COLLEGE OF PHARMACY
UNIVERSITY OF UTAH

L. S. SKAGGS PHARMACY INSTITUTE

UTAH MEDICAID DUR REPORT
NOVEMBER 2022

GUIDELINE RECOMMENDATION OVERVIEW: CDC TREATMENT GUIDELINE FOR SEXUALLY TRANSMITTED INFECTIONS (2021)

Report finalized: October 2022
Report presented: November 2022

Drug Regimen Review Center

Monet Luloh, PharmD, Clinical Pharmacist
Valerie Gonzales, PharmD, Clinical Pharmacist
Lauren Heath, PharmD, MS, BCACP, Clinical Pharmacist
Kristin Knippenberg, MFA, Administrator and Editor
Joanne LaFleur, PharmD, MSPH, Director and Associate Professor

CONTENTS

LIST OF TABLES

ABBREVIATIONS

AASLD	American Association for the Study of Liver Diseases
ACIP	Advisory Committee on Immunization Practices
AEs	adverse events
ART	antiretroviral therapy
BCA	bichloroacetic acid
BV	bacterial vaginosis
CDC	Centers for Disease Control and Prevention
CLSI	Clinical and Laboratory Standards Institute
CNS	central nervous system
DHHS	US Department of Health and Human Services
DUR	Drug Utilization Review
FDA	US Food and Drug Administration
HAV	hepatitis A virus
HBIG	hepatitis B immune globulin
HBV	hepatitis B virus
HBsAg	hepatitis B surface antigen
HCV	hepatitis C virus
HIV	human immunodeficiency virus
HPV	human papillomavirus
HSV	herpes simplex virus
IG	immunoglobulin
IHPS	infantile hypertrophic pyloric stenosis
IM	intramuscularly
IUD	intrauterine device
IV	intravenously
LGV	lymphogranuloma venereum
MIC	minimum inhibitory concentration
MSM	men who have sex with men
NAAT	nucleic acid amplification test
NGU	nongonococcal urethritis
NSAIDs	nonsteroidal anti-inflammatory drugs
OTC	over-the-counter
PDL	Preferred Drug List
PID	pelvic inflammatory disease
PrEP	pre-exposure prophylaxis
STIs	sexually transmitted infections
TCA	trichloroacetic acid
US	United States
USPSTF	US Preventive Services Task Force
VVC	vulvovaginal candidiasis
WHO	World Health Organization

EXECUTIVE SUMMARY

This report summarizes drug therapy recommendations for the treatment of sexually transmitted infections (STIs) and vulvovaginal candidiasis (VVC) according to the 2021 Centers for Disease Control and Prevention (CDC) STI guideline.[1] The 2021 CDC STI guideline provided evidence-based treatment recommendations for STIs caused by bacterial, viral, or parasitic pathogens; the majority are bacterial (n=12, 57%), and the remainder are viral (n=6, 29%) and parasitic (n=3, 14%). The treatment of human immunodeficiency virus (HIV) and viral hepatitis were considered outside the scope of the CDC guideline,[1] and therefore also this report. However, our report addresses CDC guideline-recommended treatment regimens for viral STI-related sequelae (ie, genital warts due to human papillomavirus [HPV] infection or genital herpes from herpes simplex virus [HSV] infection). In addition, we discuss the vaccination schedules for vaccine-preventable viral STIs (ie, hepatitis A virus [HAV], hepatitis B virus [HBV], HPV) as recommended by the CDC and the Advisory Committee on Immunization Practices (ACIP).[2-4]

Treatment regimens by the 2021 CDC guideline were considered "recommended" (preferred) or "alternative." CDC guideline authors rated the alternative regimens as inferior to recommended regimens for the majority of patients.[1] Generally, when provided (the guideline did not give an alternative regimen for all infections), an alternative regimen may be selected over the recommended regimen due to the presence of a contraindication, allergy, or medical comorbidity.[1] In this report, we use language consistent with the guideline to differentiate between recommended or alternative regimens. See **Appendix A** for summary tables of agents that could be used as part of a CDC-recommended or -alternative regimen for treating bacterial or parasitic STIs, and viral STI-related sequelae.

The 2021 CDC STI guideline updated the recommended treatment regimens from the prior guideline (2015)[5] for *Neisseria gonorrhoeae*, *Chlamydia trachomatis, Trichomonas vaginalis*, and pelvic inflammatory disease (PID) in order to encourage antimicrobial stewardship and limit drug resistance.[1] Key changes in the updated guideline include the following[1,5]:

- Azithromycin is no longer a recommended treatment for uncomplicated *Neisseria gonorrhoeae* infections in adults, adolescents, or children weighing >45 kg. The new recommended regimen is ceftriaxone intramuscularly (IM).
- For the treatment of *Chlamydia trachomatis* infection in adults and adolescents, the updated 2021 guideline removed azithromycin (single oral dose) as a recommended option, but continues to recommend a 7-day course of oral doxycycline. Treatment with azithromycin is now considered an alternative regimen.
- For the treatment of *Trichomonas vaginalis* infection, the 2021 guideline recommends different regimens per the patient's sex. For the treatment of non-recurrent trichomoniasis infections, men should receive a single, oral, high-dose (2 grams) of metronidazole; whereas a multi-dose regimen of oral metronidazole (500 mg twice a day) for 7 days is recommended for women.
- For the treatment of mild-to-moderate PID, the 2021 CDC STI guideline recommends that oral metronidazole be used as part of the combination regimen with doxycycline for outpatient management. Previously, the 2015 guideline recommended outpatient regimens with or without metronidazole.

An overview of CDC-recommended treatment options are provided in **Table 2** (bacterial infections), **Table 4** (viral infections), **Table 5** (parasitic infections), and **Table 7** (VVC infections). Guideline-recommended agents for STIs include the following (only includes formulations used in preferred regimens):

- **Bacterial STIs:** ceftriaxone (IM; IV), cefotaxime (IM; IV), benzathine penicillin G (IM), cefotetan (IV), doxycycline (oral; IV), cefoxitin (IV), metronidazole (oral; IV; intravaginal 0.75% gel), azithromycin (oral), levofloxacin (oral), ciprofloxacin (oral), erythromycin ethyl succinate/base (oral), erythromycin (ophthalmic 0.5% ointment), probenecid (oral), ceftizoxime (IM), clindamycin (intravaginal 2% cream), tinidazole (oral), moxifloxacin (oral), aqueous crystalline penicillin G (continuous infusion; IV), procaine penicillin G (IM)
- **Viral STI-related sequelae (ie, genital warts, genital herpes):** imiquimod (topical 3.75% or 5% cream), podofilox (topical 0.5% solution or gel), sinecatechins (topical 15% ointment), bichloroacetic acid (topical 80−90% solution), trichloroacetic acid (topical 80−90% solution), acyclovir (oral), famciclovir (oral), valacyclovir (oral)
- **Parasitic STIs:** permethrin (topical 1% cream rinse; 5% cream), pyrethrin and piperonyl butoxide (topical), ivermectin (topical 1% lotion; oral), metronidazole (oral), tinidazole (oral)
- **VVC:** fluconazole (oral), clotrimazole (intravaginal 1% or 2% cream), miconazole (intravaginal 2% or 4% cream; 100 mg, 200 mg, or 1.2 gram vaginal suppository), tioconazole (intravaginal 6.5% ointment), terconazole (intravaginal 0.4% or 0.8% cream; 80 mg vaginal suppository), butoconazole (intravaginal 2% cream)

Selection of a recommended regimen generally depends on age, sex, causative organism, comorbidities, and stage of treatment (ie, initial vs recurrent). Appropriate treatment is important to prevent transmission to others, and sequelae from persistent infection.[1]

Section 9.0 of this review summarizes the patient-administered oral or topical agents that are among CDC recommended STI regimens that are either listed as non-preferred or not included on the Utah Medicaid Preferred Drug List (PDL). Despite such occurrences, the PDL includes at least 1 guideline-recommended regimen agent for the initial treatment of each infection as preferred (or covered OTC) among major populations[*]. The Utah Medicaid Drug Utilization Review (DUR) Board may consider continuing to ensure patients have access without requiring a prior authorization to at least 1 recommended patient-administered regimen for the initial treatment of each addressed STI. In cases where a topical and oral agent are included as a recommended regimen for the same STI (eg, VVC), consideration can be made for including both formulations as preferred (or covered OTC). The current PDL (October 2022) appears to satisfy patient accessibility to guideline-recommended STI treatment regimens.

[*] The guideline-recommended treatment for a particular infection sometimes differed by patient characteristics (eg, sex, age, comorbidity). "Major populations" includes patient populations for whom a different recommended agent is listed in Table 2, Table 4, Table 5, or Table 7.

1.0 INTRODUCTION

Sexually transmitted infections (STIs), previously termed sexually transmitted diseases (STDs),[5] are caused by pathogens that are spread via sexual contact.[1,6] However, many STIs may also be transmitted from mother-to-baby during pregnancy, labor, or nursing.[6] STI management encompasses detecting the infection early, appropriate treatment, and preventing the transmission to others.[7] Treatment goals include resolving the infection/symptoms and preventing the spread to others.[1] Individuals with an untreated asymptomatic STI are at increased risk for severe complications (eg, infertility, pelvic inflammatory disease [PID]) and transmission of the STI to others.[1,8]

Based on data from 2018, the Centers for Disease Control and Prevention (CDC) estimated that approximately 1 in 5 individuals or 20% of the United States (US) population had an STI, equating to about 68 million infections.[9] In 2018, there were 26 million *new* STI infections, with nearly half occurring among adolescents and young adults aged 15−24 years.[9] The direct lifetime medical expenses of these new infections totaled approximately $16 billion, with a large proportion ($13.7 billion) attributed to human immunodeficiency virus (HIV).[9] Notably, gonorrhea, chlamydia, and syphilis were responsible for approximately $1.1 billion.[9]

In 2021, the CDC published updated recommendations from the previous 2015 guideline[5] for the treatment of STIs.[1] The 2021 guideline serves as a resource to primary care clinicians on the appropriate management of STIs for individuals who have or may be at risk of an STI. The 2021 CDC STI guideline addresses the following information (not a comprehensive list)[1]:

- Screening recommendations for detecting STIs among special populations (eg, pregnant women, adolescents, men who have sex with men [MSM])
- Guidance for primary prevention methods, counseling, and partner management
- Diagnostic considerations
- Pharmacologic treatment regimens

The objective of this report is to review the recommended pharmacologic treatment or prophylaxis of STIs according to the 2021 CDC STI guideline. The treatment of HIV and viral hepatitis were considered outside the scope of the CDC guideline, and therefore also this report; but guideline-recommended treatment regimens for viral STI-related sequelae (ie, genital warts due to human papillomavirus [HPV] infection or genital herpes from herpes simplex virus [HSV] infection) are addressed. In addition, we discuss the vaccination schedules for vaccine-preventable viral STIs (ie, hepatitis A virus [HAV], hepatitis B virus [HBV], HPV) as recommended by the CDC and the Advisory Committee on Immunization Practices (ACIP).[2-4] Furthermore, we highlight the Utah Medicaid Preferred Drug List (PDL) status of the recommended therapies that are used in the outpatient setting (administered by the patient) to ensure accordance with the guideline-recommended treatment regimens.

Table 1 outlines the numerous STIs reviewed in this report, organized by the type of causative pathogen. Vulvovaginal candidiasis, a common vaginal yeast infection, is not considered a sexually transmitted disease,[10] yet treatment of this condition is provided in the 2021 CDC STI guideline due to the high prevalence among women either at risk for an STI or who experience vaginal symptoms (eg, discharge, pruritus) that tend to coincide with some STIs.[1]

Table 1. CDC 2021 Guideline-Reviewed STIs, Organized by Causative Pathogen[1]

Bacterial	• Bacterial vaginosis • Chancroid • Cervicitis • Chlamydia	• Epididymitis • Gonorrhea • Granuloma inguinale (Donovanosis) • Lymphogranuloma venereum	• Nongonococcal urethritis • PID[a] • Proctitis • Syphilis
Viral	• HAV/HBV/HCV[b] • HIV[b] • HPV (ie, anogenital warts) • Genital herpes (HSV-1 and HSV-2)		
Parasitic	• Pediculosis Pubis (ie, pubic lice) • Scabies • Trichomoniasis		

Abbreviations: CDC, Center for Disease Control and Prevention; HAV, hepatitis A virus; HBV, hepatitis B virus; HCV, hepatitis C virus; HIV, human immunodeficiency virus; HPV, human papillomavirus; HSV, herpes simplex virus; PID, pelvic inflammatory disease; STIs, sexually transmitted infections

[a] PID is often bacterial in origin, primarily due to N. gonorrhoeae and C. trachomatis, but may also be caused by other pathogenic etiologies

*[b] Only vaccine prevention and for some infections (ie, HAV, HBV, HCV) postexposure prophylaxis were reviewed; treatment of these infections were considered outside the scope of the 2021 CDC STI guideline. Refer to **Appendix B** for information on the disease states of these infections, links to other guidelines with treatment recommendations, and CDC guideline-recommended postexposure prophylaxis, if applicable.*

2.0 METHODS

Since the purpose of this report is to review recommendations on drug therapies for the treatment of STIs from the 2021 CDC STI guideline,[1] we did not perform a formal systematic literature search for information from other sources. However, for background context, information from websites (eg, CDC, World Health Organization [WHO], UpToDate) or journal articles were used to supplement the content provided in the guideline.

3.0 2021 CDC STI GUIDELINE OVERVIEW AND KEY RECOMMENDATION CHANGES

The 2021 CDC STI guideline did not provide evidence ratings for their recommendations but it did provide a brief rationale for recommending particular agents based on clinical evidence.[1] Recommended regimens should be used primarily for the majority of patients unless contraindicated on the basis of allergy or medical conditions. Alternative regimens are considered inferior and may have disadvantages compared to recommended regimens, but can be considered when a recommended regimen is unable to be used.[1] Alternative regimens are not provided for all STIs, in which case, consulting with an infectious disease specialist is recommended. Refer to **Appendix A** for summary tables that outline the

agents that could be used as part of a CDC-recommended or -alternative regimen for treating bacterial or parasitic STIs, and viral STI-related sequelae (ie, genital warts, genital herpes).

Compared to the previous guideline iteration published in 2015, the 2021 CDC STI guideline updated recommended treatment regimens for *Neisseria gonorrhoeae*, *Chlamydia trachomatis*, *Trichomonas vaginalis*, and pelvic inflammatory disease (PID) in order to encourage antimicrobial stewardship and limit drug resistance.[1,11] These key changes are summarized as follows:

- **Treatment of uncomplicated *Neisseria gonorrhoeae* infections:** For adults and adolescents, the 2015 guideline recommended dual therapy with intramuscular (IM) ceftriaxone and oral azithromycin.[5,11] However, due to potential concerns of harming the microbiome and the impact on other pathogens, the 2021 guideline recommends only ceftriaxone.[1] This change also impacted the treatment of uncomplicated gonorrhea infections in children weighing >45 kg since the recommended regimen in this patient population deferred to the regimen used in adults and adolescents.[1,5] In addition, the dose of ceftriaxone was increased from 250 mg to 500 mg for patients weighing <150 kg, and to 1 gram for patients weighing ≥150 kg.[1,5,11]
- **Treatment of *Chlamydia trachomatis* infection:** For adults and adolescents, the updated 2021 guideline removed azithromycin (single oral dose) as a recommended option, but continues to recommend a 7-day course of oral doxycycline.[1,5,11] Treatment with azithromycin is now considered an alternative regimen.[1]
- **Treatment of *Trichomonas vaginalis* infection:** In contrast to the 2015 guideline that recommended the same dosing of metronidazole for men and women, the 2021 guideline recommends different regimens depending on the patient's sex.[1] For men, the recommended treatment for non-recurrent trichomoniasis infections is 2 grams of metronidazole administered as a single oral dose.[1] Oral metronidazole 500 mg twice a day for 7 days (previously an alternative regimen in the 2015 guideline) is the recommended treatment for women.[1,5] Tinidazole, administered as a single oral dose is no longer a recommended regimen for non-recurrent trichomonas, but may be used as an alternative agent for both women (non-pregnant) and men.[1,5]
- **Treatment of PID:** Oral metronidazole with doxycycline is preferred in the 2021 guideline for the outpatient management of mild-to-moderate PID.[1] In contrast, doxycycline could be used either with or without metronidazole in recommended outpatient regimens per the 2015 guideline.[5] The updated recommendation to use metronidazole *with* doxycycline was based on the therapeutic benefit of anaerobic coverage to prevent long-term sequelae associated with PID (eg, ectopic pregnancy, infertility).[1]

The following sections outline the recommended pharmacologic treatment regimens, including alternative regimens and prophylaxis, if applicable, for the STIs listed in **Table 1**.

4.0 BACTERIAL SEXUALLY TRANSMITTED INFECTIONS

Of the STIs addressed in the 2021 CDC guideline,[1] the majority result from bacterial infections. Bacterial STIs continue to be a common cause of infection, especially among sexually active individuals. In the US, from 2014 to 2019, the rates of chlamydia, gonorrhea, and certain stages of syphilis (primary, secondary, congenital) increased by 19–279%, depending on the bacterial STI.[12] **Table 2** provides an

overview of the recommended antimicrobial treatment regimens for bacterial STIs and the intended patient population. Please refer to the specific STI section for details on alternative regimens.

Table 2. CDC 2021 Guideline-Recommended Treatment Regimens for Bacterial STIs[a] [1,13]

Bacterial Infection	Recommended Treatment Regimen and Dosing	Indicated Population
Acute Epididymitis	*Presumptive treatment (prior to receiving laboratory results) is warranted in symptomatic sexually active men, in order to minimize the spread of infection. Following initiation of empiric treatment, treatment should be dictated by antimicrobial susceptibilities and bacterial cultures. All sex partners exposed within the preceding 60 days prior to symptom onset should be presumptively treated for chlamydia or gonorrhea, based on the causative pathogen.*	
	Ceftriaxone 500 mg[b] IM (as a one-time dose) **AND** Doxycycline 100 mg PO twice per day for 10 days	Men with acute epididymitis, probably caused by chlamydia or gonorrhea
	Ceftriaxone 500 mg[b] IM (as a one-time dose) **AND** Levofloxacin 500 mg PO once daily for 10 days	Men with acute epididymitis, probably caused by enteric pathogens (via insertive anal intercourse), chlamydia, or gonorrhea
	Levofloxacin 500 mg PO once daily for 10 days	Men with acute epididymitis, probably caused by enteric pathogens only
Bacterial Vaginosis	Metronidazole 500 mg PO twice per day for 7 days **OR** Metronidazole gel 0.75%, 5 g applied intravaginally (1 full applicator), once per day for 5 days **OR** Clindamycin cream 2%, 5 g applied intravaginally (1 full applicator), at bedtime for 7 days	Symptomatic women, including women that are pregnant
Cervicitis[c]	*Presumptive treatment (ie, prior to diagnostic results) for chlamydia and gonorrhea should be provided for high-risk women and treatment for trichomoniasis and bacterial vaginosis should be provided if identified. In the event trichomoniasis, gonorrhea, or chlamydia is detected, all sex partners exposed within the preceding 60 days should receive presumptive treatment for the specific infection.*	

Abbreviations: CDC, Centers for Disease Control and Prevention; g, gram; HIV, human immunodeficiency virus; IM, intramuscularly; kg, kilogram; LGV, lymphogranuloma venereum; mg, milligram; NAAT, nucleic acid amplification test; NGU, nongonococcal urethritis; PO, orally; STI, sexually transmitted infections

Table 2. CDC 2021 Guideline-Recommended Treatment Regimens for Bacterial STIs[a] [1,13]

Bacterial Infection	Recommended Treatment Regimen and Dosing	Indicated Population
	Doxycycline 100 mg PO twice per day for 7 days	High-risk women includes: • Women at increased risk (eg, women aged <25 years with a new sex partner, sex partner with a known STI) • A patient who's infection is unable to be tested with a NAAT • A patient for whom follow-up cannot be guaranteed May consider delaying treatment for low-risk women
Chancroid	Azithromycin 1 g PO (as a one-time dose) **OR** Ceftriaxone 250 mg IM (as a one-time dose) **OR** Ciprofloxacin 500 mg PO twice a day for 3 days **OR** Erythromycin base 500 mg PO three times a day for 7 days	All infected patients
Chlamydial Infections	*Presumptive treatment should be provided to all sex partners exposed within the previous 60 days prior to symptom onset or diagnosis, or at the very least, the most recent sex partner regardless of last sexual contact; and mothers of neonates/infants with chlamydial ophthalmia and/or pneumonia.*	
	Doxycycline 100 mg PO twice per day for 7 days	Adults and adolescents
	Azithromycin 1 g PO (as a one-time dose)	• Pregnant women • Children <8 years of age who weigh ≥45 kg[d]; for infections pertaining to the nasopharynx, rectal, and urogenital regions
	Azithromycin 1 g PO (as a one-time dose) **OR** Doxycycline 100 mg PO twice per day for 7 days	Children ≥8 years of age; for infections pertaining to the nasopharynx, rectal, and urogenital regions
	Erythromycin (ethyl succinate or base) 50 mg/kg per day PO, divided into 4 daily doses for 14 days	• Neonates[e]; for ophthalmia and pneumonia • Children and infants (<45 kg); for infections pertaining to the nasopharynx, rectal, and urogenital regions

Abbreviations: CDC, Centers for Disease Control and Prevention; g, gram; HIV, human immunodeficiency virus; IM, intramuscularly; kg, kilogram; LGV, lymphogranuloma venereum; mg, milligram; NAAT, nucleic acid amplification test; NGU, nongonococcal urethritis; PO, orally; STI, sexually transmitted infections

Table 2. CDC 2021 Guideline-Recommended Treatment Regimens for Bacterial STIs[a] [1,13]

Bacterial Infection	Recommended Treatment Regimen and Dosing	Indicated Population
Gonococcal Infections	*Presumptive treatment should be provided to all sex partners exposed within the previous 60 days prior to symptom onset or diagnosis, or if exposure occurred >60 days before, the most recent sex partner; and mothers of neonates with gonorrhea-related ophthalmia, disseminated infections, or scalp abscess. In addition, newborns at high risk for infection due to an untreated gonorrhea infection in the mother should be presumptively treated.*	
	Ceftriaxone 500 mg[b] IM (as a one-time dose)[f]	• Adults and adolescents <150 kg with uncomplicated infections pertaining to the urethra, pharynx, cervix, or rectum • Children who weigh >45 kg with an uncomplicated infection (ie, cervicitis, urethritis, vulvovaginitis, proctitis, or pharyngitis)
	Ceftriaxone 500 mg IM (as a one-time dose)[f]	Pregnant women
	Ceftriaxone 1 g IM (as a one-time dose). Consider a single conjunctival saline lavage in the infected eye	Conjunctivitis in adults or adolescents
	Ceftriaxone 1 g IV or IM every 24 hours[f]	Disseminated gonococcal infection – Gonococcal-related arthritis and arthritis-dermatitis syndrome in adults or adolescents[g]
	Ceftriaxone 1–2 g IV every 24 hours[f]	Disseminated gonococcal infection – Gonococcal meningitis or endocarditis in adults or adolescents
	Ceftriaxone 25–50 mg/kg IV or IM (as a one-time dose); max dose: 250 mg[h]	• Infants and children that weigh ≤45 kg with an uncomplicated infection (ie, cervicitis, urethritis, vulvovaginitis, proctitis, or pharyngitis) • Neonates or infants with ophthalmia; Treatment
	Ceftriaxone 20–50 mg/kg IV or IM (as a one-time dose); max dose: 250 mg	Asymptomatic neonates

Abbreviations: CDC, Centers for Disease Control and Prevention; g, gram; HIV, human immunodeficiency virus; IM, intramuscularly; kg, kilogram; LGV, lymphogranuloma venereum; mg, milligram; NAAT, nucleic acid amplification test; NGU, nongonococcal urethritis; PO, orally; STI, sexually transmitted infections

Table 2. CDC 2021 Guideline-Recommended Treatment Regimens for Bacterial STIs[a] [1,13]

Bacterial Infection	Recommended Treatment Regimen and Dosing	Indicated Population
	Ceftriaxone 25–50 mg/kg IV or IM (administered as a single dose) once a day for 7 days[i] **OR** Cefotaxime 25 mg/kg IV or IM every 12 hours for 7 days[i]	Disseminated gonococcal infection in neonates
	Ceftriaxone 50 mg/kg IV or IM (administered as a single dose) every 24 hours for 7 days; max dose: 2 g	Disseminated gonococcal infection – Bacteremia or arthritis in infants and children who weigh ≤45 kg
	Ceftriaxone 1 g IV or IM (administered as a single dose) every 24 hours for 7 days	Disseminated gonococcal infection – Bacteremia or arthritis in children who weigh >45 kg
	Erythromycin 0.5% ophthalmic ointment in both eyes (as a one-time dose) applied at birth	All neonates within 24 hours of birth; Prophylaxis
Granuloma Inguinale (Donovanosis)	Azithromycin 1 g PO once a week or 500 mg PO once a day, for >3 weeks until all lesions have fully healed	All infected patients, including patients that are pregnant or have HIV
Lymphogranuloma Venereum (LGV)	*Presumptive treatment is warranted for all individuals suspected of having LGV. Additionally, presumptive treatment for chlamydia should be provided for all asymptomatic sex partners exposed within the preceding 60 days.*	
	Doxycycline 100 mg PO twice a day for 21 days	All patients with a clinical presentation consistent with LGV, including patients who have HIV
Nongonococcal Urethritis (NGU)	*Presumptive treatment should be started when an NGU diagnosis has been established. Heterosexual men with recurrent or persistent NGU where T. vaginalis is prevalent should be presumptively treated. Following initiation of empiric treatment, treatment should be dictated by antimicrobial susceptibilities and bacterial cultures. Additionally, presumptive treatment for chlamydia should be provided for all sex partners exposed within the preceding 60 days.*	
	Doxycycline 100 mg PO twice a day for 7 days	Men, including HIV-positive men who have non-recurrent or persistent NGU
	Metronidazole 2 g PO (as a one-time dose) **OR** Tinidazole 2 g PO (as a one-time dose)	Men, including heterosexual and HIV-positive men who have recurrent or persistent NGU due to *T. vaginalis*

Abbreviations: CDC, Centers for Disease Control and Prevention; g, gram; HIV, human immunodeficiency virus; IM, intramuscularly; kg, kilogram; LGV, lymphogranuloma venereum; mg, milligram; NAAT, nucleic acid amplification test; NGU, nongonococcal urethritis; PO, orally; STI, sexually transmitted infections

Table 2. CDC 2021 Guideline-Recommended Treatment Regimens for Bacterial STIs[a] [1,13]

Bacterial Infection	Recommended Treatment Regimen and Dosing	Indicated Population
	Doxycycline 100 mg PO twice a day for 7 days **THEN** Azithromycin 1 g PO (initial one-time dose) **THEN** Azithromycin 500 mg PO once a day for the next 3 days	Men, including HIV-positive men who have recurrent or persistent NGU due to **macrolide sensitive** *M. genitalium*
	Doxycycline 100 mg PO twice a day for 7 days **THEN** Moxifloxacin 400 mg PO once a day for 7 days	• Men, including HIV-positive men who have recurrent or persistent NGU due to **macrolide resistant** *M. genitalium* • Men, including HIV-positive men who have recurrent or persistent NGU due to *M. genitalium* (**macrolide-resistance testing is unavailable**)
Pelvic Inflammatory Disease	*Presumptive treatment is warranted for women at risk for an STI or those who are sexually active, if they are symptomatic (ie, lower abdominal or pelvic pain), no other etiologies are identified, or tenderness of the cervix, uterus, or pelvic region is present based on physical examination. Regardless of the PID etiology, sex partners within the previous 60 days prior to symptom onset should be presumptively treated for gonorrhea and chlamydia.*	
	IV Regimens	
	Ceftriaxone 1 g IV every 24 hours **AND** Doxycycline 100 mg PO or IV every 12 hours **WITH** Metronidazole 500 mg PO of IV every 12 hours	Women, that have any of the following: • Surgical emergencies (eg, appendicitis) • Pregnant • Tubo-ovarian abscess • Nausea and vomiting, temperature (oral) >101°F, severe illness • Unable to tolerate, adhere, or lack a response to an oral regimen
	Cefotetan 2 g IV every 12 hours **AND** Doxycycline 100 mg PO or IV every 12 hours	
	Cefoxitin 2 g IV every 6 hours **AND** Doxycycline 100 mg PO or IV every 12 hours	

Abbreviations: CDC, Centers for Disease Control and Prevention; g, gram; HIV, human immunodeficiency virus; IM, intramuscularly; kg, kilogram; LGV, lymphogranuloma venereum; mg, milligram; NAAT, nucleic acid amplification test; NGU, nongonococcal urethritis; PO, orally; STI, sexually transmitted infections

Table 2. CDC 2021 Guideline-Recommended Treatment Regimens for Bacterial STIs[a] [1,13]

Bacterial Infection	Recommended Treatment Regimen and Dosing	Indicated Population
	IM Regimens	
	Ceftriaxone 500 mg IM (as a one-time dose) **AND** Doxycycline 100 mg PO twice a day for 14 days **WITH** Metronidazole 500 mg PO twice a day for 14 days	Women with mild-to-moderate acute PID
	Cefoxitin 2 g IM (as a one-time dose) **AND** Probenecid 1 g PO (as a one-time dose), administered simultaneously with cefoxitin **AND** Doxycycline 100 mg PO twice a day for 14 days **WITH** Metronidazole 500 mg PO twice a day for 14 days	
	Ceftizoxime or cefotaxime (or another third-generation cephalosporin administered IM) **AND** Doxycycline 100 mg PO twice a day for 14 days **WITH** Metronidazole 500 mg PO twice a day for 14 days	
Proctitis	*Presumptive treatment (prior to receiving laboratory results) is recommended for individuals whom upon evaluation have anorectal exudate, including the presence of polymorphonuclear leukocytes. In the event objective evaluation is unavailable, presumptive treatment should still be provided to patients with a clinical presentation and subjective etiology (ie, patient reports receptive anal contact) indicative of acute proctitis. Presumptive treatment for genital herpes should also be provided if perianal or mucosal ulcers are present. Additionally, all sex partners within the previous 60 days who were exposed to chlamydia or gonorrhea should be presumptively treated for the causative infection.*	

Abbreviations: CDC, Centers for Disease Control and Prevention; g, gram; HIV, human immunodeficiency virus; IM, intramuscularly; kg, kilogram; LGV, lymphogranuloma venereum; mg, milligram; NAAT, nucleic acid amplification test; NGU, nongonococcal urethritis; PO, orally; STI, sexually transmitted infections

Table 2. CDC 2021 Guideline-Recommended Treatment Regimens for Bacterial STIs[a] [1,13]

Bacterial Infection	Recommended Treatment Regimen and Dosing	Indicated Population
	Ceftriaxone 500 mg[b] IM (as a one-time dose) **AND** Doxycycline 100 mg PO twice a day for 7 days[j]	All patients with acute proctitis, including those who have HIV[k]
Syphilis	*Presumptive treatment should be provided for all individuals suspected of having syphilis that is considered to be contagious (ie, primary, secondary, or early latent syphilis); including those with risk factors, all sex partners exposed within the previous 90 days prior to the index patient's diagnosis, and sex partners exposed >90 days prior when serologic results are unavailable and for whom follow-up is not guaranteed. In geographic areas with high syphilis rates, sex partners of individuals with an unknown duration of syphilis and high serologic titers (ie, >1:32) should receive presumptive treatment.*	
	Benzathine penicillin G 2.4 million units IM (as a one-time dose)	Adults, including pregnant women and individuals living with HIV who have: • Primary syphilis • Secondary syphilis • Early latent syphilis
	Benzathine penicillin G 7.2 million units total, divided into 3 doses (2.4 million units IM each) administered once a week	Adults, including pregnant women and individuals living with HIV who have: • Late latent syphilis • Tertiary syphilis
	Aqueous crystalline penicillin G 18–24 million units daily, administered as continuous infusion or 3–4 million units IV every 4 hours, for 10–14 days	Adults, including pregnant women and individuals living with HIV who have: • Neurosyphilis • Otosyphilis • Ocular syphilis
	Benzathine penicillin G 50,000 units/kg IM (as a one-time dose) Maximum dose: 2.4 million units (adult dose)	Infants (aged ≥30 days) and children with: • Syphilis (not congenital)
	Aqueous crystalline penicillin G 200,000–300,000 units/kg per day, administered as 50,000 units/kg IV every 4–6 hours for 10 days	Infants (aged ≥30 days) and children with congenital syphilis

Abbreviations: CDC, Centers for Disease Control and Prevention; g, gram; HIV, human immunodeficiency virus; IM, intramuscularly; kg, kilogram; LGV, lymphogranuloma venereum; mg, milligram; NAAT, nucleic acid amplification test; NGU, nongonococcal urethritis; PO, orally; STI, sexually transmitted infections

Table 2. CDC 2021 Guideline-Recommended Treatment Regimens for Bacterial STIs[a] [1,13]

Bacterial Infection	Recommended Treatment Regimen and Dosing	Indicated Population
	Aqueous crystalline penicillin G 100,000–150,000 units/kg per day, administered as 50,000 units/kg IV every 12 hours for the first 7 days, then every 8 hours for the next 3 days (total treatment duration: 10 days) **OR** Procaine penicillin G 50,000 units/kg IM once a day for 10 days	Neonates (infants <30 days old) with highly probable or confirmed congenital syphilis
	Aqueous crystalline penicillin G 100,000–150,000 units/kg per day, administered as 50,000 units/kg IV every 12 hours for the first 7 days, then every 8 hours for the next 3 days (total treatment duration: 10 days) **OR** Procaine penicillin G 50,000 units/kg IM once a day for 10 days **OR** Benzathine penicillin G 50,000 units/kg IM (as a one-time dose)[l]	Neonates (infants <30 days old) with possible congenital syphilis
	Benzathine penicillin G 50,000 units/kg IM (as a one-time dose)[m]	Neonates (infants <30 days old) with less likely congenital syphilis

Abbreviations: CDC, Centers for Disease Control and Prevention; g, gram; HIV, human immunodeficiency virus; IM, intramuscularly; kg, kilogram; LGV, lymphogranuloma venereum; mg, milligram; NAAT, nucleic acid amplification test; NGU, nongonococcal urethritis; PO, orally; STI, sexually transmitted infections

Table 2. CDC 2021 Guideline-Recommended Treatment Regimens for Bacterial STIs[a] [1,13]

Bacterial Infection	Recommended Treatment Regimen and Dosing	Indicated Population

[a] When more than one regimen is provided, they are listed alphabetically for agents that have a similar efficacy and tolerability profile; whereas a non-alphabetical order indicates the preference of the regimens based on agent-specific efficacy and tolerability differences.

[b] The dose of ceftriaxone should be increased to 1 g in patients weighing ≥150 kg

[c] If the patient lives in a high prevalence area or is at risk for gonorrhea, concomitant gonorrhea treatment should be considered

[d] Evidence is limited about the effectiveness and optimal dosing for azithromycin in infants and children that weigh <45 kg

[e] Among infants <6 weeks of age, infantile hypertrophic pyloric stenosis has been reported with oral erythromycin and azithromycin use. Infants treated with these agents should be monitored for symptoms and signs of infantile hypertrophic pyloric stenosis

[f] In cases where a chlamydial infection has not been ruled out, patients should also receive doxycycline 100 mg by mouth twice a day for 7 days, or if the patient is pregnant, 1 gram of azithromycin as a single oral dose

[g] For arthritis-dermatitis syndrome, the physician may switch to an oral medication (as advised by antimicrobial susceptibility testing) after a "substantial clinical improvement" has been observed for 24–48 hours, totaling a treatment duration of ≥7 days

[h] The maximum dose is 250 mg for neonates, infants, and children (≤45 kg); the maximum dose pertains to the IV and IM routes of administration for ophthalmia, but for uncomplicated gonococcal infections the maximum dose pertains only to the IM route of administration

[i] For meningitis, the treatment duration should be extended to 10–14 days

[j] Presumptive treatment for LGV with a longer treatment duration of doxycycline for 21 days is recommended for patients that present with hemorrhagic rectal discharge, tenesmus, or mucosal or perianal ulcers, and a positive rectal test for C. trachomatis

[k] The 2021 CDC STI guideline does not address the treatment of acute proctitis during pregnancy

[l] The 1-day course is not recommended for neonates that have an abnormal or missing evaluation (ie, long bone radiographs, CSF examination, complete blood count and platelets), CSF results that are unable to be interpreted due to contamination, or for whom follow-up cannot be guaranteed

[m] For infants where the maternal nontreponemal titer is reduced by at least four-fold after treatment for early syphilis or consistently maintained a low-titer for latent syphilis, treatment may not be provided, given that frequent serologic evaluation will be performed every 2—3 months for a total of 6 months

Abbreviations: CDC, Centers for Disease Control and Prevention; g, gram; HIV, human immunodeficiency virus; IM, intramuscularly; kg, kilogram; LGV, lymphogranuloma venereum; mg, milligram; NAAT, nucleic acid amplification test; NGU, nongonococcal urethritis; PO, orally; STI, sexually transmitted infections

4.1 Acute Epididymitis

STI-attributing pathogens (eg, *N. gonorrhoeae, C. trachomatis, M. genitalium)* or enteric microorganisms (eg, *E. coli*), either transmitted sexually or non-sexually, can cause acute epididymitis (defined as symptoms lasting <6 weeks).[1] Acute epididymitis due to an STI is more common among men <35 years of age, whereas an infection due to an enteric organism is more common among men ≥35 years of age, and usually due to secondary causes.[1,14] However, the sexual transmission of enteric organisms may occur in men, regardless of age, who practice anal intercourse and are the insertive partner.[1] Non-sexual causes due to *E. coli* or other Gram-negative bacteria include indwelling urinary catheters, bacteriuria secondary to urinary retention (eg, benign prostatic hyperplasia), or recent surgery.[1,14]

Acute epididymitis is characterized as unilateral scrotal pain, inflammation, and swelling of the epididymis, located behind the testis.[1,14] In some cases, the infection may include the testis (epididymo-orchitis).[1] Individuals with epididymitis due to an STI often experience urethritis, which tends to be asymptomatic.[1]

Presumptive treatment (ie, prior to receiving laboratory results) is recommended for all sexually active men to minimize the spread of the infection to others and prevent any complications.[1] Furthermore, all sex partners exposed within the preceding 60 days prior to symptom onset should be presumptively treated for chlamydia or gonorrhea, based on the causative pathogen (*refer to Sections 4.5. and 4.6., respectively*). The selection of a treatment regimen is based on the most likely causative pathogen related to the patient's risk for an STI (ie, chlamydia, gonorrhea) or enteric infection. Treatment goals include curing the infection, improving symptoms and signs of the infection, preventing the transmission of STIs (ie, chlamydia, gonorrhea) to others (if applicable), and reducing the risk of epididymitis-related complications (eg, chronic scrotal pain, infertility). Acute epididymitis is often treated in an outpatient setting; however, inpatient hospitalization and referral to a specialist should be considered for patients with a fever or severe pain (suggesting a more serious condition [eg, abscess, testicular infarction, testicular torsion, necrotizing fasciitis]), or when an individual is unable to adhere to outpatient treatment. In addition, a history of diabetes and fever, older age, and an elevated C-reactive protein level may be predictive factors for severe acute epididymitis, indicating the need for hospitalization.[1]

Recommended treatment regimen for men, including those who have HIV, are as follows[1]:

- Probably caused by chlamydia or gonorrhea:
    - Ceftriaxone 500 mg IM (one-time dose) AND
    - Doxycycline 100 mg by mouth twice a day for 10 days
- Probably caused by chlamydia, gonorrhea, or enteric pathogens:
    - Ceftriaxone 500 mg IM (one-time dose) AND
    - Levofloxacin 500 mg by mouth once a day for 10 days
- Probably due to enteric pathogens only:
    - Levofloxacin 500 mg by mouth once a day for 10 days

Men with acute epididymitis, either suspected or confirmed to be a result of chlamydia or gonorrhea should refrain from having sexual intercourse until all affected people have been treated (ie, patient, all sex partners within the prior 60-day period) and symptoms have subsided.[1]

For patients that are receiving regimens containing ceftriaxone, it is recommended to increase the dose to 1 gram for people weighing ≥150 kg.[1] Levofloxacin as monotherapy is only preferred if the acute epididymitis is probably only caused by enteric pathogens. Once additional laboratory results are obtained, treatment should be dictated by antimicrobial susceptibilities and bacterial cultures. To supplement the antibiotic therapy, scrotal elevation, bed rest, and nonsteroidal anti-inflammatory drugs (NSAIDs) are recommended to be used until the scrotal inflammation and fever have reduced.[1]

For men who do not experience an improvement in their symptoms within 72 hours after treatment, a follow-up visit should occur to reassess the diagnosis and therapeutic management, especially when scrotal tenderness and swelling continue after completing the antibiotic regimen.[1] However, a minor level of discomfort may occur for a couple of weeks after completing the antibiotic therapy, but ultimately, it should completely resolve after a few weeks.[1]

4.2 Bacterial Vaginosis

Bacterial vaginosis (BV) is the result of a microbial imbalance from exchanging the normal flora (*Lactobacillus* species) with higher concentrations of anaerobic bacteria (eg, *Prevotella* species, *G. vaginalis, A. vaginae*).[1] The mechanism underlying the microbial shift that causes BV, including if it is acquired from a single sexually transmitted microorganism remains unknown.[1]

Globally, BV is a highly prevalent STI and the most common cause of vaginal discharge.[1] A higher prevalence of BV has been reported in women utilizing a copper-containing intrauterine device (IUD) for contraception; however, an increased risk of developing BV has not been associated with hormonal contraception use and might be protective.[1] Although BV has recognizable symptoms, most women in the US are asymptomatic (84%), according to a survey published in 2007.[1,15]

Only *symptomatic* women are recommended for treatment.[1] Treatment not only helps resolve the infection/symptoms but also helps minimize the risk of acquiring other STIs (eg, HIV, *C. trachomatis, N. gonorrhoeae, M. genitalium*, human papillomavirus [HPV]) and the risk of adverse pregnancy-related outcomes (preterm birth, postpartum endometritis, premature rupture of membranes, and intra-amniotic infection) associated with symptomatic BV.[1]

Recommended treatment regimens for symptomatic women, including those who are pregnant, are as follows[1]:

- Metronidazole 500 mg by mouth twice a day for 7 days OR
- Metronidazole gel 0.75%, 5 grams applied intravaginally (1 full applicator) once a day for 5 days OR
- Clindamycin cream 2%, 5 grams applied intravaginally (1 full applicator) at bedtime for 7 days

Alternative treatment regimens for symptomatic women, including those who are pregnant, are as follows[1]:

- Clindamycin 300 mg by mouth twice a day for 7 days OR
- Clindamycin ovules 100 mg inserted vaginally once a day at bedtime for 3 days OR
- Secnidazole 2 gram oral granules (as a one-time dose) sprinkled onto food (eg, yogurt, pudding, unsweetened applesauce) OR
- Tinidazole 1 gram by mouth once a day for 5 days OR

- Tinidazole 2 grams by mouth once a day for 2 days

Women are encouraged to use condoms or abstain from sexual activity while being treated for BV.[1] There is a lack of evidence supporting the use of douching for the symptomatic relief or treatment of BV, and in fact, could potentially increase the risk for reinfection.[1]

Metronidazole is secreted into breast milk, but oral doses <2 grams are considered compatible with breastfeeding.[1] Clindamycin cream or ovules may weaken latex-based condoms and vaginal diaphragms[1]; thus, these types of products are not recommended to be used within 72 hours following application.[1,16]

A follow-up visit is not required for infections that have resolved after treatment.[1] For women who experience recurrent or persistent BV, clinicians may use the same recommended regimens as the first occurrence or switch to another recommended option. Limited evidence supports other treatment options (eg, 750 mg metronidazole vaginal suppository) that might be tried after completing a recommended regimen, including suppressive therapy (eg, 2 grams of oral metronidazole and 150 mg of fluconazole).[1]

4.3 Cervicitis

The most common etiology of cervicitis is *N. gonorrhoeae* or *C. trachomatis*.[1] However, other STIs have been known to cause cervicitis such as genital herpes (primarily caused by herpes simplex virus-2 [HSV-2]), trichomoniasis, or *M. genitalium.* Women presenting with cervicitis are often asymptomatic, but some women may experience intermenstrual bleeding (eg, particularly after vaginal intercourse) and abnormal vaginal discharge.[1]

The following at-risk patient populations should be treated with antimicrobials presumptively (ie, before diagnostic test results are obtained) for *N. gonorrhoeae* or *C. trachomatis*[1]:

- Women at increased risk of infection
    - Women aged <25 years with a new sex partner
    - A sex partner with other partners
    - A sex partner with a known STI
- A patient for whom follow-up cannot be guaranteed
- A patient who's infection is unable to be tested with a nucleic acid amplification test (NAAT)

Delaying treatment until diagnostic results are available may be considered for women who are low-risk for contracting an STI.[1]

Recommended treatment regimen for all women, including those who are pregnant and/or who have HIV, is as follows[1]:

- Doxycycline 100 mg by mouth twice a day for 7 days

Alternative treatment regimen for all women, including those who are pregnant and/or who have HIV, is as follows[1]:

- Azithromycin 1 gram by mouth (as a one-time dose)

Women should refrain from having sexual intercourse until symptoms have resolved and all affected people have been treated (ie, patient, all sex partners within the previous 60 days) to prevent reinfection and transmission.[1] This translates to abstaining until finishing the 7 day treatment course for the recommended regimen, or for 7 days after the single-dose alternative regimen. In the event trichomoniasis, gonorrhea, or chlamydia is detected, all sex partners exposed within the preceding 60 days should receive presumptive treatment for the specific infection.[1]

For patients that live in a high prevalence area or are at risk for gonorrhea, concomitant gonorrhea treatment should be considered (*refer to Section 4.6*). If identified, treatment for BV and trichomoniasis should be provided (*refer to Sections 4.2. and 6.3, respectively*).[1]

For women that received treatment for cervicitis, a follow-up visit should occur to ensure the infection has been cured.[1] A follow-up visit may be considered for women who had treatment deferred and tested negative for *N. gonorrhoeae* or *C. trachomatis.* Women diagnosed with cervicitis due to gonorrhea, chlamydia, or trichomoniasis should receive repeat testing after 3 months of treatment to ensure complete resolution. In addition, women that experience recurrent or persistent cervicitis after receiving treatment should be reassessed for treatment failure or potential reinfection.[1]

4.4 Chancroid

Globally and within the US, the prevalence of chancroid infections have declined.[1] The STI is considered rare, with only 7 cases reported to the CDC in 2016.[1,17] However, chancroid may still be present in certain regions of the Caribbean and Africa.[1] Typically, sporadic outbreaks of painful genital ulcers occur when an individual is infected.[1]

Even with appropriate pharmacologic treatment, serious cases may include rectal or genital scarring or urogenital fistulas as a result of developing suppurative buboes.[1,17]

Recommended treatment regimens for all infected patients are as follows[1]:

- Azithromycin 1 gram by mouth (as a one-time dose) OR
- Ceftriaxone 250 mg intramuscularly (IM) (as a one-time dose) OR
- Ciprofloxacin 500 mg by mouth twice a day for 3 days OR
- Erythromycin base 500 mg by mouth three times a day for 7 days

Ceftriaxone 250 mg IM and oral azithromycin are single-dose regimens,[1] potentially allowing for better patient compliance versus other recommended options. Although ciprofloxacin is associated with a low risk of negative fetal outcomes in pregnancy, it carries a potential risk for toxicity during lactation; thus, guideline authors advise using a different recommended agent for pregnant or lactating patients.[1]

A follow-up visit should occur within 3−7 days after starting therapy to asses if the treatment was successful.[1] Typically, if the infection was treated successfully, symptomatic relief of ulcers is achieved within 3 days and signs should be resolved within 7 days after treatment. However, the complete healing of ulcers depends on the size, with larger ulcers taking >2 weeks to heal. In addition, healing may be slower in people living with HIV or for uncircumcised men, requiring additional or extended courses of treatment.[1]

4.5 Chlamydial Infections

In the US, chlamydial infections (ie, *C. trachomatis*) are the most commonly reported bacterial STI with an estimated prevalence of 2.4 million,[9] of which, the highest prevalence is among individuals ≤24 years of age.[1] Patients are commonly asymptomatic, resulting in increased potential for the development of serious sequelae in women such as PID, infertility, and ectopic pregnancy.[1] Treatment should be provided as soon as possible for all infected individuals, including presumptively for all sex partners within the previous 60 days prior to symptom onset or diagnosis, to minimize the risk of potential complications and prevent continual transmission and reinfection. At the very least, the most recent sex partner should be presumptively treated, regardless of last sexual contact (<60 days, >60 days).[1]

4.5.1 Chlamydial Infection in Adults and Adolescents

Recommended treatment regimen for adults and adolescents, including patients who have HIV, is as follows[1]:

- Doxycycline 100 mg by mouth twice a day for 7 days
    - A delayed-release formulation (once daily dosing) has shown to be as effective as the immediate-release formulation (twice daily dosing) for the treatment of *urogenital* infections, with fewer gastrointestinal adverse events (AEs), but tends to be more expensive

Alternative treatment regimens for adults and adolescents, including patients who have HIV, are as follows[1]:

- Azithromycin 1 gram by mouth (as a one-time dose) OR
- Levofloxacin 500 mg by mouth once a day for 7 days

To prevent possible reinfection and/or transmission, patients with a chlamydia infection should refrain from having sexual intercourse until all affected individuals have been treated (ie, patient, all sex partners) or symptoms have resolved, if present.[1] Patients should refrain from participating in sex for 7 days after one-time therapy or until the 7-day regimen is completed. Even with a negative HIV diagnosis, HIV pre-exposure prophylaxis (PrEP) should be offered to MSM with a rectal chlamydia infection.[1]

Doxycycline is an effective treatment for *C. trachomatis* infections in the urogenital, oropharyngeal, and rectal regions.[1] When nonadherence is suspected, an alternative regimen may be used. Prior to the use of azithromycin, susceptibility testing should be considered due to the lower efficacy in treating rectal infections. In the 2021 guideline, erythromycin has been removed as an alternative agent due to the high risk of nonadherence from gastrointestinal-related AEs.[1]

For nonpregnant people, testing for therapeutic failure 4 weeks after completing either a recommended or alternative treatment regimen is unnecessary, unless suspicion of nonadherence or reinfection exists or symptoms persist.[1] A follow-up visit should occur approximately 3 months after treatment to retest for chlamydia due to the high chance of reinfection. In the event following-up at 3 months is not feasible, the patient should be retested at the next routine visit <12 months after completing the initial pharmacotherapy.[1]

4.5.2 Chlamydial Infection During Pregnancy

Pregnant patients should be treated to prevent possible transmission to the neonate during labor.[1] If chlamydial infections occur in the neonate/infant (ie, chlamydial ophthalmia and/or pneumonia), presumptive treatment should be provide to the mother.[1]

Recommended treatment regimen for pregnant patients is as follows[1]:

- Azithromycin 1 gram by mouth (as a one-time dose)

Alternative treatment regimen for pregnant patients is as follows[1]:

- Amoxicillin 500 mg by mouth 3 times a day for 7 days

Due to the risk of tooth discoloration, doxycycline is contraindicated during the second and third trimesters.[1] Evidence suggests that the preferred agent, azithromycin, is safe during pregnancy. Amoxicillin is recommended as an alternative agent due to the potential concern of *C. trachomatis* resistance to penicillin-class antibiotics. Erythromycin is also no longer recommended as an alternative agent for pregnant patients due to the high incidence of gastrointestinal-related AEs and the possibility of negative maternal and fetal outcomes.[1]

Unlike the general population, testing to ensure to infection has been cured is recommended at approximately 4 weeks after completing treatment.[1] Unresolved infections can result in serious sequelae that may put the mother and baby at an increased risk of complications (eg, ophthalmia neonatorum). However, similar to non-pregnant patients, all pregnant individuals should also be retested at 3 months after therapy.[1]

4.5.3 Chlamydial Infection in Neonates

Treating pregnant patients and conducting appropriate prenatal screening are the best approaches for minimizing transmission of *C. trachomatis* infections to neonates during labor.[1] Although other regions of the body that contain mucosal membranes are also susceptible to infection (eg, oropharynx, rectum, urogenital tract), the eye is the most identifiable among neonatal chlamydial infections.[1]

4.5.3.1 Ophthalmia Neonatorum (Conjunctivitis in Newborns)

Chlamydial conjunctivitis usually manifests 5−12 days after delivery.[1] For all infants ≤30 days old diagnosed with conjunctivitis, an etiology of *C. trachomatis* should be considered, especially when a maternal history of chlamydia exists.[1]

Recommended treatment regimens for neonates is as follows[1]:

- Erythromycin (ethyl succinate or base) 50 mg/kg per day by mouth, divided into 4 daily doses for 14 days

There is limited data regarding the efficacy of oral azithromycin for treating chlamydial ophthalmia neonatorum, but some evidence suggests a short-course may effectively treat chlamydial infections in neonates.[1] Notably, among infants <6 weeks of age, infantile hypertrophic pyloric stenosis (IHPS) has been reported with oral erythromycin and azithromycin use. Infants treated with these agents should be monitored for symptoms and signs of IHPS.[1]

Since erythromycin is estimated to be effective in 80% of cases, a second course of treatment may be needed for some infants.[1] Therefore, the follow-up visit should evaluate whether a subsequent course is required. For neonates treated for ophthalmia neonatorum, the risk of concurrent chlamydial pneumonia should be considered.[1]

4.5.4 Chlamydial Infection in Infants and Children

Chlamydial infections of certain body regions (ie, urogenital tract, nasopharynx, rectum) that were transmitted perinatally can last for 2−3 years.[1] However, they might also occur due to other causes, such as sexual abuse.[1]

Recommended treatment regimens for infants and children are as follows[1]:

- Weighing <45 kg:
    - Erythromycin (ethyl succinate or base) 50 mg/kg per day by mouth, divided into 4 daily doses for 14 days
- Weighing ≥45 kg, but <8 years of age:
    - Azithromycin 1 gram by mouth (as a one-time dose)
- ≥8 years of age:
    - Azithromycin 1 gram by mouth (as a one-time dose) OR
    - Doxycycline 100 mg by mouth twice a day for 7 days

Evidence is limited about the effectiveness and optimal dosing for azithromycin in children and infants that weigh <45 kg.[1] Therefore, azithromycin as a one-time dose is only recommended for children that weigh at least 45 kg, regardless of age. A follow-up visit at approximately 4 weeks after completing treatment is recommended to ensure that the infection has been cured.[1]

4.5.4.1 Chlamydial Pneumonia in Infants

Subacute chlamydial pneumonia may develop in infants between 1 to 3 months old due to an untreated material infection that spread to the neonate during delivery.[1] Decisions to initiate treatment are often based on the clinical presentation of the infant, including radiologic chest results (ie, positive bilateral diffuse infiltrates), infant age, and whether the mother is considered high-risk for chlamydia (eg, age <25 years, numerous sex partners, prior chlamydial infection). For cases where follow-up is doubtful and a high certainty of a chlamydial infection exists, the infant may be presumptively treated with the shorter-duration alternative regimen despite a lack of laboratory results.[1]

Recommended treatment regimens for infants is as follows[1]:

- Erythromycin (ethyl succinate or base) 50 mg/kg per day by mouth, divided into 4 daily doses for 14 days

Alternative treatment regimen for infants is as follows[1]:

- Azithromycin suspension 20 mg/kg per day by mouth once a day for 3 days

Similar to ophthalmia neonatorum, regimens using erythromycin may require additional courses of therapy due to the lower effectiveness (ie, 80%).[1] There is limited data regarding the efficacy of

azithromycin for treating chlamydial pneumonia. Therefore, follow-up is recommended to ensure the pneumonia has been successfully treated and symptoms have resolved (eg, cough, tachypnea) regardless of the regimen used. Despite resolution of the infection, some infants may continue to have lasting effects (eg, abnormal pulmonary function tests) into childhood.[1]

4.6 Gonococcal Infections

Second to chlamydial infections (ie, *C. trachomatis*), *N. gonorrhoeae* is the next most prevalent bacterial STI in the US, with an estimated 1.6 million new infections occurring annually.[1] Interestingly, gonorrhea has a higher prevalence within certain geographic regions (eg, southeastern US) and subpopulations (ie, adolescents, young adults).[1,18]

The 2015 CDC STI guideline-recommended treatment included dual therapy with azithromycin and ceftriaxone.[5] However, due to the potential concerns of harming the microbiome and the impact on other pathogens, the 2021 guideline recommends only ceftriaxone.[1] In the US, ceftriaxone is the only remaining antibiotic to be highly effective as a one-time dose at all of the various anatomical sites for a potential gonorrhea infection, with a higher dose (1 gram) indicated for individuals weighing ≥150 kg.[1]

Although the Clinical and Laboratory Standards Institute (CLSI) does not have established criteria to indicate ceftriaxone or cefixime (alternative agent) resistance, isolates with a minimum inhibitory concentration (MIC) of ≥0.5 ug/mL tend to be considered resistant.[1] However, for surveillance purposes to detect potential trends in gonococcal susceptibility, the Gonococcal Isolate Surveillance Project (GISP), the primary US surveillance system for tracking gonorrhea resistance,[19] has set lower MIC threshold standards for cephalosporins than the CLSI to provide increased sensitivity to emerging gonococcal resistance patterns.[1] Although the percentage of isolates with ceftriaxone and cefixime MICs ≥0.125 ug/mL have remained low in the US (0.1% and 0.3% during 2019, respectively), higher MICs for ceftriaxone and cefixime (1.5−4.0 ug/mL and 1.5−8.0 ug/mL, respectively) have been detected in other countries.[1] Thus, the CDC plans to track any changes in the MIC of ceftriaxone to remain vigilant against *N. gonorrhoeae* antimicrobial resistance and promote antibiotic stewardship.[1]

4.6.1 Gonococcal Infection in Adults and Adolescents

Among men, gonococcal infections often result in symptomatic urethral infections, encouraging the pursuit of medical treatment and subsequently minimizing the risk of potential sequelae.[1] Whereas, women are frequently asymptomatic or have non-specific symptoms, causing the infection to be unidentified until symptoms develop from a severe complication (eg, PID).[1] Untreated *N. gonorrhoeae* infections can result in epididymitis in men and PID in women.[18] Rarely (an estimated 0.5−3% of untreated gonorrhea cases),[20] invasive infections can occur in secondary anatomical sites via the blood circulation, causing disseminated gonococcal infections (DGI) (eg, arthritis or arthritis-dermatitis syndrome, endocarditis, or meningitis).[1,18,20] Once the infection has disseminated, hospitalization is recommended and medications are generally given intravenously (IV) rather than IM.[1]

To prevent possible transmission, individuals with a gonorrhea infection should refrain from having sexual intercourse for 7 days until all affected people have been treated (ie, patient, all sex partners) and symptoms have resolved, if present.[1] Presumptive treatment should be provided to all sex partners exposed within the previous 60 days prior to symptom onset or diagnosis; or if exposure occurred >60

days before, the most recent sex partner. Individuals co-infected with chlamydia should also receive doxycycline 100 mg by mouth twice a day for 7 days, unless contraindicated. Individuals who have presumably failed gonococcal treatment with a cephalosporin should have cultures and susceptibility testing performed, the physician should consult with an STI or infectious disease specialist, and the case should be reported to the CDC within 24 hours. Additionally, consultation with an STI or infectious disease expert is recommended for pregnant patients with a cephalosporin allergy or other contraindications to ceftriaxone (recommended regimen).[1]

Testing to ensure the infection has been cured after treatment depends on the anatomical site of the infection.[1] However, repeat cultures and susceptibility testing should be obtained for individuals who continue to experience symptoms after completing the appropriate treatment regimen since some symptoms (eg, cervicitis, urethritis, proctitis) may be caused by other pathogens, or to evaluate for potential treatment failure or reinfection. Due to the high chance of reinfection, a follow-up visit should occur at approximately 3 months to retest for gonorrhea in all treated adults and adolescents. In the event following-up at 3 months is not feasible, the patient should be retested at the next routine visit <12 months after completing the initial pharmacotherapy.[1]

4.6.1.1 Uncomplicated Urethral, Cervical, or Rectal Gonococcal Infections in Adults and Adolescents

Recommended treatment regimen for adults and adolescents, including pregnant patients and those who have HIV, is as follows[1]:

- Ceftriaxone 500 mg IM (one-time dose)

Alternative treatment regimens for adults and adolescents are as follows, *if ceftriaxone is unavailable*[1]:

- Gentamicin 240 mg IM (one-time dose) AND
- Azithromycin 2 grams by mouth (one-time dose) OR
- Cefixime 800 mg by mouth (one-time dose)

Combination therapy with gentamicin IM and oral azithromycin is recommended for patients who have a confirmed or suspected IgE-mediated penicillin allergy.[1] However, the risk of cross-reactivity for penicillin is <1% with third-generation cephalosporins, such as ceftriaxone. During pregnancy, gentamicin should be used cautiously due to the increased risk for fetal birth defects, ototoxicity, and nephrotoxicity.[1]

A test to evaluate if the infection has been cured after completing either a recommended or alternative regimen is not required for uncomplicated rectal or urogenital infections.[1]

4.6.1.2 Uncomplicated Pharyngeal Gonococcal Infection in Adults and Adolescents

Pharyngeal gonococcal infections are more challenging to cure than infections at other anatomical sites, such as the urethra, cervix, and rectum.[1] While individuals with pharyngeal infections due to *N. gonorrhoeae* rarely develop complications, it is easily transmitted to others since infected individuals are commonly asymptomatic, potentially contributing to antimicrobial resistance. There are a limited number of antibiotic therapies that effectively cure (>90%) pharyngeal infections; thus, no alternative regimens are provided in the guideline. In situations where an alternative regimen is warranted (ie, an

individual has an allergic or other serious reaction, including Steven Johnson syndrome), an infectious disease specialist should be consulted.[1]

Recommended treatment regimen for adults and adolescents, including pregnant patients and those living with HIV, is as follows[1]:

- Ceftriaxone 500 mg IM (one-time dose)

To ensure the infection has been cured, a follow-up visit for repeat testing should occur between 7−14 days after treatment, preferably after the seventh day to minimize the chance of a false-positive.[1]

4.6.1.3 Gonococcal Conjunctivitis in Adults and Adolescents

Non-neonatal gonococcal conjunctivitis is rare, and there is limited evidence regarding adult treatment (one published study).[1] In the only published study, all adults (n=12) were successfully treated with a one-time dose of IM ceftriaxone.[1,21] However, given the lack of robust data and the uncommon nature of gonococcal conjunctivitis, an infectious disease specialist should be consulted.[1]

Recommended treatment regimen for adults and adolescents is as follows[1]:

- Ceftriaxone 1 gram IM (one-time dose)

In addition to ceftriaxone, a single conjunctival saline lavage may be used in the infected eye.[1]

4.6.1.4 Arthritis-Dermatitis Syndrome and Gonococcal-Related Arthritis in Adults and Adolescents

Recommended treatment regimen for adults and adolescents is as follows[1]:

- Ceftriaxone 1 gram IM or IV every 24 hours

Alternative treatment regimens for adults and adolescents are as follows[1]:

- Cefotaxime 1 gram IV every 8 hours OR
- Ceftizoxime 1 gram every 8 hours

The physician may switch to an oral medication (as advised by antimicrobial susceptibility testing) after a "substantial clinical improvement" has been observed for 24−48 hours, totaling a treatment duration of >7 days.[1] Notably, the 2021 guideline does not state a preferred administration route for ceftizoxime (an alternative agent), which can be administered either IV or IM.[22] However, other resources that claim to be in alignment with the 2021 guideline recommend ceftizoxime should be administered IV.[23]

4.6.1.5 Gonococcal Endocarditis and Meningitis in Adults and Adolescents

Recommended treatment regimen for adults and adolescents is as follows[1]:

- Ceftriaxone 1−2 gram IV every 24 hours

The duration of treatment should be dictated by the patient's clinical presentation in collaboration with an infectious disease specialist.[1] Parenteral therapy for meningitis is recommended to be continued for 10−14 days, and >4 weeks for endocarditis.[1]

4.6.2 Gonococcal Infection in Neonates

Similar to chlamydia infections in neonates, treating pregnant patients and appropriate prenatal screening are the best approaches for minimizing the transfer of *N. gonorrhoeae* infections to neonates from cervical exposure during labor.[1] An infection attributed to *N. gonorrhoeae* typically occurs 2−5 days after birth and can manifest in the eye, scalp (from electrodes for monitoring purposes), or in more serious cases, disseminate to other sites resulting in meningitis, sepsis, or arthritis. Mothers of neonates with gonorrhea-related ophthalmia, disseminated infections, or scalp abscess should be presumptively treated for *N. gonorrhoeae*.[1]

For ceftriaxone-containing regimens, caution should be used when administering the agent to newborns with hyperbilirubinemia, especially those who are premature.[1] If ceftriaxone is unable to be used due to concurrent administration of intravenous calcium, cefotaxime administered either IM or IV as a one-time dose of 100 mg/kg may be used. An infectious disease specialist should be consulted for the treatment of all gonococcal infections in neonates, except infections that occur in the absence of symptoms and as prophylaxis (*discussed in detail below*).[1]

4.6.2.1 Asymptomatic Gonococcal Infection in Neonates

For newborns at high risk for a gonorrhea infection due to an untreated infection in the mother, presumptive treatment should be administered, even when signs of an infection are not present.[1]

Recommended treatment regimen for neonates is as follows[1]:

- Ceftriaxone 20−50 mg/kg IM or IV as a one-time dose
    - Maximum dose: 250 mg

4.6.2.2 Ophthalmia Neonatorum (Conjunctivitis in Newborns)

In the US, cases of ophthalmia neonatorum due to *N. gonorrhoeae* are rare, most likely due to most states legally mandating ocular prophylaxis with erythromycin.[1] If left untreated, the infection can cause ocular perforation, corneal scarring, and permanent visual loss shortly after delivery (<24 hours).[1,24] Thus, the US Preventive Services Task Force (USPSTF) recommends prophylaxis for all neonates <24 hours after delivery due to the safety benefits and proven effectiveness.[1,24] Ophthalmic erythromycin ointment is the only US Food and Drug Administration (FDA)-approved prophylactic agent for gonococcal ophthalmia neonatorum.[1]

4.6.2.2.1 Prophylaxis

Recommended prophylaxis regimen for neonates is as follows[1]:

- Erythromycin 0.5% ophthalmic ointment in both eyes (as a one-time dose) applied at birth

Regardless of the delivery method (ie, cesarean or vaginally), erythromycin should be applied to the neonate's eyes immediately after birth.[1] If the ointment is not applied while in the delivery room, an appropriate tracking system should be used to ensure that prophylaxis is administered in a timely manner (<24 hours after birth).[1]

In the event erythromycin ointment is unavailable, ceftriaxone administered either IV or IM, as a one-time dose of 25−50 mg/kg (maximum 250 mg) may be used for neonates at risk of *N. gonorrhoeae* acquisition, especially when a concern for maternal gonorrhea exists or no prenatal care was provided.[1] Nevertheless, this is not a recommended alternative regimen for prophylaxis management and is suggested for use when the preferred therapy is unavailable.[1]

4.6.2.2.2 Treatment

Recommended treatment regimen for neonates is as follows[1]:

- Ceftriaxone 25−50 mg/kg IM or IV as a one-time dose
    - Maximum dose: 250 mg

Antibiotics applied topically are not recommended for treating ophthalmia neonatorum because they are often "inadequate" and are superfluous when systemic antibiotics are administered.[1] Neonates with ophthalmia neonatorum should be assessed for symptoms of an disseminated infection.[1]

4.6.2.3 Disseminated Gonococcal Infections in Neonates

Recommended treatment regimens for neonates are as follows[1]:

- Ceftriaxone 25−50 mg/kg per day IM or IV (administered as a single dose) once a day for 7 days OR
- Cefotaxime 25 mg/kg per day IM or IV every 12 hours for 7 days

For the treatment of meningitis, the treatment duration of either regimen should be extended to 10−14 days.[1]

4.6.3 Gonococcal Infection in Infants and Children

Sexual abuse is the most common reason for gonococcal infections to occur among infants and children.[1] Sexually abused children with pharyngeal or anorectal *N. gonorrhoeae* infections are often asymptomatic. However, vaginitis is frequently reported among preadolescent girls, but the manifestation of PID from an untreated vaginal infection is less likely to occur in preadolescent girls relative to adult women.[1]

For the treatment of gonococcal infections, including disseminated infections (ie, arthritis, bacteremia), only the parenteral administration of ceftriaxone is recommended to be used.[1]

4.6.3.1 Uncomplicated Urogenital and Pharyngeal Infections in Infants and Children

Recommended treatment regimens for cervicitis, vulvovaginitis, pharyngitis, urethritis, or proctitis in infants and children is as follows[1]:

- Children and infants weighing ≤45 kg:
    - Ceftriaxone 25−50 mg/kg IM or IV (as a one-time dose)
        - Maximum dose: 250 mg IM
- Children weighing >45 kg:
    - Ceftriaxone 500 mg IM (as a one-time dose)

4.6.3.2 Arthritis or Bacteremia in Infants and Children

Recommended treatment regimens for infants and children is as follows[1]:

- Children and infants weighing ≤45 kg:
    - Ceftriaxone 50 mg/kg IV or IM (administered as a single dose) every 24 hours for 7 days
        - Maximum dose: 2 grams
- Children weighing >45 kg:
    - Ceftriaxone 1 gram IV or IM (administered as a single dose) every 24 hours for 7 days

4.7 Granuloma Inguinale (Donovanosis)

In the US, granuloma inguinale (donovanosis) is very uncommon, but cases have been reported in other regions such as South Africa, India, and South America.[1] The causative organism is *Klebsiella granulomatis*, a gram-negative intracellular bacteria. The disease is characterized as painless, ulcerative genital lesions that gradually grow and are highly vascular, and as such, easily bleed, promoting secondary bacterial infections. The infection can spread to the surrounding areas of the body (eg, pelvis) or disseminate to the mouth, bones, or intra-abdominal tissues. Individuals with granuloma inguinale (donovanosis) can be infected with other STI pathogens.[1]

Treatment with antibiotics, usually for an extended duration (>3 weeks), helps to stop the growth of the lesions and aid the healing process.[1] However, even with effective treatment, individuals can experience a recurrence 6−18 months later. Sexual partners within the previous 60-day period prior to the manifestation of symptoms may be offered treatment. However, in the absence of symptoms, the value of treating sex partners has not been determined.[1]

Recommended treatment regimen for all individuals, including patients who are pregnant or who have HIV, is as follows[1]:

- Azithromycin 1 gram by mouth once a week or 500 mg once a day for >3 weeks until all lesions have fully healed

Alternative treatment regimens for all individuals, including patients who are pregnant[†] or who have HIV, are as follows[1]:

- Doxycycline 100 mg by mouth twice a day for >3 weeks until all lesions have fully healed OR
- Erythromycin base 500 mg by mouth 4 times per day for >3 weeks until all lesions have fully healed OR
- Trimethoprim-sulfamethoxazole (double strength: 160 mg/800 mg) 1 tablet twice a day for >3 weeks until all lesions have fully healed

For individuals who do not experience an improvement in symptoms within the first couple of days of treatment, an additional antibiotic may be added to any of the above regimens (recommended or alternative).[1] Until symptoms and signs of the infection resolve, patients should be followed to ensure the infection is being appropriately treated.[1]

[†] Pregnant and lactating patients should receive a regimen that contains azithromycin or erythromycin due to the better compatibility during pregnancy and/or breastfeeding.

4.8 Lymphogranuloma Venereum

Lymphogranuloma venereum (LGV) is caused by the L1, L2, or L3 strains of *C. trachomatis*, which result in various clinical presentations.[1] Proctocolitis is the most frequent clinical presentation, which can produce symptoms synonymous with inflammatory bowel disease (eg,mucoid or hemorrhagic discharge from the rectum, localized pain, tenesmus, constipation), but other manifestations include lymphadenopathy and genital ulcer disease. Untreated rectal infections can progress to colorectal fistulas and strictures. Notably, individuals can also be asymptomatic with rectal LGV.[1]

Although LGV is uncommon in the US, the highest incidence seems to be among sexually active people aged 15−40 years.[25] In particular, the acquisition of proctocolitis-related LGV seems to be higher among MSM and HIV-positive individuals.[25]

Presumptive treatment should be provided to individuals presenting with a clinical presentation consistent with LGV, including the following examples[1]:

- Proctocolitis symptoms (eg, tenesmus, hemorrhagic discharge, ulceration)
- Severe unilateral or bilateral inguinal lymphadenopathy with buboes, especially in patients who recently had a genital ulcer
- Genital ulcer, provided other etiologies have been excluded

Treatment goals include curing the infection and preventing chronic tissue injury, although tissue scarring can occur as a natural response to the infection.[1] To prevent the formation of femoral and/or inguinal ulcers, buboes may need to be drained or aspirated.[1]

Recommended treatment regimen for all individuals, including patients who have HIV, is as follows[1]:

- Doxycycline 100 mg by mouth twice a day for 21 days

Alternative treatment regimens for all individuals, including patients who have HIV, are as follows[1]:

- Azithromycin 1 gram by mouth once a week for 3 weeks OR
- Erythromycin base 500 mg by mouth 4 times per day for 21 days

Longer durations of pharmacotherapy may be needed for patients with markers of severe disease such as buboes, fistulas, or other indicators (eg, HIV-positive).[1] Only the regimen using azithromycin suggests a NAAT test 4 weeks after completing treatment to ensure the infection is cured. During pregnancy, azithromycin tends to be generally safe at the recommended dose and frequency, but no published evidence exists to confirm this regimen. Erythromycin may be used during pregnancy, but it tends to cause gastrointestinal AEs, whereas doxycycline may discolor developing teeth. For pregnant patients, a test of cure is required 4 weeks after the initial positive diagnosis test (ie, NAAT), regardless of the treatment regimen used.[1]

Until symptoms and signs of the infection resolve, patients should be followed to ensure the infection is being treated.[1] Even with a negative HIV diagnosis, HIV PrEP should be offered to MSM with a chlamydia infection in the rectal region. A follow-up visit should occur for all patients approximately 3 months after treatment is completed to retest for chlamydia. In the event a 3 month follow-up is not feasible, the patient should be retested at the next routine visit <12 months after completing the initial

pharmacotherapy. Presumptive treatment with the recommended regimen for chlamydia (doxycycline 100 mg by mouth twice a day for 7 days) should be used in asymptomatic sex partners who were exposed within the preceding 60 days of symptom onset.[1]

4.9 Nongonococcal Urethritis

Nongonococcal urethritis (NGU), a generic diagnosis, can be caused by a variety of bacterial pathogens, including *C. trachomatis* (<50% of cases), *M. genitalium* (10−25% of cases), and *T. vaginalis* (1−8% of cases, depending on geographic area and population).[1] Other bacterial etiologies include *N. meningitidis*, *Haemophilus* species, and adenovirus. Despite the possibility of numerous bacterial causes, in almost half of the reported cases, no pathogens are detected.[1]

Presumptive treatment should be started when an NGU diagnosis has been established, although ideally, treatment should be targeted to the causative pathogen based on bacterial cultures and antimicrobial susceptabilities.[1] Additionally, presumptive treatment for chlamydia should be provided for all sex partners exposed within the preceding 60 days.[1]

Recommended treatment regimen for men, including those living with HIV is as follows[1]:

- Doxycycline 100 mg by mouth twice a day for 7 days

Alternative treatment regimens for men, including those living with HIV, are as follows[1]:

- Azithromycin 1 gram by mouth (as a one-time dose) OR
- Azithromycin 500 mg by mouth (as a one-time dose) THEN
- Azithromycin 250 mg by mouth once a day for 4 days

Men should refrain from having sexual intercourse until all affected individuals have been treated (ie, patient, all sex partners) to prevent possible reinfection and transmission.[1] This translates to abstaining until finishing the 7 day treatment course for the recommended regimen and the infected individual no longer has any symptoms, or for 7 days after the single one-time dose alternative regimen.[1]

Regardless of the total number of doses required in the regimen, the first dose should be administered in the clinic and overseen by the clinician to ensure adherence.[1] For *M. genitalium* infections, a multiday dosing regimen of azithromycin may inhibit resistance compared to the single-dose regimen, according to pharmacokinetic data. Erythromycin is no longer recommended as an alternative agent due to the more frequent dosing administration (ie, 4 times per day) and gastrointestinal-related AEs. In addition, levofloxacin, previously an alternative agent, is no longer recommended due to the reduced efficacy for treating NGU, especially when the causative organism is *M. genitalium*.[1]

Men diagnosed with a specific pathological cause of gonorrhea, chlamydia, or trichomoniasis should follow up in 3 months after being treated for repeat testing and offered partner management.[1] For men with persistent symptoms or relapse after completing initial treatment, a follow-up test for *T. vaginalis* and *M. genitalium* should be conducted. In the absence of objective findings (ie, laboratory results, documented signs of localized inflammation), retreatment should not be based solely on the manifestation of symptoms.[1]

4.9.1 Recurrent or Persistent Nongonococcal Urethritis

After completing an initial treatment regimen, reinfection or treatment failure may result in persistent or recurrent NGU.[1] Commonly, *M. genitalium* has been associated with recurrent or persistent NGU, particularly with doxycycline treatment regimens. The initial regimen may be repeated for men who did not previously adhere to the regimen or were reinfected by an untreated sex partner. Bacterial cultures and antimicrobial susceptibilities should be used to determine therapeutic decisions for men who did not re-acquire the infection and were compliant with the initial treatment regimen.[1]

Persistent or recurrent NGU may be caused by *T. vaginalis*, especially in regions where the bacterium is prevalent, and can occur with heterosexual intercourse; thus, these individuals should be treated presumptively with the recommended regimen.[1]

Recommended treatment regimens for men, including those living with HIV, are as follows[1]:

- Metronidazole 2 grams by mouth (as a one-time dose) OR
- Tinidazole 2 grams by mouth (as a one-time dose)

In the event the disease is not likely to be caused by *T. vaginalis* (ie, negative NAAT for *T. vaginalis,* NGU in MSM), men should be tested using an FDA-approved NAAT test for *M. genitalium.*[1] Preferably, treatment should be guided by resistance testing because >90% cure rates have been observed with this approach.[1] The following recommended regimens should be used when resistance testing is available, and are utilized based on macrolide sensitivity or resistance.[13]

Recommended treatment regimen for men, including those who have HIV, with macrolide *sensitive* *M. genitalium* is as follows[1,13]:

- Doxycycline 100 mg by mouth twice a day for 7 days THEN
- Azithromycin 1 gram by mouth (initial one-time dose) THEN
- Azithromycin 500 mg by mouth once a day for the next 3 days (Total azithromycin dose: 2.5 grams, including the initial 1 gram dose)

Recommended treatment regimen for men, including those who have HIV, with macrolide *resistant* *M. genitalium* is as follows[1,13]:

- Doxycycline 100 mg by mouth twice a day for 7 days THEN
- Moxifloxacin 400 mg by mouth once a day for 7 days

Treatment should still be provided when resistance testing is unavailable, although it may not cure the infection.[1] However, the empiric recommended regimen (same recommended regimen for macrolide resistant *M. genitalium)* of combination therapy with doxycycline (reduces bacterial load) and moxifloxacin increases the probability of treatment success. While most strains of *M. genitalium* are moxifloxacin-sensitive, some strains may be resistant. The alternative regimen should be used when a contraindication to moxifloxacin exists or is unavailable.[1] Because this regimen is based on limited evidence and the prevalence of macrolide resistance is high, repeat testing for *M. genitalium* should be conducted 21 days after completing this treatment.[1,13]

Recommended treatment regimen for men, including those who have HIV, when *M. genitalium* macrolide-resistance testing is unavailable is as follows[1,13]:

- Doxycycline 100 mg by mouth twice a day for 7 days THEN
- Moxifloxacin 400 mg by mouth once a day for 7 days

Alternative treatment regimen for men, including those who have HIV, when *M. genitalium* macrolide-resistance testing is unavailable is as follows[13]:

- Doxycycline 100 mg twice a day for 7 days THEN
- Azithromycin 1 gram by mouth (initial one-time dose) THEN
- Azithromycin 500 mg by mouth once a day for 3 days

A referral to a urologist or infectious disease expert is recommended for men that continue to have recurrent or persistent NGU after completing the appropriate treatment regimen for *T. vaginalis* or *M. genitalium.*[1]

4.10 Pelvic Inflammatory Disease

Pelvic inflammatory disease (PID) is an infection that involves the upper reproductive tract of females, including the ovaries, uterus, and fallopian tubes, and may extend into the pelvic region.[1,26] An estimated 50% of acute PID cases are caused by *C. trachomatis* and *N.gonorrhoeae*,[1] but other pathogens may be involved, such as *M. genitalium,* anaerobes, *H. influenzae, T. vaginalis, M. hominis, G. vaginalis* (bacterium involved in the manifestation of BV), and enteric gram-negative rods.[1,26] The risk of developing PID from chlamydia or gonorrhea is decreased when these infections are treated early; however, it is unclear whether the incidence of PID is affected by BV treatment.[1]

Long-term sequelae of PID (eg, chronic pelvic pain, ectopic pregnancy, infertility) can be prevented with prompt treatment[26]; thus, treatment should be provided immediately after a diagnosis has been established.[1] Presumptive treatment is warranted for women at risk for an STI or those who are sexually active, if they are symptomatic (ie, lower abdominal or pelvic pain), no other etiologies are identified, or tenderness of the cervix, uterus, or pelvic region is present based on physical examination.[1] Treatment regimens, either administered IV or IM, depending on disease severity, consist of broad-spectrum antibiotics. Regardless of a negative endocervical screening, all treatment regimens should include antibiotics that are effective against *C. trachomatis* and *N. gonorrhoeae.*[1] The decision to hospitalize an adolescent or adult woman with PID should be based on the physician's clinical judgment and if any of the following criteria are met[1]:

- When surgical emergencies (eg, appendicitis) may be required
- Pregnancy
- Tubo-ovarian abscess
- Nausea and vomiting, temperature (oral) >101°F, severe illness
- Unable to tolerate, adhere, or lack a response to an oral regimen

To prevent possible transmission, women should refrain from having sexual intercourse until treatment is finished, symptoms are no longer present, and sex partners have been appropriately treated.[1] Regardless of the PID etiology, sex partners within the previous 60 days prior to symptom onset should

be presumptively treated for *N. gonorrhoeae* and *C. trachomatis* since asymptomatic infection tends to be common.[1]

Women may continue to use any form of contraception while receiving any of the treatment regimens.[1] However, if a woman has an intrauterine device (IUD), particularly copper-containing, the physician can consider removing the device if no improvement is observed within 48–72 hours of starting treatment due to the inherent risk of PID with IUDs. However, the risk of PID is usually restricted to the first 3 weeks after the IUD is placed. Thus, it may be sensible not to remove the IUD since evidence from a systematic review suggests that removing an IUD had no impact on treatment outcomes.[1]

Women should experience symptomatic improvement (eg, decreased tenderness, defervescence) within 72 hours of starting treatment, regardless of the administration route.[1] Hospitalization, ensuring the appropriate antibiotic regimen, and subsequent diagnostic evaluation are recommended for women who fail to respond promptly (<72 hours) to an outpatient regimen. A follow-up retest visit should occur at approximately 3 months for all women with PID caused by gonorrhea or chlamydia. In the event following-up at 3 months is not feasible, the patient should be retested at the next routine visit <12 months after completing the pharmacotherapy.[1]

4.10.1 Intravenous Regimens

Recommended IV/oral treatment regimens for women are as follows[1]:

Option 1:

- Ceftriaxone 1 gram IV every 24 hours AND
- Doxycycline 100 mg by mouth or IV every 12 hours WITH
- Metronidazole 500 mg by mouth or IV every 12 hours

Option 2:

- Cefotetan 2 grams IV every 12 hours AND
- Doxycycline 100 mg by mouth or IV every 12 hours

Option 3:

- Cefoxitin 2 grams IV every 6 hours AND
- Doxycycline 100 mg by mouth or IV every 12 hours

Alternative IV/IM treatment regimens for women are as follows[1]:

Option 1:

- Ampicillin-sulbactam 3 grams IV every 6 hours AND
- Doxycycline 100 mg by mouth or IV every 12 hours

Option 2:

- Clindamycin 900 mg IV every 8 hours AND
- Gentamicin 2 mg/kg loading dose IM or IV, then 1.5 mg/kg every 8 hours (maintenance dose)
    - 3–5 mg/kg once a day may be used as an alternative maintenance dose

Typically, agents administered via IV can be transitioned to oral within 24−48 hours of improvement, but ultimately, the decision of when to initiate oral therapy should be individualized.[1] The bioavailability for

metronidazole and doxycycline is similar between routes of administration, with the oral route preferred over IV, whenever feasible. Once improvement has been demonstrated with parenteral therapy, it is recommended to transition to oral combination therapy with doxycycline (100 mg twice a day) and metronidazole (500 mg twice a day) for a total treatment duration of 14 days.[1]

When using gentamicin and clindamycin (an alternative regimen), transitioning to oral therapy with doxycycline (100 mg twice a day) or clindamycin (450 mg four times a day) can be considered after 24–28 hours of improvement, for a total treatment duration of 14 days.[1] For women who have tubo-ovarian abscess, oral therapy with doxycycline and either clindamycin or metronidazole should be used to provide adequate anaerobic coverage.[1]

4.10.2 Intramuscular Regimens

Women with mild-to-moderate acute PID can be considered for outpatient treatment (IM regimens).[1] IV therapy should be considered for women who do not respond to IM treatment within 72 hours of initiation. Metronidazole is now recommended to be used as part of the combination regimen *with* doxycycline for the outpatient management of mild-to-moderate PID.[1] Previously, the 2015 guideline recommended outpatient regimens with or without metronidazole.[5] The updated recommendation to use metronidazole with doxycycline was based on the therapeutic benefit of anaerobic coverage to prevent long-term sequelae of PID.[1] For ceftriaxone-containing regimens (ie, *option 1*), an increased dose (1 gram) should be administered in women weighing ≥150 kg.[1]

Recommended IM/oral treatment regimens for women are as follows[1]:

Option 1:

- Ceftriaxone 500 mg IM (as a one-time dose) AND
- Doxycycline 100 mg by mouth twice a day for 14 days WITH
- Metronidazole 500 mg by mouth twice a day for 14 days

Option 2:

- Cefoxitin 2 grams IM (as a one-time dose) AND
- Probenecid 1 gram by mouth (as a one-time dose), administered simultaneously with cefoxitin AND
- Doxycycline 100 mg by mouth twice a day for 14 days WITH
- Metronidazole 500 mg by mouth twice a day for 14 days

Option 3:

- Ceftizoxime or cefotaxime, or another third-generation cephalosporin administered IM AND
- Doxycycline 100 mg by mouth twice a day for 14 days WITH
- Metronidazole 500 mg by mouth twice a day for 14 days

Alternative regimens, which contain agents administered orally and in some cases IV, can be considered for women that (1) live in communities with low gonorrhea prevalence and who are at low risk for acquisition, (2) are likely to follow-up, and (3) have an allergy to cephalosporins.[1] The following alternative regimens using quinolones can be considered for women who meet this criteria, but are not generally recommended due to the emergence of quinolone-resistant *N. gonorrhoeae*[1]:

Option 1:

- Levofloxacin 500 mg by mouth once a day OR
- Moxifloxacin 400 mg by mouth once a day AND
- Metronidazole 500 mg by mouth twice a day for 14 days

Option 2:

- Azithromycin 500 mg IV once a day for 1–2 doses THEN
- Azithromycin 250 mg by mouth once a day AND
- Metronidazole 500 mg by mouth twice a day for 12–14 days

A diagnostic test for *N. gonorrhoeae* should be performed prior to initiating treatment.[1] In addition, treatment should be guided by antimicrobial susceptibility, especially when *N. gonorrhoeae* is present. An infectious disease specialist should be consulted when susceptibility testing is unavailable or when *N. gonorrhoeae* is quinolone-resistant.[1]

4.11 Proctitis, Proctocolitis, and Enteritis

Proctitis, proctocolitis, and enteritis are gastrointestinal syndromes that can be sexually acquired.[1] These syndromes predominantly affect individuals who are receptive during anal intercourse or other related sexual practices (eg, oral-anal, digit-anal). Sexual practices and behaviors that enable the transmission of enteric pathogens might promote the acquisition of other STIs, including HIV. For patients at risk for acquiring HIV, PrEP for HIV should be considered. While a specific treatment regimen is provided by the guideline for acute proctitis, proctocolitis and enteritis treatment should be guided by susceptibility testing and targeted to the causative pathogen.[1]

4.11.1 Acute Proctitis

Proctitis is inflammation localized to the rectum and often causes tenesmus, anorectal pain, or discharge from the rectum.[1] The most common sexually transmitted pathogens attributed to proctitis are *C. trachomatis* (including L1, L2, and L3 strains associated with LGV), *N. gonorrhoeae, T. pallidum*, and herpes simplex virus (HSV). Some etiologies of proctitis (ie, LGV and genital HSV) are more prevalent in specific patient populations (ie, individuals living with HIV). In addition, other pathogens may contribute to the etiology of proctitis in individuals living with HIV (eg, *M. genitalium*), including MSM (eg, *N. meningitidis*).[1]

Presumptive treatment for acute proctitis should be provided to individuals whom upon evaluation have anorectal exudate (eg, pus), including the presence of polymorphonuclear leukocytes.[1] In the event objective evaluation is unavailable (eg, Gram stain, anoscopy), presumptive treatment should still be provided to patients with a clinical presentation and subjective etiology (ie, patient reports receptive anal contact) indicative of acute proctitis. Additionally, all sex partners within the previous 60 days who were exposed to chlamydia or gonorrhea should be presumptively treated for the causative infection.[1]

Recommended treatment regimen for individuals, including those living with HIV, is as follows:

- Ceftriaxone 500 mg IM (as a one-time dose) AND
- Doxycycline 100 mg by mouth twice a day for 7 days

For individuals weighing ≥150 kg, the dose of ceftriaxone should be increased to 1 gram.[1] In addition, presumptive treatment for LGV with a longer doxycycline treatment duration of 21 days is recommended for patients with hemorrhagic rectal discharge, tenesmus, or mucosal or perianal ulcers, and a positive rectal test for *C. trachomatis*. Presumptive treatment for genital herpes should also be provided to patients with perianal or mucosal ulcers discovered upon examination using an anoscope. No guidance is provided on the treatment of acute proctitis during pregnancy.[1]

Individuals should refrain from having sexual intercourse until all affected individuals have been treated (ie, patient, all sex partners) to prevent possible reinfection and transmission.[1] This implies abstaining until finishing the 7 day treatment course and symptoms are no longer present.[1]

The specific pathogenic etiology and symptom severity dictates the approach for follow-up.[1] In patients with proctitis due to chlamydia or gonorrhea, a follow-up visit should occur 3 months after treatment to retest for the presence of the respective causative pathogen.[1]

4.12 Syphilis

Syphilis is caused by the bacterium *T. pallidum*, which can be acquired either sexually or vertically from mother-to-baby during labor.[1,27] Syphilis is categorized into stages based on clinical manifestations.[1] It has the potential to disseminate to other organ systems (eg, central nervous system [CNS], auditory system, visual system) at any time after inoculation.[1] The various stages of syphilis are as follows, along with the corresponding distinctive manifestations[1,28]:

- Primary syphilis: typically presents as a painless ulcer (chancre) at the site of exposure (eg, genitals, anus, mouth), but may also include numerous, atypical, or painful lesions. The ulcer may resolve within 3–6 weeks, irrespective treatment.
- Secondary syphilis: may present as a widespread cutaneous rash, lymphadenopathy, mucocutaneous lesions, alopecia, weight loss, muscle aches, and sore throat. Over time, the symptoms will resolve (without therapeutic intervention), allowing the infection to get progressively worse.
- Tertiary syphilis: may present as gummatous lesions, signs of late neurosyphilis (eg, general paresis, tabes dorsalis), cardiovascular syphilis, and mental abnormalities (eg, alterations in personality, memory loss).
- Latent syphilis: presents with no symptoms, but the infection is detected through serologic testing.

The preferred antibiotic for treating syphilis, regardless of the stage, is the parenteral administration of penicillin G.[1] However, the dosage, duration of treatment, and preparation (ie, aqueous procaine, benzathine, aqueous crystalline) used depends on the patient's symptoms, and consequently, stage of syphilis. Longer treatment durations are recommended for infections that have persisted for longer than 12 months (ie, late latent syphilis), have an unknown duration, or are considered tertiary syphilis.[1]

For individuals suspected of having contagious syphilis (ie, primary, secondary, or early latent syphilis), including those with risk factors, presumptive treatment should be provided to limit transmission.[1] In addition, all sex partners exposed to primary, secondary, or early latent syphilis within the previous 90 days should be presumptively treated for early syphilis, regardless of serologic results. For sex partners exposed >90 days prior, presumptive treatment should be provided when serologic results are

unavailable and for whom follow-up is not guaranteed. In geographic areas with high syphilis rates, sex partners of individuals with an unknown duration of syphilis and high serologic titers (ie, >1:32) should also receive presumptive treatment.[1]

There is the potential for an acute febrile reaction, referred to as Jarisch-Herxheimer reaction, to occur within the initial 24 hours of starting penicillin.[1] The reaction can occur in anyone, but tends to be more prevalent among individuals with early syphilis (ie, primary, secondary, early latent),[27] possibly due to the higher bacterial loads present during the early years of infection.[1] The use of antipyretics (eg, acetaminophen, aspirin) are encouraged to help manage symptoms of the reaction.[1]

Reinfection or treatment failure is suggested by at least a four-fold consistent increase in nontreponemal test titer lasting for >2 weeks, or the manifestation of recurrent or progressive symptoms.[1] In cases where reinfection or treatment failure is indicated, treatment should be repeated with weekly injections of IM benzathine penicillin G 2.4 million units at an extended duration of 3 weeks. This regimen is recommended for patients who have no neurologic abnormalities or any indication of neurosyphilis; thus, retreatment should also be based on CSF results. Typically, further courses of treatment are not recommended for patients with primary or secondary syphilis that continue to have elevated serologic titers, regardless of an additional extended duration of therapy and negative neurologic findings. However, repeating the 3-week treatment can be considered for patients living with HIV infection or latent syphilis who are unlikely to follow-up or have an initially high titer (>1:32) that fails to lessen four-fold within or by 2 years after treatment. Individuals that continue to have elevated serologic test titers, despite repeating treatment should receive serologic and clinical follow-up at least every 12 months. Treatment of neurosyphilis (a potential cause of treatment failure) should be provided based on positive cerebrospinal fluid (CSF) results. Additionally, based on clinical presentation, otosyphilis and/or ocular syphilis should be treated (*please refer to Section 4.12.4*).[1]

4.12.1 Primary and Secondary Syphilis

All adults, children, and infants (≥1 month) should have a clinical evaluation and serologic testing conducted 6–12 months after completing the appropriate therapeutic regimen; more frequent follow up may be considered for patients who are unlikely to follow-up at the longer duration or when a concern for reinfection exists.[1] Individuals living with HIV should have more frequent follow-up serologic testing and clinical visits (ie, 3, 6, 9, 12, and 24 months). Repeating treatment with benzathine penicillin G at an extended duration (weekly injections for 3 weeks) should be based on the likelihood of reinfection and/or treatment failure.[1]

4.12.1.1 Primary and Secondary Syphilis in Adults

Recommended treatment regimen for adults, including pregnant patients and those living with HIV, is as follows[1]:

- Benzathine penicillin G 2.4 million units IM (as a one-time dose)

Patients with an allergy to penicillin who may not follow-up or be adherent should be desensitized and treated with the recommended regimen.[1]

Based on limited evidence, the following **alternative** regimens may be used for non-pregnant patients who have a penicillin allergy[1]:

- Doxycycline 100 mg by mouth twice a day for 14 days OR
- Tetracycline 500 mg by mouth four times a day for 14 days OR
- Ceftriaxone 1 gram IM or IV once a day for 10 days[‡]

Evidence has not shown an increased therapeutic benefit by adding other antibiotics (eg, amoxicillin) or extra doses of benzathine penicillin G to the recommended regimen, including among patients with comorbid HIV.[1] Parenteral penicillin G has shown benefit in preventing transmission to others and late-stage sequelae, and resolution of symptoms, if present (eg, healing ulcers). If an alternative non-penicillin regimen is used for certain non-pregnant patients, adherence is likely to be higher with doxycycline rather than tetracycline based on the dosing frequency and side effect profile (more gastrointestinal AEs with tetracycline).[1]

4.12.1.2 Primary and Secondary Syphilis in Infants and Children

Recommended treatment regimen for infants (aged ≥30 days) and children is as follows[1]:

- Benzathine penicillin G 50,000 units/kg IM (as a one-time dose)
    - Dose not to exceed 2.4 million units (adult dose)

Infants and children with primary or secondary syphilis should be evaluated to determine the acquisition of the infection (ie, congenital or acquired from sexual abuse), and care should be executed by a pediatric infectious disease specialist.[1]

4.12.2 Latent Syphilis

Latent syphilis is characterized by asymptomatic presentation, with evidence of syphilis identified by serologic testing.[1] Early latent syphilis occurs within the initial 12 months of the infection; infections with a longer (>12 months) or unknown duration are referred to as late latent syphilis or syphilis of unknown duration, respectively.[1]

Treatment of latent syphilis is aimed at preventing sequelae associated with long-term infection due to the inability to spread via sexual contact; however, the infection can still be spread vertically to a neonate from an infected mother, which can result in congenital syphilis (*refer to Section 4.12.6*).[1]

Quantitative nontreponemal serologic titers should be performed at 6, 12, and 24 months after treatment and evaluated against the titer taken during the treatment period.[1] Individuals living with HIV should have more frequent serologic and clinical follow-up at 6, 12, 18, and 24 months after treatment. Repeating treatment with benzathine penicillin G at weekly intervals for a longer duration of 3 weeks should be based on the likelihood of reinfection and/or treatment failure.[1]

[‡] The alternative regimen of ceftriaxone is based on limited clinical evidence, including pharmacologic and biologic data; therefore, the ideal dose and duration have not been established.

4.12.2.1 Latent Syphilis in Adults

Recommended treatment regimen for *early* latent syphilis in adults, including pregnant patients and those living with HIV, is as follows[1]:

- Benzathine penicillin G 2.4 million units IM (as a one-time dose)

Recommended treatment regimen for *late* latent syphilis or syphilis of an unknown duration in adults, including pregnant patients and those living with HIV, is as follows[1]:

- Benzathine penicillin G 7.2 million units total, divided into 3 doses (2.4 million units IM each) administered once a week

Patients with an allergy to penicillin who may not follow-up or be adherent should be desensitized and treated with the recommended regimen.[1]

Non-pregnant individuals with a penicillin allergy diagnosed with latent syphilis are likely to respond to the same **alternative** antibiotics suggested for primary and secondary syphilis (*refer to Section 4.12.1.1*).[1] Notably, only doxycycline and tetracycline (at the recommended doses for primary and secondary syphilis) are recommended for syphilis infections that have been present for >12 months (ie, late latent syphilis) or an unknown duration, with both agents used for 28 days. It is recommended that these alternative regimens be combined with frequent follow-up, particularly in individuals living with HIV, due to the limited efficacy evidence available within this patient population.[1]

4.12.2.2 Latent Syphilis in Infants and Children

A pediatric infectious disease specialist should oversee the treatment of infants (aged ≥30 days) and children with latent syphilis.[1] Infants and children diagnosed with latent syphilis should be evaluated, including a CSF examination. In addition, an investigation to determine the acquisition of the infection (ie, congenital or acquired from sexual abuse) should be conducted and the respective infection should be appropriately treated. The recommended regimen below is indicated for non-penicillin allergic infants and children with acquired syphilis, and no abnormal neurologic findings based on the CSF examination.[1]

Recommended treatment regimen for infants (aged ≥1 month) and children is as follows[1]:

- Benzathine penicillin G 50,000 units/kg IM (as a one-time dose)
    - Dose not to exceed 2.4 million units (adult dose)

4.12.3 Tertiary Syphilis in Adults

Prior to treatment initiation, individuals should undergo a CSF examination, regardless of neurologic symptoms.[1] The recommended regimen should only be used in adults without an allergy to penicillin and no indication of neurosyphilis, including upon CSF examination. A neurosyphilis treatment regimen should be used for individuals with abnormal CSF results. While individuals with cardiovascular complications due to syphilis (ie, cardiovascular syphilis) should be managed in collaboration with an infection disease specialist, some clinicians treat these individuals with a pharmacologic regimen designed for neurosyphilis. Individuals with a penicillin allergy should be managed in collaboration with an infectious disease expert.[1]

Recommended treatment regimen for adults, including pregnant patients and those living with HIV, is as follows[1]:

- Benzathine penicillin G 7.2 million units total, divided into 3 doses (2.4 million units IM each) administered once a week

4.12.4 Neurosyphilis, Ocular Syphilis, and Otosyphilis in Adults

The potential for the infection to spread to the CNS (neurosyphilis), auditory system (otosyphilis), or visual system (ocular syphilis) can manifest during any stage.[1] However, otosyphilis and ocular syphilis tend to be diagnosed during the early stages of syphilis (eg, primary, secondary). Manifestations of ocular syphilis and otosyphilis may occur independently or as a result of neurosyphilis.[1]

An early sign of neuro-involvement that may develop within a couple of months to years after the initial inoculation is syphilitic meningitis (eg, stroke, cranial nerve dysfunction, abnormal mental status). Other neurologic symptoms, such as general paresis and tabes dorsalis may manifest later during the course of the disease (10 to >30 years). Ocular syphilis is typically associated with extensive inflammation of the uvea (panuveitis), but can involve other components of the eye resulting in optic neuropathy, conjunctivitis, retinal vasculitis, posterior interstitial keratitis, and other eye-related conditions. Ultimately, ocular syphilis can result in loss of sight. Symptoms associated with otosyphilis include vertigo, tinnitus, and sensorineural hearing loss. Hearing loss can occur in one or both ears, worsen suddenly, and have an unexpected onset; thus, hearing loss has the potential to be permanent. Regardless of neurological findings, the treatment regimen is the same for neurosyphilis, ocular syphilis and otosyphilis.[1]

Recommended treatment regimen for adults, including pregnant patients and those living with HIV, is as follows[1]:

- Aqueous crystalline penicillin G 18–24 million units daily, administered as a continuous infusion or 3–4 million units IV every 4 hours, for 10–14 days

Alternative treatment regimen for adults, including pregnant patients and those living with HIV, is as follows[1]:

- Procaine penicillin G 2.4 million units IM once a day for 10–14 days AND
- Probenecid 500 mg by mouth 4 times a day for 10–14 days

Based on limited evidence, the following **alternative** regimen may be used for non-pregnant patients with neurosyphilis who have a penicillin allergy[1]:

- Ceftriaxone 1–2 grams IM or IV once a day for 10–14 days
    - Small observational studies indicate that this regimen may be potentially effective among individuals living with HIV

The recommended alternative regimen may be considered for individuals likely to comply with therapy.[1] The 14-day treatment duration for neurosyphilis is shorter than the 21-day treatment duration for late latent syphilis. Thus, treatment for late latent syphilis can be considered upon completion of the neurosyphilis regimen to provide a similar total duration of treatment (ie, 21 days). As adjunctive

treatment for ocular syphilis and otosyphilis, systemic steroids are often used; however, these agents have not demonstrated a therapeutic benefit.[1]

Upon completing neurosyphilis treatment, additional CSF examinations are not recommended for non-infected HIV individuals, or HIV-positive individuals on antiretroviral therapy (ART) that have shown a response to treatment (ie, clinically and serologically).[1]

4.12.5 Syphilis During Pregnancy

Regardless of the stage of syphilis, pregnant patients should be treated with parenteral penicillin G.[1] The treatment regimen, including dose and frequency, should be based on the stage of the infection (*refer to the previous sections for the appropriate recommended regimen, according to the stage of infection*). For patients unlikely to receive prenatal care, treatment should be provided based on a positive serologic test when determining pregnancy status. To prevent congenital syphilis, an additional IM dose of benzathine penicillin G 2.4 million units can be considered one week after the initial single-dose administration in pregnant women with primary, secondary, or early latent syphilis. In situations where a documented penicillin allergy exists, the pregnant patient should be desensitized and treated with penicillin. Although the Jarisch-Herxheimer reaction can cause fetal distress and induce premature labor, it should not be a reason to delay or avoid treatment.[1]

In pregnant women, reinfection or treatment failure is suspected when a four-fold sustained increase in nontreponemal titer occurs for >2 weeks after treatment.[1] Due to rapid titer elevations directly after treatment, a follow-up titer should not be performed until 8 weeks after treatment, unless symptoms persist. Treatment failure should be suspected when (1) the maternal antibody labor titer has increased four-fold compared to the initial titer prior to treatment, (2) labor ensues within 30 days of treatment, or (3) signs of infection are observed at the time of labor.[1]

4.12.6 Congenital Syphilis

In the US, cases of congenital syphilis have increased since 2012, with 1,870 cases reported during 2019 (a 477% increase compared to 2012).[1] The prevention and identification of congenital syphilis relies heavily on the appropriate management of pregnant patients and, consequently, on the ability to obtain routine serologic testing throughout pregnancy.[1]

4.12.6.1 Neonatal Congenital Syphilis

Various treatment regimens are recommended based on the likelihood of congenital syphilis in neonates. Desensitization should occur in neonates suspected of having congenital syphilis who have a penicillin allergy (or other secondary reaction due to penicillin).[1] If penicillin products are unavailable or a premature neonate is unable to tolerate IM injections and has no clinical indication of congenital syphilis (*possible or less likely congenital syphilis*), IV ceftriaxone can be considered, but it should be used in consultation with an infectious disease expert due to the limited evidence in favor of the agent for treating congenital syphilis, and used cautiously in neonates with jaundice. A dose of 50−75 mg/kg IV every 24 hours may be used, but the dose should be adjusted in premature neonates. A treatment duration for ceftriaxone is not specified, but in infants (aged ≥30 days) and children, the treatment duration is 10–14 days.[1]

Follow-up serologic testing and evaluations should occur every 2–3 months for neonates with a positive nontreponemal serologic test, until a negative result is obtained.[1] For neonates that were not treated (ie, congenital syphilis was less plausible or unlikely), it is expected that nontreponemal antibody titers will decline by 3 months of age, and be negative by 6 months of age. Treatment should be initiated at 6 months of age if the nontreponemal test remains positive. Treated neonates that continue to have positive nontreponemal serologic titers at 6–12 months of age should have a CSF examination, and may require retreatment with a 10-day regimen.[1]

4.12.6.1.1 Congenital Syphilis – Highly Probable or Confirmed

Recommended treatment regimens for neonates (infants <30 days old) with highly probable or confirmed congenital syphilis are as follows[1]:

- Aqueous crystalline penicillin G 100,000–150,000 units/kg per day, administered as 50,000 units/kg IV every 12 hours for the first 7 days, then every 8 hours for the next 3 days (total treatment duration: 10 days) OR
- Procaine penicillin G 50,000 units/kg IM once a day for 10 days

The procaine penicillin G regimen should be used when aqueous crystalline penicillin G is unavailable due to a shortage.[1]

4.12.6.1.2 Congenital Syphilis – Possible

Recommended treatment regimens for neonates (infants <30 days old) with possible congenital syphilis are as follows[1]:

- Aqueous crystalline penicillin G 100,000–150,000 units/kg per day, administered as 50,000 units/kg IV every 12 hours for the first 7 days, then every 8 hours for the next 3 days (total treatment duration: 10 days) OR
- Procaine penicillin G 50,000 units/kg IM once a day for 10 days OR
- Benzathine penicillin G 50,000 units/kg IM (as a one-time dose)[§]

The 1-day regimen can be considered for incubating syphilis without an evaluation in neonates who have a negative nontreponemal test and the maternal risk of untreated syphilis is low, based on the physician's clinical judgment.[1] Due to the increased risk of acquiring congenital syphilis, a 10-day regimen is recommended for neonates who have been exposed to an untreated early syphilis maternal infection, even when the neonate presents without any signs of congenital syphilis (ie, nonreactive nontreponemal test, regular evaluation) and the patient is likely to follow-up.[1]

If an aqueous crystalline penicillin G shortage occurs, the procaine penicillin G or benzathine penicillin G regimens should be used.[1] In situations where the 1-day regimen with benzathine penicillin G would be inappropriate, procaine penicillin G is preferred.[1]

[§] The 1-day course is not recommended for neonates who have an abnormal or missing evaluation (ie, long bone radiographs, CSF examination, complete blood count and platelets), when CSF results are unable to be interpreted due to contamination, or for whom follow-up cannot be guaranteed

4.12.6.1.3 Congenital Syphilis – Less Likely

Recommended treatment regimen for neonates (infants <30 days old) with less likely congenital syphilis is as follows[1]:

- Benzathine penicillin G 50,000 units/kg IM (as a one-time dose)

For infants where the maternal nontreponemal titer is reduced by at least four-fold after treatment for early syphilis or consistently maintained a low titer for latent syphilis, treatment may not be provided, given that frequent serologic testing will be performed every 2–3 months for a total of 6 months.[1]

4.12.6.1.4 Congenital Syphilis – Unlikely

Treatment for congenital syphilis is generally not recommended if it is unlikely to be present.[1] However, a one-time IM administration of benzathine penicillin G 50,000 units/kg may be considered, especially for neonates with a positive nontreponemal titer, and for whom follow-up is uncertain.[1]

4.12.6.2 Congenital Syphilis in Infants and Children

Recommended treatment regimen for infants (aged ≥30 days) and children with congenital syphilis is as follows[1]:

- Aqueous crystalline penicillin G 200,00–300,000 units/kg per day, administered as 50,000 units/kg every 4–6 hours for 10 days

Infants or children with a penicillin allergy (or other reaction secondary to penicillin) should be desensitized and treated with the recommended regimen.[1]

Weekly injections of benzathine penicillin G 50,000 units/kg IM for <3 weeks can be considered for infants and children with no abnormalities present upon examination, including CSF findings, and no symptoms of congenital syphilis.[1] Upon completion of the 10-day recommended regimen, a one-time dose of benzathine penicillin G 50,000 units/kg IM (maximum dose: 2.4 million units) can be considered to provide a similar treatment duration among individuals with no abnormal findings and no symptoms. For children who have other treponemal infections, these regimens should suffice.[1]

Follow-up serologic testing and clinical evaluations should occur every 3 months until a four-fold reduction is observed in the titer or the serologic test is negative.[1] Retreatment with a 10-day regimen of parenteral penicillin G should be considered for infants and children with titers that have a sustained increase for >2 weeks, or titers that fail to reduce by four-fold after 12–18 months. For patients with abnormal CSF results that persist beyond 18 months and are not attributed to other causes, retreatment for neurosyphilis should be initiated and managed in collaboration with an infectious disease expert.[1]

If aqueous crystalline penicillin G is unavailable due to a shortage, similar agents used in neonates should be used to treat congenital syphilis in infants and children.[1] As a first-line option, IM procaine penicillin G 50,000 units/kg (maximum dose: 2.4 million units) daily for 10 days should be used, even among those without any evidence of infection. As an alternative for patients without infection manifestations, benzathine penicillin G 50,000 units/kg IM (maximum dose: 2.4 million units) as a one-time dose may be used. Ceftriaxone can be considered if procaine penicillin G is unavailable, but it should be used in consultation with an infectious disease expert due to the limited evidence in favor of

the agent to treat congenital syphilis. Generally, 75 mg/kg (infants) or 100 mg/kg (children) IV or IM daily for 10–14 days can be considered, but the dose may need to be adjusted based on actual body weight. Procaine penicillin G is preferred for infants or children who have an abnormal or missing evaluation, CSF results are unable to be interpreted due to contamination, or for whom follow-up cannot be guaranteed.[1]

5.0 VIRAL SEXUALLY TRANSMITTED INFECTIONS

5.1 Vaccines for Viral Sexually Transmitted Infections

The acquisition of some viral STIs (ie, hepatitis A and B, human papillomavirus) can be prevented with vaccinations.[1] **Table 3** summarizes the vaccine-preventable viral STIs and the recommended population who should be offered the vaccine, according to the Advisory Committee on Immunization Practices (ACIP).[2-4]

For hepatitis A virus (HAV), vaccination is an effective preventable method (100% protective antibody levels after the second dose) for minimizing the transmission to at-risk individuals who were unvaccinated from infancy.[1] Only the monovalent vaccines (ie, Havrix, Vaqta) should be administered in infants at least 1 year of age.[1] Doses administered at <1 year of age are not valid since a suboptimal immune response may occur.[29] A combination hepatitis A and hepatitis B vaccine (Twinrix), administered as a 3-dose series, is available for adults ≥18 years of age who are at risk of acquiring HAV or hepatitis B virus (HBV).[1] When administered at the recommended schedule, Twinrix achieves comparable immunogenicity to the monovalent vaccines.[1]

Like the HAV vaccines, the HBV vaccines are recommended routinely for infants, unvaccinated pediatrics, and unvaccinated adults at increased risk of acquisition.[1] There are three single-antigen hepatitis B vaccines available in the US: Recombivax HB, Engerix-B, and Heplisav-B.[1] The first three-antigen vaccine (PreHevbrio) for HBV was approved by the FDA in November 2021,[30] but the 2021 STI guideline[1] predates the approval of this new vaccine; thus the guideline does not comment on its use. However, ACIP (2022) recommends this vaccine for adults ≥18 years of age.[4] In addition to PreHevbrio, Heplisav-B is also indicated for adults ≥18 years of age; therefore, only Recombivax HB and Engerix-B should be administered in pediatrics.[31] Additionally, due to insufficient evidence on pregnancy-related risks for Heplisav-B and PreHevbrio, pregnant women that require the vaccine should be administered Recombivax, Engerix-B, or Twinrix.[4] In general, when selecting a vaccine, the provider should consider the dosing schedule that will ensure completion of the series[1]; the dosing schedule varies by the age of the receiver, whether the recipient has a compromised immune system, and product. All of the vaccines are recommended to be routinely administered as a 3-dose series, except Heplisav-B, which is administered as a 2-dose series.[1] A 4-dose regimen of Engerix-B is recommended for adults (≥20 years of age) on hemodialysis or other immunocompromised individuals.[4]

Gardasil 9 is the only human papillomavirus (HPV) vaccine available in the US.[1,32] Gardasil 9 is a 9-valent vaccine that targets the same HPV types of the predecessor vaccine (Gardasil), in addition to types 31, 33, 45, 52 and 58.[1] Routine HPV vaccination is recommended for all adolescents 11–12 years of age, with the youngest possible age of administration being 9 years.[2] A 2-dose series may be used in healthy adolescents who receive the vaccine prior to turning 15 years of age, whereas the 3-dose schedule is recommended for immunocompromised individuals and those 15–45 years of age. The vaccine may be

routinely administered to individuals up to 26 years of age. Adults between 27–45 years of age should have a collaborative discussion with their clinician prior to receiving the vaccine.[2] The HPV vaccine is not recommended to be administered during pregnancy.[1,2] Gardasil 9 may be administered in people with atypical Pap smear results or HPV screening, previous documentation of anogenital warts, or anogenital precancer.[1] The vaccine cannot treat anogenital warts or existing HPV infections; therefore, it is used as a preventative method in unexposed individuals.[1]

Table 3. Vaccine-Preventable Viral STIs and Recommended Vaccinations per ACIP Guidelines[2-4]

Vaccine (Brand Name)	Recommended Dosing	Schedule[a]		Indicated Population[b]
Hepatitis A [2020 ACIP Guideline][3]				
Inactivated Hep A monovalent vaccine (**Havrix**)	• 0.5 mL IM (1–18 yrs of age) • 1 mL IM (≥19 yrs of age)	• Children/Adolescents (aged 1–18 yrs) • Adults (aged ≥19 yrs)	1st dose: 0 month 2nd dose: 6–12 months	• All infants 12–23 months of age • Unvaccinated pediatrics 2–18 years of age • MSM • Injection drug users • Individuals with illegal drug use • Individuals with chronic liver disease • Homeless individuals • Individuals with an exposure risk due to their occupation • Individuals that travel internationally • HIV-positive individuals or individuals with hepatitis C • Pregnant women at an increased risk or request the vaccine
Inactive Hep A monovalent vaccine (**Vaqta**)	• 0.5 mL IM (1–18 yrs of age) • 1 mL IM (≥19 yrs of age)	• Children/Adolescents (aged 1–18 yrs) • Adults (aged ≥19 yrs)	1st dose: 0 month 2nd dose: 6–18 months	
Combination Hep A and Hep B vaccine (**Twinrix**)[c]	1 mL IM (≥18 yrs of age)	Adults (aged ≥18 yrs)	**Standard:** 1st dose: 0 month 2nd dose: 1 month 3rd dose: 6 months **Accelerated:** 1st dose: 0 day 2nd dose: 7 days 3rd dose: 21–30 days 4th dose: 12 months	

Table 3. Vaccine-Preventable Viral STIs and Recommended Vaccinations per ACIP Guidelines[2-4]

Vaccine (Brand Name)	Recommended Dosing	Schedule[a]		Indicated Population[b]
Hepatitis B [2022 ACIP Guideline][4]				
Recombinant Hep B single-antigen vaccine (**Recombivax HB**)[33]	• 0.5 mL IM (birth–19 yrs of age) • 1 mL IM (≥20 yrs of age)	• Infants (aged <1 yr) • Children (aged 1–10 yrs) • Adolescents (aged 11–19 yrs)[d] • Adults (aged ≥20 yrs) • Individuals on hemodialysis or other immunocompromised individuals, irrespective of age	1st dose: 0 month 2nd dose: 1 month 3rd dose: 6 months	• All infants • Unvaccinated pediatrics <19 years of age • Unvaccinated adults (19–59 years of age) • Unvaccinated adults ≥60 years of age with or without risk factors • Unvaccinated, uninfected sexually active individuals with ≥1 sex partner • Individuals who are being evaluated or treated for an STI • MSM • Injection drug users • Individuals with chronic liver disease • Dialysis patients • Individuals with an exposure risk due to their occupation (eg, HCP) • Individuals that travel internationally • HIV-positive individuals or individuals with hepatitis C
Recombinant Hep B single-antigen vaccine (**Engerix-B**)[34]	• 0.5 mL IM (birth–19 yrs of age) • 1 mL IM (aged ≥20 yrs) • 2 mL IM (adults on hemodialysis)	• Infants (aged <1 yr of age) • Children (aged 1–10 yrs of age) • Adolescents (aged 11–19 yrs) • Adults (aged ≥20 yrs)	1st dose: 0 month 2nd dose: 1 month 3rd dose: 6 months	
		Adults (aged ≥20 yrs) on hemodialysis or other immunocompromised individuals	1st dose: 0 month 2nd dose: 1 month 3rd dose: 2 months 4th dose: 6 months	
Recombinant Hep B single-antigen vaccine (**Heplisav-B**)	1 mL IM[e] (aged ≥18 yrs)	Adults (aged ≥18 yrs)	1st dose: 0 month 2nd dose: 1 month	
Recombinant Hep B three-antigen vaccine (**PreHevbrio**)[f]	1 mL IM (aged ≥18 yrs)	Adults (aged ≥18 yrs)	1st dose: 0 month 2nd dose: 1 month 3rd dose: 6 months	
Human Papillomavirus [2019 ACIP Guideline][2]				
Recombinant HPV 9-valent vaccine (**Gardasil 9**)	0.5 ML IM (9–45 years of age)	Children and adolescents (aged 9–14 yrs, not immunocompromised)	**2-dose Regimen:** 1st dose: 0 month 2nd dose: 6–12 months	• Unvaccinated children and adults (males and females) aged 9–26 yrs

Table 3. Vaccine-Preventable Viral STIs and Recommended Vaccinations per ACIP Guidelines[2-4]

Vaccine (Brand Name)	Recommended Dosing	Schedule[a]		Indicated Population[b]
		• Adolescent and young adults (aged 15–26 yrs) • Immunocompromised individuals • Adults (aged 27–45 yrs)	**3-dose Regimen:** 1st dose: 0 month 2nd dose: 2 months 3rd dose: 6 months	• Individuals that have not completed the entire series up to 26 yrs of age • Not routinely recommended in adults aged >26 yrs, but a shared decision approach can be used for adults 27–45 yrs of age

Abbreviations: ACIP, Advisory Committee on Immunization Practices; HCP, health care personnel; HIV, human immunodeficiency virus; IM, intramuscular; MSM, men who have sex with men; STI, sexually transmitted infection; yrs, years

[a] For the most up-to-date immunization schedules for pediatrics and adults, please refer to the CDC website available at: https://www.cdc.gov/vaccines/schedules/index.html

[b] May not be a comprehensive list for all vaccines (ie, hepatitis A and B vaccines); please refer to the most recent ACIP guidelines for at-risk populations who should be offered the vaccine

[c] Twinrix is not recommended to be used for postexposure prophylaxis

[d] Adolescents aged 11—15 years may receive the 3-dose series with 0.5 mL at the listed schedule (pediatric strength) or a 2-dose series of 1 mL at 0- and 4—6 months (adult strength)

[e] Since the vaccine is supplied as a single-dose 0.5 mL prefilled syringe, 2 syringes (0.5 mL each) should be administered to equal the recommended 1 mL dose

[f] PreHevbrio was approved by the US Food and Drug Administration (FDA) in November 2021; thus, FDA-approval predated the updated CDC 2021 STI Guideline, published in July.[1] However, it is recommended by ACIP in the 2022 hepatitis B guideline.[4]

5.2 Treatment of Sexually Transmitted Viral-Related Sequelae

The treatment of most viral STIs (ie, HBV, HCV, HIV) were considered outside the scope of the 2021 CDC STI guideline[1]; therefore, readers should refer to the appropriate clinical practice guideline for evidence-based treatment recommendations. **Appendix B** includes additional information on the disease states of viral hepatitis (ie, HAV, HBV, HCV) and HIV, links to other guidelines with treatment recommendations of these infections, and CDC guideline-recommended postexposure prophylaxis, if applicable.

The following sections address the 2021 CDC guideline recommended treatment regimens for viral STI-related sequelae (ie, genital warts, genital herpes). **Table 4** provides a general overview of the recommended treatment regimens and the intended population. For additional information, please refer to the specific STI section.

Table 4. CDC 2021 Guideline-Recommended Treatment Regimens for Viral STI-Related Sequelae[a] [1,13]

Viral STI – Sequelae	Recommended Treatment Regimen and Dosing	Indicated Population	
HPV—Genital Warts	*Applied by the patient:*	Individuals with external anogenital warts	
	Imiquimod 3.75% cream[b] applied nightly at bedtime for <8 weeks or 5% cream[b] applied at bedtime 3 times a week for <16 weeks **OR** Podofilox 0.5% solution or gel applied twice a day for 3 days, followed by 4 days of no treatment[c] **OR** Sinecatechins 15% ointment[b] applied three times a day until the warts have completely resolved, but use should not exceed >16 weeks		
	Administered by the provider in a health care setting:		• Individuals with vaginal[d], cervical[e, f], or intra-anal warts[d, e] • Pregnant women • For individuals with urethral meatus warts, only cryotherapy with liquid nitrogen or surgical removal is recommended
	Cryotherapy with liquid nitrogen or cryoprobe **OR** Surgical removal (ie, laser, electrosurgery, tangential scissor excision, curettage, or tangential shave excision) **OR** Bichloroacetic acid or trichloroacetic acid 80–90% solution, repeated weekly as needed		
HSV—Genital Herpes	*Presumptive treatment is warranted for all individuals suspected of having an initial episode of genital herpes*		
	Acyclovir 400 mg PO three times a day for 7–10 days[g] **OR** Famciclovir 250 mg PO three times a day for 7–10 days[g] **OR** Valacyclovir 1 g PO twice a day for 7–10 days[g]	Individuals, including those who have HIV with an initial episode of genital herpes	
	Acyclovir 400 mg PO twice a day **OR** Valacyclovir 500 mg PO once a day[h] **OR**	Suppressive treatment for individuals with recurrent HSV-2 genital herpes	

Abbreviations: CDC, Centers for Disease Control and Prevention; g, gram; HPV, human papillomavirus; HSV, herpes simplex virus; mg, milligram; PO, orally; STI, sexually transmitted infections

Table 4. CDC 2021 Guideline-Recommended Treatment Regimens for Viral STI-Related Sequelae[a] [1,13]

Viral STI – Sequelae	Recommended Treatment Regimen and Dosing	Indicated Population
	Valacyclovir 1 g PO once a day **OR** Famciclovir 250 mg PO twice a day	
	Acyclovir 400–800 mg PO two-to-three times a day **OR** Famciclovir 500 mg PO twice a day **OR** Valacyclovir 500 mg PO twice a day	Suppressive treatment for individuals living with HIV who have recurrent genital herpes[i]
	Acyclovir 400 mg PO three times a day **OR** Valacyclovir 500 mg PO twice a day	Suppressive treatment for pregnant women with recurrent genital herpes[i, j]
	Acyclovir 800 mg PO twice a day for 5 days **OR** Acyclovir 800 mg PO three times a day for 2 days **OR** Famciclovir 1 g PO twice a day for 1 day **OR** Famciclovir 125 mg PO twice a day for 5 days	Episodic treatment for individuals with recurrent HSV-2 genital herpes
	OR Famciclovir 500 mg PO (as a one-time dose) **THEN** Famciclovir 250 mg PO twice a day for 2 days	
	OR Valacyclovir 500 mg PO twice a day for 3 days **OR** Valacyclovir 1 g PO once a day for 5 days	
	Acyclovir 400 mg PO three times a day for 5–10 days **OR**	Episodic treatment for individuals living with HIV who have recurrent genital herpes[i]

Abbreviations: CDC, Centers for Disease Control and Prevention; g, gram; HPV, human papillomavirus; HSV, herpes simplex virus; mg, milligram; PO, orally; STI, sexually transmitted infections

Table 4. CDC 2021 Guideline-Recommended Treatment Regimens for Viral STI-Related Sequelae[a] [1,13]

Viral STI – Sequelae	Recommended Treatment Regimen and Dosing	Indicated Population
	Famciclovir 500 mg PO twice a day for 5–10 days **OR** Valacyclovir 1 g PO twice a day for 5–10 days	

[a] ***When more than one regimen is provided, they are listed alphabetically for agents that have a similar efficacy and tolerability profile; whereas a non-alphabetical order indicates the preference of the regimens based on agent-specific efficacy and tolerability differences.***

[b] *Has the potential to weaken vaginal diaphragms and condoms; therefore, these methods may be less effective at preventing pregnancy with concurrent use*

[c] *This regimen may be repeated up to 4 times, as needed*

[d] *Due to the risk of perforation and fistula development, a cryoprobe is not recommended to be used in the vagina and presumably in the anal canal*

[e] *A specialist should be consulted for appropriate management*

[f] *Prior to starting treatment, women with exophytic cervical warts should have a biopsy performed to rule out high-grade squamous intraepithelial lesions*

[g] *If the lesions are not completely healed by the end of the 10-day course, the duration may be extended*

[h] *For individuals that have frequent recurrent episodes (≥10 episodes annually), the lower dose of valacyclovir (500 mg) may not be as effective as the higher strength (1 gram) regimen or the regimen with acyclovir*

[i] *It appears that the regimens may be used for either HSV-1 or HSV-2 recurrent genital herpes. These regimens most likely apply to HSV-2 since recurrent episodes are uncommon with HSV-1.*

[j] *Daily suppressive treatment for recurrent genital herpes in pregnant individuals should start at 36 weeks' gestation*

Abbreviations: CDC, Centers for Disease Control and Prevention; g, gram; HPV, human papillomavirus; HSV, herpes simplex virus; mg, milligram; PO, orally; STI, sexually transmitted infections

5.2.1 Human Papillomavirus Infections

HPV can be transmitted via sexual contact, including anal or vaginal intercourse, and non-penetrative sexual activities (eg, oral sex).[1] Although unlikely, HPV can also be transmitted from an infected mother to her infant during labor.[1]

Of the 150 different types of identified HPV, ≥40 are considered to be localized to the genital region.[1] Most HPV infections are self-limited, with the majority of individuals presenting with no symptoms. Certain types of HPV are known to be oncogenic (eg, HPV types 18 and 16), resulting in various types of anogenital cancers (eg, penile, cervical, vaginal, anal, vulvar), as well as oropharyngeal cancer. In contrast, other types (eg, HPV types 11 and 6) are known to cause recurrent respiratory papillomatosis (rarely) and genital warts. Prior to the availability of vaccines, an estimated 355,000 new cases of genital warts were reported annually.[1]

5.2.1.1 Treatment

Since there is no treatment for the virus itself, the CDC STI guideline focused on providing recommendations for conditions that may emerge as a result of the HPV infection (eg, genital warts, precancerous lesions).[1] Targeted ART is not recommended for HPV since subclinical genital infections usually spontaneously resolve.[1]

The following section discusses the CDC STI guideline recommendations for treating anogenital warts as a result of an HPV infection.

5.2.1.1.1 Anogenital Warts

The development of anogenital warts may occur months or years after the initial inoculation with HPV; therefore, individuals may have HPV with no visible signs of infection.[1] Individuals with anogenital warts are typically asymptomatic, but the warts can cause discomfort (eg, itchiness, pain) depending on the location and size. Warts may have a varied appearance of being flat, raised, or pedunculated growths. While warts have the potential to occur at any site of anogenital epithelium, including within the anogenital tract, warts are commonly located on the shaft of the penis, surrounding the vaginal introitus, or under the penile foreskin (among uncircumcised individuals). In the US, the occurrence of anogenital warts has decreased among young women, adolescents, and heterosexual men due to the routine vaccination against HPV, including types 6 and 11, which are attributed to more than 90% of non-oncogenic anogenital wart cases.[1]

Although anogenital warts may spontaneously resolve, even without treatment, it is possible that the quantity or size of the warts may worsen.[1] Available treatments eradicate the appearance of warts but most likely do not eliminate HPV infectivity. Thus, the recurrence of anogenital warts is common upon completing treatment, especially within the first 3 months and for individuals living with HIV. It is unclear whether the reduction in viral DNA achieved with treatment translates to a decline in future transmission.[1]

The 2021 CDC STI guideline provides a variety of preferred options for the treatment of anogenital warts, either applied by the patient or administered by the clinician.[1] No recommended option is

preferred over another, and a single treatment regimen may not be suitable for all patients. Therefore, an individualized shared decision approach should be implemented to determine the best treatment for the patient. Despite limited evidence about the risk and benefits of combining treatment options, some clinicians may use a combination of treatments (eg, cryotherapy during clinic visits with a topical agent applied by the patient between visits).[1]

Recommended treatment regimens for *external anogenital warts* among all individuals, including those living with HIV, are as follows[1]:

Applied by the patient:

- Imiquimod 3.75% or 5% cream OR
- Podofilox 0.5% solution or gel OR
- Sinecatechins 15% ointment

Administered by the provider in a health care setting:

- Cryotherapy with liquid nitrogen or cryoprobe OR
- Surgical removal (ie, laser, electrosurgery, tangential scissor excision, curettage, or tangential shave excision) OR
- Trichloroacetic acid or bichloroacetic acid 80–90% solution

Imiquimod should be applied at bedtime, either 3 times a week for <16 weeks with the 5% cream, or nightly for <8 weeks with the 3.75% cream.[1] After applying the cream (6–10 hours), the treatment area should be thoroughly cleaned, regardless of the product strength. Local inflammatory reactions may occur during use (eg, irritation, redness, vesicles). Notably, imiquimod cream and sinecatechins ointment may weaken vaginal diaphragms and condoms; therefore these methods may be less effective at preventing pregnancy with concomitant use.[1]

Regardless of formulation, podofilox should be applied (either by using a finger or cotton swab) to the treatment area (< 10 cm^2) twice a day for 3 days (total daily volume should not exceed 0.5 mL), followed by 4 days of no treatment.[1] This regimen may be repeated up to four times, as needed. The clinician is advised to apply the initial dose to show the appropriate technique. The solution or gel should be allowed to dry completely after each application. Patients may experience irritation or minor pain localized to the treated area after applying the medication. Before and after handling the product, patients are advised to wash their hands.[1]

Sinecatechins 15% ointment should be applied as a thin layer using a finger (0.5 cm layer per wart) three times a day until the warts have completely resolved or up to a maximum of 16 weeks.[1] It is recommended to avoid oral, anal, and genital sexual contact while the ointment is applied. Due to undetermined efficacy and safety, sinecatechins should not be used among people who are immunocompromised. Common adverse events include ulceration, redness, burning or itching, edema, induration, pain, and vesicular rash.[1]

While the 2021 CDC STI guideline mentions topical cidofovir, intralesional interferon, and photodynamic therapy as other regimens that may be considered, only the use of podophyllin resin is discussed in detail.[1] The decision to use a non-recommended agent should be made collaboratively between the patient and provider due to the limited supportive evidence and the tendency to cause more AEs

compared to recommended agents. Podophyllin resin 10−25% should be applied by a provider within a health care setting due to the strict application methods used to ensure patient safety. To avoid excessive application and potential systemic toxicity, the amount of podophyllin resin should be restricted to <0.5 mL or applied to an area <10 cm^2 for each application, should not be applied to an area of damaged skin, allowed to dry completely after application, and the treatment area should be washed 1–4 hours after the resin is applied.[1]

A trained physician should execute the treatment of internal warts; therefore, all recommended treatments are performed within a health care setting and are not for patient use.

Recommended treatment regimen for individuals with *urethral meatus warts* are as follows[1]:

- Cryotherapy with liquid nitrogen OR
- Surgical removal

Recommended treatment regimen for individuals with *vaginal, cervical, or intra-anal warts* are as follows[1]:

- Cryotherapy with liquid nitrogen OR
- Surgical removal OR
- Trichloroacetic acid or bichloroacetic acid 80–90% solution

Due to the risk of perforation and fistula development, a cryoprobe is not recommended to be used in the vagina,[1] and presumably in the anal canal; therefore, if cryotherapy is used, it should be performed using liquid nitrogen.[1] Prior to starting treatment, women with exophytic cervical warts should have a biopsy performed to rule out high-grade squamous intraepithelial lesions. A specialist should be consulted for the management of cervical and intra-anal warts.[1]

Usually, a treatment response is observed within 3 months of initiating therapy, but this can depend on adherence and whether the patient is immunosuppressed.[1] A different treatment modality may be used in patients that remain unresponsive after completing the recommended treatment course or experience serious AEs. When treatment is administered correctly, complications (eg, scars, fistulas, vulvodynia) are rarely an issue.[1]

5.2.1.1.1.1 Treatment of Anogenital Warts During Pregnancy

The patient-applied regimens (ie, podofilox, sinecatechins, imiquimod) are not recommended for use during pregnancy.[1] Even though imiquimod appears to be low risk during pregnancy, it is recommended to be avoided until additional evidence is available supporting its use. The treatment of anogenital warts can be considered during pregnancy, but the response may be inadequate (eg, incomplete resolution) until after labor. Cesarean delivery is only recommended for pregnant women with anogenital warts when excessive bleeding is expected with vaginal delivery or the pelvic outlet is blocked; it should not be used exclusively to prevent HPV transmission to the neonate. Rarely, respiratory papillomatosis may occur among infected infants and children, but the risk is low.[1]

5.2.1.1.2 Cervical Cancer

Long-term infections with oncogenic HPV types, particularly 16 and 18 are known to be attributed to roughly all cervical cancers, and a variety of penile, anal, vaginal, and oropharyngeal cancers.[1] Of the HPV-related cancers, only routine screening is recommended for cervical cancer. Please refer to the 2021 CDC STI guideline for US cervical cancer screening recommendations from the USPSTF, American Cancer Society, and American College of Obstetricians and Gynecologists.[1]

5.2.2 Genital Herpes

Genital herpes, a permanent, chronic infection, can be caused by either herpes simplex virus (HSV)-1 or HSV-2.[1] HSV is transmitted by exposed contact with mucosal tissue, herpetic lesions, or genital or oral secretions.[35] In addition, viral shedding of HSV can occur from natural-appearing genital or oral mucosa. Typically, HSV-2 is only spread from genital-genital contact with an infected individual. Yet, an HSV-1 genital infection can result from receiving oral sex from an individual infected with oral HSV-1.[35] HSV-1 anogenital infections tend to be increasing with a higher prevalence among young women and MSM.[1] In the US, approximately 47.8% and 11.9% of individuals between the age of 14–49 years are infected with HSV-1 or HSV-2, respectively.[1,36]

Most infections of genital herpes are transmitted by individuals that are asymptomatic or undiagnosed due to unrecognized or mild symptoms.[1] Asymptomatic transmission to susceptible sex partners due to viral shedding occurs commonly within the first year of inoculation with HSV-2.[1] Individuals should refrain from sexual activity while the infected person is symptomatic (ie, lesions are present), including prodromal symptoms (eg, genital pain, pruritus, paresthesias), which begin hours to days prior to the emergence of herpetic lesions.[1,35]

Systemic treatment with antiviral agents focuses on long-term management rather than acute episodes.[1] The goals of treatment are to prevent or treat symptomatic recurrent outbreaks, improve the patient's quality of life, and adequately suppress viral concentrations to prevent the spread to others, primarily during sexual contact. Treatment with topical antivirals is not recommended due to negligible benefits; however, treatment with 3 oral antivirals, acyclovir, valacyclovir, and famciclovir, has been shown to moderately manage the symptoms of genital herpes in the event of an initial or recurrent episode, or as suppressive treatment when used daily.[1] Treatment is categorized based on an initial outbreak (ie, initial episode) or recurrent outbreaks (ie, suppressive, episodic). Generally, for individuals with asymptomatic HSV-2 *without* recurrences, neither episodic nor suppressive treatment should be used, and the risk of preventing transmission with suppressive treatment is unclear within this patient population.[1] Notably, treatment does not eliminate latent virus nor does the effect persist beyond drug discontinuation. No evidence suggests using acyclovir, valacyclovir, or famciclovir as PrEP among unexposed individuals to prevent HSV acquisition.[1]

5.2.2.1 Treatment of an Initial Episode of Genital Herpes

It is recommended that all patients presenting with an initial episode of genital herpes receive presumptive treatment regardless of initial symptom severity because subsequent infections may result in more aggressive (eg, severe ulcerations, neurologic complications) and persistent symptoms.[1]

Recommended initial treatment regimens for individuals, including those living with HIV, are as follows[1]:

- Acyclovir 400 mg by mouth three times a day for 7–10 days OR
- Famciclovir 250 mg by mouth three times a day for 7–10 days OR
- Valacyclovir 1 gram by mouth twice a day for 7–10 days

The duration may be extended if the lesions are not completely healed by the end of the 10-day course.[1] Although the lower strength of acyclovir (200 mg) taken five times a day is effective for treating initial genital herpes episodes, it is not recommended due to the higher dosing frequency, which may negatively impact patient compliance.[1]

5.2.2.2 Suppressive Treatment for Recurrent Genital Herpes

Relative to HSV-2, recurrent episodes are unlikely to occur with HSV-1 genital herpes, and viral shedding rapidly diminishes within the first year of inoculation.[1] Thus, the decision to initiate daily suppressive therapy should be made collaboratively between the provider and patient, and reserved for individuals who have frequent recurrences (ie, ≥10 episodes per year). It is unknown whether suppressive treatment prevents HSV-1 transmission to sexual partners.[1]

Even though suppressive treatment is typically not indicated for genital herpes among asymptomatic individuals with HSV-2 and symptomatic HSV-1, it may be considered for individuals with significant psychosocial distress due to the diagnosis.[1]

Most individuals presenting with an initial symptomatic episode of genital herpes due to HSV-2 will develop a recurrent episode.[1] Oral acyclovir, valacyclovir, and famciclovir are recommended to be administered as daily suppressive treatment to decrease the recurrence rate and reduce the risk of transmission to sexual partners. Annually, clinicians should evaluate whether long-term suppressive therapy is required since the recurrence rate of HSV-2 genital herpes often decreases with time. However, suppressive treatment may not need to be discontinued; the development of HSV antiviral resistance and emergence of medication-related adverse events rarely occur.[1]

Recommended suppressive regimens for individuals with recurrent **HSV-2** genital herpes are as follows[1]:

- Acyclovir 400 mg by mouth twice a day OR
- Valacyclovir 500 mg by mouth once a day OR
- Valacyclovir 1 gram by mouth once a day OR
- Famciclovir 250 mg by mouth twice a day

For individuals that have frequent recurrent episodes, the lower dose of valacyclovir (500 mg) may not be as effective as the higher strength (1 gram) regimen or the regimen with acyclovir.[1] For suppressing viral shedding, famciclovir seems to be not as effective as valacyclovir.[1]

5.2.2.2.1 Suppressive Treatment for Recurrent Genital Herpes in Individuals with HIV

Suppressive treatment is also effective at decreasing HSV-related symptoms among individuals living with HIV.[1] This treatment decreases the risk of genital ulcer disease, often associated with ART initiation, especially within the first 6 months. However, daily suppressive antiviral treatment, including episodic

treatment (*refer to Section 5.2.2.3.1*) does not decrease the risk of sexual transmission of either HIV or HSV, slow HIV disease progression, or reduce HIV-related inflammation.[1]

Recommended suppressive treatment regimens for individuals living with HIV who have recurrent genital herpes[**] are as follows[1]:

- Acyclovir 400–800 mg by mouth two-to-three times a day OR
- Famciclovir 500 mg by mouth twice a day OR
- Valacyclovir 500 mg by mouth twice a day

5.2.2.2.2 Suppressive Treatment for Recurrent Genital Herpes During Pregnancy

The probability of neonatal HSV transmission depends on the maternal HSV status during the later stages of pregnancy and neonatal exposure to infected lesions and viral shedding during labor.[1] If maternal acquisition of genital herpes is close to the time of labor, the risk of transmission to the neonate is 30–50%; however, the risk of transmission is <1% when the maternal acquisition of genital herpes occurs during earlier stages of pregnancy or for women who have a history of prenatal recurrent herpes.[1]

The use of acyclovir during pregnancy is considered to be safe, regardless of the trimester.[1] It may also be used during breastfeeding. Although evidence is limited about prenatal exposure, animal studies suggest that valacyclovir and famciclovir pose a low risk for teratogenic effects from use during pregnancy. Therefore, presumably due to more robust evidence, oral acyclovir is preferred for pregnant women with an initial episode of genital herpes or recurrent herpes. Acyclovir should be administered IV for severe HSV. Suppressive treatment in pregnant women with recurrent genital herpes should be initiated at 36 week's gestation.[1]

Recommended suppressive regimens for pregnant patients with recurrent genital herpes[**] are as follows[1]:

- Acyclovir 400 mg by mouth three times a day OR
- Valacyclovir 500 mg by mouth twice a day

Neonates born with genital herpes should be evaluated immediately.[1] For newborns with suspected or confirmed genital herpes, acyclovir 20 mg/kg IV every 8 hours for 14 days should be administered. A 21-day duration should be used for disseminated HSV infections.[1]

5.2.2.3 Episodic Treatment for Recurrent Genital Herpes

Like suppressive treatment, episodic treatment may be used among individuals with recurrent genital herpes; however, in contrast to suppressive daily treatment, the antiviral is taken as needed to resolve emergent outbreaks during episodic treatment.[37] Episodic treatment should be started immediately at the onset of symptoms (ie, <1 day of lesion appearance or at the first indication of prodrome).[1] Episodic treatment decreases lesion healing time and the duration of viral shedding.[37] The antivirals listed below

[**] It appears that the regimens may be used for either HSV-1 or HSV-2 recurrent genital herpes. Suppressive/episodic treatment for recurrent genital herpes most likely applies to HSV-2 since recurrent episodes are uncommon with HSV-1.

were considered equally efficacious as episodic treatment for genital herpes by the 2021 CDC STI guideline creators.[1]

Recommended episodic treatment regimens for individuals with recurrent **HSV-2** genital herpes are as follows[1]:

- Acyclovir 800 mg by mouth twice a day for 5 days OR
- Acyclovir 800 mg by mouth three times a day for 2 days OR
- Famciclovir 1 gram by mouth twice a day for 1 day OR

- Famciclovir 500 mg by mouth (as a one-time dose) THEN
- Famciclovir 250 mg by mouth twice a day for 2 days

- Famciclovir 125 mg by mouth twice a day for 5 days OR
- Valacyclovir 500 mg by mouth twice a day for 3 days OR
- Valacyclovir 1 gram by mouth once a day for 5 days

Due to the higher dosing frequency, acyclovir 400 mg three times daily for 5 days is not recommended, even though it is effective as an episodic regimen for recurrent HSV-2 genital herpes.[1]

5.2.2.3.1 Episodic Treatment for Recurrent Genital Herpes in Individuals with HIV

Episodic treatment tends to be used for an extended duration among individuals living with HIV relative to the general population.

Recommended episodic treatment regimens for individuals living with HIV who have recurrent genital herpes** are as follows[1]:

- Acyclovir 400 mg by mouth three times a day for 5–10 days OR
- Famciclovir 500 mg by mouth twice a day for 5–10 days OR
- Valacyclovir 1 gram by mouth twice a day for 5–10 days

5.2.2.3.2 Episodic Treatment for Recurrent Genital Herpes During Pregnancy

The 2021 CDC STI guideline did not provide or mention any episodic treatment regimens for recurrent HSV genital herpes among pregnant individuals.[1] Please refer to **Section 5.2.2.2.2** for recommended suppressive regimens that may be used in pregnant women with recurrent genital herpes.

5.2.2.4 Severe HSV Disease

For HSV infections that have disseminated or manifested conditions that require hospitalization (hepatitis, pneumonitis) and/or involve the CNS (eg, encephalitis, meningitis), acyclovir 5–10 mg/kg IV every 8 hours is recommended, even among individuals living with HIV.[1] IV treatment should be continued until clinical improvement is achieved, and then treatment should be transitioned to oral therapy for a total duration of >10 days. An extended treatment duration is recommended for infections with CNS complications. For example, HSV-2 meningitis should be treated for at least 10–14 days and encephalitis should be treated intravenously for at least 14–21 days.[1]

5.2.2.5 Antiviral-Resistant HSV Infection

As the name implies, acyclovir-resistant HSV genital herpes is an infection resistant to acyclovir, along with valacyclovir and famciclovir (most strains).[1] Therefore, the standard recommended agents would be ineffective. The preferred regimen is foscarnet 40–80 mg/kg IV every 8 hours until symptom resolution.[1] The alternative, cidofovir 5 mg/kg IV once weekly, may also be considered. Both agents require extensive laboratory monitoring for nephrotoxicity. Other effective regimens include imiquimod 5% cream applied to the genital herpetic lesions for 8 hours three times a week, or topical cidofovir 1% gel applied 2–4 times a day. Notably, topical cidofovir must be compounded.[1]

6.0 PARASITIC SEXUALLY TRANSMITTED INFECTIONS

Only 3 STIs addressed by the 2021 CDC STI guideline are caused by parasitic organisms.[1] These parasitic STIs are pediculosis pubis (also referred to as pubic lice), scabies, and trichomoniasis.[1]

Table 5 outlines the recommended treatment regimens and the intended population. For information on alternative treatment regimens, please refer to the specific section on that topic.

Table 5. CDC 2021 Guideline-Recommended Treatment Regimens for Parasitic STIs[a] [1]

Parasitic Infection	Recommended Treatment Regimen and Dosing	Indicated Population
Pediculosis Pubis (ie, pubic lice)	Permethrin 1% cream rinse[b] applied to the affected region; rinse with water after 10 minutes **OR** Pyrethrin and piperonyl butoxide[b] applied to the affected region; rinse with water after 10 minutes	• Sexually active adolescents and adults • Pregnant women • Individuals living with HIV
Scabies	Permethrin 5% cream applied to all body regions (from neck to feet/toes[c]), rinse after 8–14 hours **OR** Ivermectin 1% lotion applied to all body regions (from neck to feet/toes[c]), rinse after 8–14 hours[d] **OR** Ivermectin 200 µg/kg PO with food (as a one-time dose), repeat in 2 weeks	All individuals diagnosed with scabies including pregnant women[e] and individuals living with HIV
Trichomoniasis	*Presumptive treatment is warranted for all recent sex partners*	
	Metronidazole 500 mg PO twice a day for 7 days	• Women[f], including those living with HIV, with an initial infection or subsequent infection due to sexual exposure from an infected partner • Men, including those who have HIV, with a recurrent infection due to treatment failure
	Metronidazole 2 g PO (as a one-time dose)	Men, including those who have HIV, with an initial infection or subsequent infection due to sexual exposure from an infected partner
	Metronidazole or tinidazole[g] 2 g PO once a day for 7 days	Women[f], including those living with HIV, with a recurrent infection due to treatment failure

Table 5. CDC 2021 Guideline-Recommended Treatment Regimens for Parasitic STIs[a] [1]

Parasitic Infection	Recommended Treatment Regimen and Dosing	Indicated Population

Abbreviations: CDC, Centers for Disease Control and Prevention; OTC, over-the-counter; PO, orally; STI, sexually transmitted infections

[a] When more than one regimen is provided, they are listed alphabetically for agents that have a similar efficacy and tolerability profile; whereas a non-alphabetical order indicates the preference of the regimens based on agent-specific efficacy and tolerability differences.

[b] These OTC products may also be used to treat other lice infections (eg, head lice) that spread from non-sexual contact. Permethrin 1% cream may be used in children as young as 2 months of age,[38] and pyrethrin and piperonyl butoxide may be used in children ≥2 years of age.[39]

[c] It is recommended to be used from the neck down in older children and adults, but when used for infants and young children, it should be applied to the head in addition to the areas below the neck

[d] Repeat application in 7 days if symptoms do not resolve

[e] Permethrin is preferred during pregnancy due to the limited evidence for ivermectin in this patient population

[f] The CDC guideline did not explicitly recommend a treatment option for use during pregnancy; however, the guideline authors did emphasize that metronidazole is probably safe during pregnancy.

[g] Tinidazole is recommended to be used in non-pregnant women only

6.1 Pediculosis Pubis

The causative parasitic organism of pediculosis pubis, or pubic lice, is *Phthirus pubis.*[1] Generally, transmission among adults occurs due to proximity during sexual exposure.[1,40] Although not common, pubic lice can be transmitted by using infected bed linens, clothing, or towels.[40] Pubic lice can also affect other body areas with coarse hair (eg, beard, eyebrows, armpits, eyelashes).[40] Most individuals seek treatment due to the symptoms (ie, pruritus), or visibly notable nits (lice eggs) or lice within the hair.[1]

The recommended treatment regimens include over-the-counter (OTC) products.[41] These agents are considered to be safe and effective when used as directed.[41] These regimens are not recommended for lice attached to the eyelashes; petroleum jelly or ophthalmic ointment should be used in these cases.[1]

Recommended treatment regimens for individuals, including pregnant and lactating women and those living with HIV, are as follows[1]:

- Permethrin 1% cream rinse applied to the affected region and rinsed with water after 10 minutes
  OR
- Pyrethrin and piperonyl butoxide applied to the affected region and rinsed with water after 10 minutes

One of the alternative regimens below may be considered upon suspected treatment failure (ie, no clinical improvement) to a recommended regimen.[1] Malathion in particular may be effective for cases of suspected *P. pubis* resistance to a recommended product.[1]

Alternative treatment regimens for individuals, including those living with HIV, are as follows[1]:

- Malathion 0.5% lotion applied to the affected region and rinsed after 8–12 hours OR
- Ivermectin 250 µg/kg by mouth (as a one-time dose) with food; dose should be repeated 1–2 weeks

Repeating treatment in 1–2 weeks is recommended when using ivermectin (alternative agent) since the initial dose may not prevent recurrent infection from unhatched eggs.[1] Due to better bioavailability, ivermectin should be taken with food. While the dose of ivermectin does not need to be adjusted among individuals with renal impairment; it is unknown whether subsequent doses among individuals with severe liver disease are considered safe. No evidence suggests ivermectin causes fetal toxicity or teratogenicity with use during pregnancy; therefore it may be used in this patient population, but permethrin is preferred. Additionally, ivermectin is likely to be compatible with use during lactation.[1] Lindane is no longer recommended as an alternative therapy due to the difficult administration, contraindications among special populations, and concern for systemic toxicity.[1,5]

A follow-up visit should occur 1 week after starting treatment if symptoms do not resolve.[1] Retreatment may be required if lice or nits are found upon examination. Individuals should refrain from sexual activity until all sex partners within the previous month have been treated, clothing and bedding have been cleaned thoroughly (eg, dry cleaned), and there is confirmation that the infection resolved.[1]

6.2 Scabies

Sarcoptes scabiei is a mite that causes a skin infestation called scabies.[1] The mite burrows into the outermost regions of the skin, but not deeper than the stratum corneum, with females laying eggs as they dig.[42] Typical symptoms are intense pruritis and a papular rash.[43] The rash and pruritis may be generalized or occur at specific anatomical sites (eg, between digits, penis, breasts, armpit, elbow).[43] Upon initial infestation, sensitization to *S. scabiei* can take 4–8 weeks; afterward the infected individual becomes symptomatic.[1,43] Yet, individuals that previously had scabies can develop symptoms within <24 hours upon reinfestation.[1] Scabies is often transmitted by prolonged, skin-to-skin exposure during sexual contact, but it can also occur indirectly from using infected towels, clothing, or bedding.[43] Infection from non-sexual contact is more risky if the infection is crusted (Norwegian) scabies, a more contagious infestation. Crusted scabies tends to be more aggressive than typical scabies and often affects older, immunocompromised (eg, HIV), or disabled individuals.[43] Therefore, if person living with HIV or someone who is immunocompromised are diagnosed with a crusted scabies infection, a specialist should be consulted to ensure appropriate management.[1]

One of the recommended treatments, permethrin 5% cream, requires a prescription unlike lower strength permethrin formulations available OTC.[43] All recommended regimens have comparable efficacy for treating scabies. Treatment selection depends on the formulation (oral or topical), dosing/application frequency, and cost.[43] Oral ivermectin may be preferred to control scabies infestation during mass outbreaks in institutional settings (eg, nursing homes, residential facilities, hospitals).[1,43] To prevent recurrent infestations and to ensure eradication, regimens containing ivermectin should be repeated in 1 or 2 weeks, depending on formulation, due to reduced ovicidal activity.[1]

Recommended treatment regimens for individuals, including those living with HIV, for non-crusted scabies are as follows[1]:

- Permethrin 5% cream[††] applied to all body regions from the neck to the feet/toes[‡‡ 43], rinsed after 8–14 hours OR
- Ivermectin 1% lotion applied to all body regions from the neck to the feet/toes[‡‡ 43], rinsed after 8–14 hours, application should be repeated in 7 days if symptoms do not resolve OR
- Ivermectin 200 µg/kg by mouth (as a one-time dose) with food; dose should be repeated in 2 weeks

Alternative treatment regimens for individuals, including those living with HIV, for non-crusted scabies is as follows[1]:

- Lindane 1% (lotion: 1 oz; cream: 30 grams) applied as a thin layer to all body regions from the neck to the feet, rinsed after 8 hours

Lindane may be used as an alternative regimen for individuals who have failed or are intolerant to the recommended treatment regimens.[1] Lindane should not be used in pregnant or lactating women,

[††] Permethrin 5% cream is preferred to ivermectin for infants and children (<5 years) who weigh <15 kg, and for treatment during pregnancy

[‡‡] When applying scabicide lotion or cream, it is recommended to be used from the neck down in older children and adults, but in addition to those areas, it should also be applied to the head when used in infants and young children.

infants and children <10 years of age, and individuals with severe dermatitis or crusted scabies. Toxicities (eg, aplastic anemia, seizures) and resistance have been reported with lindane use.[1]

Due to insufficient high-quality evidence on the treatment of crusted scabies, a recommended regimen is uncertain.[1] Treatment failure is likely to occur with a single-dose topical regimen or oral ivermectin. Therefore, a combination of topically applied 5% permethrin cream or 25% benzyl benzoate with oral ivermectin, dosed as 200 µg/kg taken on days 1, 2, 8, 9, and 15, may be considered for the treatment of crusted scabies. For more severe cases, additional doses of ivermectin may be needed on days 22 and 29.[1]

Due to the inconclusive safety of ivermectin among infants and young children (<5 years of age)[13] weighing <15 kg, permethrin is preferred.[1] Additionally, permethrin is preferred during pregnancy due to the limited evidence of ivermectin in this patient population.[1]

Due to numerous contributors (eg, treatment failure, reinfection, cross-reactivity with other household mites), retreatment should be considered for individuals with persistent symptoms or visible mites detected >2 weeks after treatment.[1] Sex partners that had contact with the infected individual within the previous month of diagnosis should be evaluated for scabies and treated if a scabies infestation occurs.[1]

6.3 Trichomoniasis

Trichomoniasis is a sexually acquired infection that results from exposure to a protozoan parasite, *Trichomonas vaginalis.*[1,44] In 2018, the CDC estimated >2 million people were infected within the US, but the majority of individuals (70–80%) were asymptomatic or had minor symptoms.[44] In the US, *T. vaginalis* predominantly affects females compared to males, with an estimated prevalence of 2.1% and 0.5%, respectively.[1] Unlike the relative prevalence of gonorrhea and chlamydia infections among female age groups, the prevalence of trichomoniasis infection seems to be similar across female age groups (ie, <24 years of age and >24 years of age).[1]

Trichomoniasis is easily transmitted from infected vaginal secretions during unprotective genital intercourse.[1] For some individuals, symptom onset may occur within 5–28 days of the initial inoculation; whereas for others, symptoms may present during later stages of infection.[44] Symptoms range in severity and may be transient. Common symptoms experienced by both men and women include irritation within the genitals, discomfort or burning during or after voiding, and penile or vaginal discharge (fishy smell).[44] *T. vaginalis* rarely affects extragenital regions (eg, rectum, mouth), even though it is possible.[1] If untreated, the infection can last for years and increases the risk of acquiring other STIs and negative pregnancy outcomes (eg, low birth weight, premature birth).[1]

Treatment may cure the infection, decrease symptoms, if present, and minimize the risk of transmission.[1,44] Nitroimidazoles (eg, metronidazole) are the only drug class with proven efficacy against trichomoniasis.[1] Thus, individuals with a nitroimidazole allergy should be desensitized in collaboration with an allergist. Non-nitroimidazole regimens (ie, boric acid, paromomycin) for those who cannot be desensitized are based on case reports; thus, the ideal alternative treatment for nitroimidazole allergic patients has not yet been determined.[1]

Recommended treatment regimen for women, including those who are pregnant and living with HIV, is as follows[1]:

- Metronidazole 500 mg by mouth twice a day for 7 days

Recommended treatment regimen for men, including those with comorbid HIV, is as follows[1]:

- Metronidazole 2 grams by mouth (as a one-time dose)

Alternative treatment regimens for women and men, including those living with HIV, is as follows[1]:

- Tinidazole 2 grams by mouth (as a one-time dose)

The tinidazole regimen was recommended as an alternative regimen despite some advantages relative to the recommended metronidazole regimens, possibly due to a higher cost. The tinidazole regimen demonstrated similar or higher cure rates (92–100% compared to 84–98% for recommended metronidazole regimens) in clinical studies and demonstrated comparable or superior symptom resolution to the single-dose 2-gram metronidazole regimen, while also having a slightly longer half-life and fewer gastrointestinal AEs.[1] Although the multi-dose regimen (ie, metronidazole 500 mg twice daily) used to be an alternative regimen for both men and women in the 2015 guideline,[5] it seems that this recommendation was changed for women only in the 2021 guideline, because there is a lack of evidence comparing the metronidazole multi-dose regimen to the single-dose regimen among men.[1] Among women, the metronidazole multi-dose regimen has been demonstrated to be more effective than the single-dose regimen, especially for symptomatic cases, or for women with a history of trichomoniasis. Topical metronidazole gel is not recommended due to being less effective than oral administration.[1]

Infected individuals should refrain from sexual activity until all affected individuals (ie, patient and all sex partners) have completed treatment and are no longer symptomatic to prevent possible reinfection.[1] Presumptive treatment should be offered to all recent sex partners. Due to the high rate of recurrence, a follow-up visit to retest for *T. vaginalis* should occur <3 months after the initial treatment for all sexually active women, including those living with HIV. In the event a 3-month follow-up is not feasible, the patient should be retested at the next routine visit <12 months after completing the initial pharmacotherapy.[1]

6.3.1 Recurrent Trichomoniasis

Recurrent trichomoniasis infections may be caused by reinfection from a sex partner, nitroimidazole-resistance, or lack of compliance to the treatment regimen.[1] Within 3 months of initial treatment, reinfection occurs for approximately 20% of individuals, which is why a test of cure is recommended during this period.[44] Women and men with a subsequent trichomoniasis infection should be retreated with the same initial metronidazole regimen (multi-dose for women and single, one-time dose for men) if reinfection occurs due to sexual exposure from an infected partner.[1] For women that experience treatment failure and without concern for re-exposure, an alternative regimen should be used (ie, tinidazole or metronidazole 2 grams once a day for 7 days). However, men with treatment failure and without a risk of re-exposure should receive the multi-dose regimen of metronidazole 500 mg twice a day for 7 days. If nitroimidazole-resistance is suspected, the CDC should be contacted to provide testing supplies and offer guidance on alternative regimens.[1]

While not a formal guideline recommendation, the following regimens can be considered for *in vitro* nitroimidazole-resistant trichomoniasis (listed in order of preference)[1]:

1. Metronidazole or tinidazole 2 grams by mouth once a day for 7 days
2. Tinidazole 2 grams by mouth once a day for 14 days AND tinidazole 500 mg (oral tablet) inserted vaginally twice a day for 14 days (*women only; not pregnant or lactating*)
3. Tinidazole 1 gram by mouth three times a day for 14 days AND paromomycin cream 6.25% (4 grams) inserted vaginally every night for 14 days (*women only; not pregnant or lactating*)

These regimens contain extended durations of high-dose metronidazole and/or tinidazole, with additional topical therapy to ensure successful treatment.[1] Preparations of paromomycin other than oral capsules are not commercially available in the US and must be compounded by a pharmacy.[45]

6.3.2 Treatment of Trichomoniasis During Pregnancy

Despite rare perinatal transmission, due to the potential for adverse pregnancy outcomes, symptomatic pregnant women should be treated with metronidazole since this agent has no evidence of teratogenic effects.[1] Due to evidence of metronidazole secretion in breast milk, some clinicians prefer lactating women to wait for 12–24 hours after metronidazole ingestion before breastfeeding, although no evidence has shown adverse effects among exposed infants. The CDC guideline did not explicitly recommend a treatment option for use during pregnancy; however, the guideline authors emphasize that metronidazole, a recommended agent for treatment of women with trichomoniasis, is probably safe during pregnancy. Treatment with tinidazole is not recommended for pregnant women, and lactating women taking a one-time dose of tinidazole 2 grams should wait to breastfeed until 72 hours after ingestion.[1]

7.0 TREATMENT OF SEXUALLY TRANSMITTED INFECTIONS IN SEXUAL ASSAULT SURVIVORS

Among female adolescent and adult sexual assault survivors, chlamydia, gonorrhea, and trichomoniasis are often detected; necessitating presumptive treatment for these infections among women.[1] Men should also receive presumptive treatment for chlamydia and gonorrhea with empiric antibiotics. Notably, the efficacy of the recommended regimens at preventing infection following sexual assault has not been studied. As a reminder, the dose of ceftriaxone should be increased to 1 gram for individuals weighing ≥150 kg.[1] For alternative regimens, please refer to the particular STI section.

Recommended empiric treatment regimen for adolescent and adult *women* is as follows[1]:

- Ceftriaxone 500 mg IM (as a one-time dose) AND
- Doxycycline 100 mg by mouth twice a day for 7 days AND
- Metronidazole 500 mg by mouth twice a day for 7 days

Recommended empiric treatment regimen for adolescent and adult *men* is as follows[1]:

- Ceftriaxone 500 mg IM (as a one-time dose) AND
- Doxycycline 100 mg by mouth twice a day for 7 days

Vaccines (ie, HBV, HPV) may be warranted for certain sexual assault survivors depending on vaccination status.[1] Additionally, the need for HIV PEP (<72 hours after a sexual assault) should be evaluated based on individualized risk.[1]

For prepubertal children who are victims of sexual assault or abuse, presumptive treatment for an STI is not recommended due to the low occurrence.[1] However, infection concerns may warrant presumptive treatment in certain environmental conditions, and may be considered once all diagnostic tests are completed. An initial examination should be performed to detect the presence of any STIs and treated accordingly based on the diagnostic results. For children that have no indication of HIV, HBV, or syphilis at the initial visit, but it is a concern, it is recommended to perform repeat serologic testing and a follow-up examination roughly 6 weeks and <3 months after the sexual exposure. This allows for adequate time to manifest symptoms and develop antibodies, if any of the concerned infections are present. HIV PEP (<72 hours after a sexual assault) may be offered to children based on the individualized risks and benefits of therapy, the accessibility of prompt treatment (ie, <72 hours), the probability the assailant was HIV-positive, and patient compliance.[1]

8.0 NON-SEXUALLY TRANSMITTED INFECTIONS – VULVOVAGINAL CANDIDIASIS

While the 2021 CDC STI guideline addresses numerous STIs, it also provides guidance on the treatment of a common non-sexually transmitted infection, vulvovaginal candidiasis (VVC).[1] Treatment of this condition was provided in the guideline due to the high prevalence among women either at risk for an STI or who experience vaginal symptoms (eg, discharge, pruritus) that tend to coincide with some STIs.[1] Other infections that result in vaginal symptoms that are sexually acquired include BV, cervicitis, and trichomoniasis, which were discussed earlier in this report.

Vulvovaginal candidiasis (VVC) is a vaginal infection primarily caused by the yeast *Candida albicans* (80–92% of cases),[10] but can also be caused by other species of *Candida*.[1] *Candida* is part of the normal vaginal flora.[46] An infection manifests when the environment of the vagina changes, promoting irregular *Candida* growth. Risk factors for a VVC infection include recent antibiotic use, hormonal contraceptive use, a dysfunctional immune system, or diabetes.[46] Common symptoms of VVC are non-specific, including vaginal soreness or pruritus, genital pain during sexual intercourse, irregular vaginal discharge, and dysuria.[1,46] VCC is ubiquitous among women, with approximately 3 out of 4 women anticipated to have ≥1 episode during their lifetime.[1] In the US, VVC results in approximately 1.4 million outpatient visits per year, and is a prevalent type of vaginal infection, second only to bacterial infections.[46]

Treatment of VVC depends on whether the infection is uncomplicated or complicated. **Table 6** outlines the indicated population of women that should receive treatment for VVC, according to infection severity. Since VVC is not acquired sexually, sex partners do not need to be treated.[1]

Table 6. Uncomplicated vs Complicated Vulvovaginal Candidiasis[1]

Severity	Indicated Population
Uncomplicated	Women that have *all* of the following: • Infrequent or irregular episodes • Mild-to-moderate symptoms • Probably caused by *C. albicans* • Immunocompetent
Complicated	Women that have *any* of the following: • Recurrent vulvovaginal candidiasis (≥3 symptomatic episodes within <12 months) • Severe symptoms • Caused by non-*albicans Candida* species • Diabetes • Immunocompromised due to a disease state (eg, HIV) or treatment (eg, corticosteroids)

8.1 Uncomplicated Vulvovaginal Candidiasis

Recommended antimycotic treatment regimens for VVC are available OTC or by prescriptions. The majority of recommended treatment options are administered intravaginally whereas there is one oral option (fluconazole); all recommended regimens for uncomplicated VVC are generally for a short duration (ie, 3 or 7 days).[1] Regimens consisting of azoles successfully alleviate symptoms and achieve negative cultures in 80–90% of patients who finish the regimen.[1]

Table 7 provides the guideline-recommended treatment regimens for uncomplicated VVC. The agents listed in the table may be used in uncomplicated or complicated cases of VVC.

Table 7. CDC 2021 Guideline-Recommended Treatment Regimens for Vulvovaginal Candidiasis

Availability	Agent and Formulation	Administration Route	Recommended Dosing and Frequency
OTC	Clotrimazole 1% cream	Intravaginal	5 g once daily for 7–14 days[a]
	Clotrimazole 2% cream		5 g once daily for 3 days
	Miconazole 4% cream		
	Miconazole 2% cream		5 g once daily for 7 days[a]
	Miconazole 100 mg vaginal suppository		1 suppository once daily for 7 days[a]
	Miconazole 200 mg vaginal suppository		1 suppository once daily for 3 days
	Miconazole 1.2 g vaginal suppository		1 suppository (as a one-time application)
	Tioconazole 6.5% ointment		5 g (as a one-time application)
Prescription	Butoconazole 2% cream	Intravaginal	5 g (as a one-time application)
	Terconazole 0.4% cream		5 g once daily for 7 days[a]
	Terconazole 0.8% cream		5 g once daily for 3 days
	Terconazole 80 mg vaginal suppository		1 suppository once daily for 3 days

Table 7. CDC 2021 Guideline-Recommended Treatment Regimens for Vulvovaginal Candidiasis

Availability	Agent and Formulation	Administration Route	Recommended Dosing and Frequency
	Fluconazole 150 mg	Oral	1 tablet (as a one-time dose)

Abbreviations: CDC, Centers for Disease Control and Prevention; OTC, over-the-counter;

[a] Possible recommended regimen during pregnancy

All of the suppositories and creams listed in these regimens weaken latex condoms and diaphragms; therefore, patients should be counseled about this risk, if a topical product is selected.[1] During pregnancy, only topical products used for 7 days are recommended; oral fluconazole should not be used due to the risk of congenital defects and spontaneous abortion. Regarding adverse effects, topical products may cause localized irritation or burning, and fluconazole may cause headache, abdominal pain, or nausea.[1]

While a follow-up visit is generally not warranted for uncomplicated VVC, women that continue to have persistent symptoms after using an OTC regimen or experience recurring symptoms <2 months after any treatment regimen should be assessed.[1]

8.2 Complicated Vulvovaginal Candidiasis

Complicated VVC cases include women with recurrent episodes (≥3 symptomatic episodes within <12 months), severe VVC symptoms (eg, edema, fissure formation, erythema), or a non–*albicans Candida* VVC infection.[1] The presence of at least one condition meeting the criteria for complicated VVC necessitates more aggressive treatment than conventional antimycotic regimens for uncomplicated cases. Complicated VVC treatment in the presence of underlying immunocompromising conditions (eg, HIV), inadequately controlled diabetes, or taking immunosuppressive treatment may not be cured by short-duration regimens and may require prolonged duration (ie, 7–14 days with topical recommended agents), in addition to management of modifiable risk factors.[1] For women living with HIV and who have complicated VVC, fluconazole 200 mg once a week can be considered as long-term prophylactic treatment, but it should not be solely implemented based on HIV status.[1]

8.2.1 Recurrent Vulvovaginal Candidiasis

The pathogenesis of recurrent VVC is not well defined and may be idiopathic or due to secondary underlying factors (eg, regular antibiotic use, immunocompromised, diabetes).[1] Among women with recurrent VVC, 10–20% of cases were due to non–*albicans Candida* species.[1] Recurrent VVC treatment requires an extended initial treatment duration relative to uncomplicated infections and a maintenance regimen. For initial treatment of a recurrence, it is recommended to start either 1) a recommended topical product for uncomplicated VVC (*refer to* ***Table 7***) for a longer duration than for an uncomplicated case (ie, for 7–10 days); or 2) oral fluconazole (100-,150-, or 200 mg) every three days for 3 doses total (ie, day1, day 4, and day 7). A recommended maintenance regimen of oral fluconazole, 100-,150-, or 200 mg once a week for 6 months should commence after completion of the initial regimen for recurrence. Or if the preferred oral fluconazole maintenance regimen is not feasible, an alternative maintenance regimen of topical products may be used as needed. For patients who continue to experience symptoms

and have positive cultures while on maintenance treatment, susceptibility tests should be acquired to determine azole resistance, and an expert should be consulted.[1]

8.2.2 Severe Vulvovaginal Candidiasis

It is recommended that patients with severe VVC be treated with an extended duration (ie, 7−14 days) of one of the topical azoles recommended in **Table 7**, or oral fluconazole 150 mg every 3 days, for 2 doses total (ie, day 1, day 4).[1]

8.2.3 Non-albicans Vulvovaginal Candidiasis

The ideal treatment of non–*albicans Candida* VVC has not been established; it is recommended that a regimen containing either a topical or oral non-fluconazole azole (based on susceptibility testing) should be used for 7–14 days.[1] If the infection recurs, intravaginal gelatin capsules of boric acid (600 mg) may be used once a day for 3 weeks; treatment success is estimated to be about 70%.[1] Referral to a specialist should be considered for patients that continue to have persistent or recurring symptoms.[1]

9.0 PRODUCT STATUS ON THE PREFERRED DRUG LIST (PDL)

When reviewing the Utah Medicaid Preferred Drug List (PDL) status of guideline-recommended agents, we focused on patient-administered oral or topical agents that were part of preferred regimens. Therefore, we did not consider agents that would be billed under the medical plan (eg, agents administered by providers in a hospital or clinic). The information below summaries the agents that are among CDC recommended STI regimens that are either listed as non-preferred or not included on the PDL.

According to the PDL published October 1, 2022, the majority of the guideline-recommended oral or topical antibiotics for the treatment of bacterial STIs (**Table 2**) are preferred on the PDL. A few recommended oral agents are not included on the PDL[§§], including azithromycin and erythromycin (ethyl succinate and base).[47] These agents are among recommended treatment regimens as follows:

- Azithromycin: recommended oral agent for chancroid, chlamydial infections, granuloma inguinale, and nongonococcal urethritis (macrolide sensitive *M. genitalium*)
- Erythromycin ethyl succinate: recommended oral agent for chlamydial infections
- Erythromycin base: recommended oral agent for chancroid and chlamydial infections

For most of these infections, at least 1 other guideline-recommended agent is preferred on the PDL with a few exceptions. For example, erythromycin (ethyl succinate/base) is the only recommended agent for the treatment of certain types of chlamydial infections in neonates, or infants and children weighing <45 kg.[1] Additionally, azithromycin is the only guideline-recommended agent for granuloma inguinale (donovanosis), but this infection is very uncommon in the US.[1]

Most of the guideline-recommended topical or oral agents for the treatment of viral STI-related sequelae (**Table 4**) are preferred on the PDL. The exception is oral famciclovir, which is non-preferred on

[§§] We have been informed that these specific unlisted agent(s) on the PDL are open access (ie, available to patients without a prior authorization or any other restrictions).

the PDL.[47] Although famciclovir is a recommended agent for the treatment of genital herpes due to HSV infection, other guideline-recommended agents for genital herpes have PDL-preferred status (eg, oral acyclovir or valacyclovir).[47] Podofilox and sinecatechins, topical treatment options for HPV genital warts are not included on the PDL[§§]. However, imiquimod, another recommended topical option for the treatment of HPV genital warts, is PDL-preferred as brand.

Regarding the agents listed in **Table 5** for the treatment of parasitic STIs, there are a few guideline-recommended topical or oral products that are either non-preferred or not included on the PDL. Oral ivermectin is not listed on the PDL[§§], and ivermectin lotion is non-preferred on the PDL.[47] Regardless, the third recommended option for the treatment of scabies, permethrin 5% cream, is PDL-preferred. OTC formulations of pyrethrum with piperonyl butoxide and permethrin 1% (ie, liquid, lotion) are covered for the treatment of pubic lice, but it is unclear if these permethrin formulations include the guideline-recommended permethrin 1% cream rinse. The first-line treatment option for trichomoniasis and for *in-vitro* nitroimidazole-resistant *T. vaginalis*, oral metronidazole, and the alternative option, tinidazole, are PDL-preferred. However, the third-line option for *in vitro* nitroimidazole-resistant trichomoniasis in women, topical paromomycin cream, must be compounded due to a lack of commercial availability, and therefore is not listed on the PDL.[47]

Comparing guideline-recommended products for the treatment of vulvovaginal candidiasis (**Table 7**) to the PDL, a few recommended products are non-preferred on the PDL or are not on the covered OTC list. OTC miconazole vaginal suppositories and tioconazole ointment are not covered.[47] In addition, intravaginal prescription products, terconazole cream, terconazole vaginal suppositories, and butoconazole are non-preferred. Nevertheless, a few other intravaginal options (clotrimazole cream and miconazole cream) and the oral option, fluconazole, are covered OTCs or preferred prescription products on the PDL.[47]

9.1 Conclusions Regarding Current PDL Placement

Overall, our comparison of CDC guideline-recommended oral or topical products for the treatment of major infections discussed in this report to PDL covered products found that at least 1 guideline-recommended initial agent is accessible (ie, as PDL-preferred status for prescription products, or covered status for OTC products) for the treatment of each infection among major populations.[***] The Utah Medicaid Drug Utilization Review (DUR) Board may consider continuing to ensure patients have access without requiring a prior authorization to at least 1 recommended patient-administered regimen for the initial treatment of each addressed STI. In cases where a topical and oral agent are included as a recommended regimen for the same STI (eg, VVC), consideration can be made for including both formulations as preferred (or covered OTC).

[***] The guideline-recommended treatment for a particular infection sometimes differed by patient characteristics (eg, sex, age, comorbidity). "Major populations" includes patient populations for whom a different recommended agent is listed in Table 2, Table 4, Table 5, or Table 7.

REFERENCES

1. Workowski K, Bachmann L, Chan P, et al. 2021 Sexually Transmitted Infections Treatment Guidelines. Centers for Disease Control and Prevention; 2021. Accessed September 12, 2022. Available at https://www.cdc.gov/std/treatment-guidelines/STI-Guidelines-2021.pdf.

2. Meites E, Szilagyi PG, Chesson HW, Unger ER, Romero JR, Markowitz LE. Human Papillomavirus Vaccination for Adults: Updated Recommendations of the Advisory Committee on Immunization Practices. MMWR Morb Mortal Wkly Rep. 2019;68(32):698-702. doi:10.15585/mmwr.mm6832a3.

3. Nelson NP, Weng MK, Hofmeister MG, et al. Prevention of Hepatitis A Virus Infection in the United States: Recommendations of the Advisory Committee on Immunization Practices, 2020. MMWR Recomm Rep. 2020;69(5):1-38. doi:10.15585/mmwr.rr6905a1.

4. Weng MK, Doshani M, Khan MA, et al. Universal Hepatitis B Vaccination in Adults Aged 19-59 Years: Updated Recommendations of the Advisory Committee on Immunization Practices - United States, 2022. MMWR Morb Mortal Wkly Rep. 2022;71(13):477-483. doi:10.15585/mmwr.mm7113a1.

5. Workowski K, Bolan G. 2015 Sexually Transmitted Infections Treatment Guidelines. Centers for Disease Control and Prevention; 2015. Accessed September 12, 2022. Available at https://www.cdc.gov/mmwr/pdf/rr/rr6403.pdf.

6. Sexually transmitted infections (STIs). Fact sheet. WHO.int. August 22, 2022. Accessed September 12, 2022. Available at https://www.who.int/news-room/fact-sheets/detail/sexually-transmitted-infections-(stis).

7. McCormack D, Koons K. Sexually Transmitted Infections. Emerg Med Clin North Am. 2019;37(4):725-738. doi:10.1016/j.emc.2019.07.009.

8. Ghanem KG, Tuddenham S. Screening for sexually transmitted infections. UpToDate.com; 2022. Last Updated May 26, 2022. Accessed September 21, 2022. Available at https://www.uptodate.com/contents/screening-for-sexually-transmitted-infections.

9. Sexually Transmitted Infections Prevalence, Incidence, and Cost Estimates in the United States. Fact sheet. CDC.gov. January 25, 2021. Accessed September 12, 2022. Available at https://www.cdc.gov/std/statistics/prevalence-2020-at-a-glance.htm.

10. Sobel JD, Mitchell C. Candida vulvovaginitis: Clinical manifestations and diagnosis. UpToDate.com; 2022. Last Updated February 9, 2022. Accessed October 9, 2022. Available at https://www.uptodate.com/contents/candida-vulvovaginitis-clinical-manifestations-and-diagnosis.

11. Sunagawa S, Baack K, Gomez L, Nichols H, Lewis T, Zeger W. STI therapy compliance pre and post 2021 CDC treatment guideline update. Am J Emerg Med. 2022, 10.1016/j.ajem.2022.07.031doi:10.1016/j.ajem.2022.07.031.

12. Dalby J, Stoner BP. Sexually Transmitted Infections: Updates From the 2021 CDC Guidelines. Am Fam Physician. 2022;105(5):514-520.

13. Sexually Transmitted Infections: Summary of CDC Treatment Guidelines - 2021. Pocket guide. CDC.gov. 2021. Accessed September 27, 2022. Available at https://www.cdc.gov/std/treatment-guidelines/pocket-guide.pdf.

14. Lynch S. Acute epididymitis. JAAPA. 2018;31(3):50-51. doi:10.1097/01.JAA.0000530304.69021.4b.

15. Koumans EH, Sternberg M, Bruce C, et al. The prevalence of bacterial vaginosis in the United States, 2001-2004; associations with symptoms, sexual behaviors, and reproductive health. Sex Transm Dis. 2007;34(11):864-869. doi:10.1097/OLQ.0b013e318074e565.

16. Clindamycin phosphate vaginal cream. Prescribing information. Pfizer Inc.; 2022. Accessed September 22, 2022. Available at https://labeling.pfizer.com/showlabeling.aspx?format=PDF&id=627.

17. StatPearls.com. Chancroid. NCBI Bookshelf; 2022. Last Updated May 23, 2022. Accessed September 19, 2022. Available at https://www.ncbi.nlm.nih.gov/books/NBK513331/.

18. Price G, Bash M. Epidemiology and pathogenesis of Neisseria gonorrhoeae infection. UpToDate.com; 2019. Last Updated October 10, 2019. Accessed September 26, 2022. Available at https://www.uptodate.com/contents/epidemiology-and-pathogenesis-of-neisseria-gonorrhoeae-infection.

19. Gonococcal Isolate Surveillance Project (GISP). Fact sheet. CDC.gov. September 1, 2022. Accessed September 26, 2022. Available at https://www.cdc.gov/std/gisp/default.htm.

20. Health Alert Template for Disseminated Gonococcal Infection (DGI). Fact sheet. CDC.gov. December 5, 2019. Accessed September 26, 2022. Available at https://www.cdc.gov/std/program/outbreakresources/HANtemplate-dgi.htm#:~:text=DGI%20occurs%20when%20the%20sexually,rare%20occasions%2C%20endocarditis%20or%20meningitis.

21. Haimovici R, Roussel TJ. Treatment of gonococcal conjunctivitis with single-dose intramuscular ceftriaxone. Am J Ophthalmol. 1989;107(5):511-514. doi:10.1016/0002-9394(89)90495-9.

22. Richards DM, Heel RC. Ceftizoxime. A review of its antibacterial activity, pharmacokinetic properties and therapeutic use. Drugs. 1985;29(4):281-329. doi:10.2165/00003495-198529040-00001.

23. Klausner J. Disseminated gonococcal infection. UpToDate.com; 2022. Last Updated July 20, 2022. Accessed September 26, 2022. Available at https://www.uptodate.com/contents/disseminated-gonococcal-infection.

24. Curry SJ, Krist AH, Owens DK, et al. Ocular Prophylaxis for Gonococcal Ophthalmia Neonatorum: US Preventive Services Task Force Reaffirmation Recommendation Statement. JAMA. 2019;321(4):394-398. doi:10.1001/jama.2018.21367.

25. StatPearls.com. Lymphogranuloma Venereum. NCBI Bookshelf; 2022. Last Updated October 9, 2022. Accessed October 10, 2022. Available at https://www.ncbi.nlm.nih.gov/books/NBK537362/.

26. Wiesenfeld H. Pelvic inflammatory disease: Treatment in adults and adolescents. UpToDate.com; 2022. Last Updated March 14, 2022. Accessed September 28, 2022. Available at https://www.uptodate.com/contents/pelvic-inflammatory-disease-treatment-in-adults-and-adolescents.

27. Peeling RW, Mabey D, Kamb ML, Chen XS, Radolf JD, Benzaken AS. Syphilis. Nat Rev Dis Primers. 2017;3:17073. doi:10.1038/nrdp.2017.73.

28. Syphilis - CDC Basic Fact Sheet. Fact sheet. CDC.gov. 2022. Accessed September 29, 2022. Available at https://www.cdc.gov/std/syphilis/stdfact-syphilis.htm.

29. Hepatitis A Questions and Answers for Health Professionals. Fact sheet. CDC.gov. July 28, 2020. Accessed October 3, 2022. Available at https://www.cdc.gov/hepatitis/hav/havfaq.htm.

30. Prehevbrio Hepatitis B Vaccine (Recombinant) injectable suspension, for intramuscular use. Prescribing information. VBI Vaccines Inc.; 2021. Accessed October 3, 2022. Available at https://www.prehevbrio.com/wp-content/uploads/2021/11/PreHevbrio-Full-Prescribing-Information.pdf.

31. Hepatitis B Questions and Answers for Health Professionals. Fact sheet. CDC.gov. March 30, 2022. Accessed October 3, 2022. Available at https://www.cdc.gov/hepatitis/hbv/hbvfaq.htm#treatment.

32. Gardasil 9 (Human Papillomavirus 9-valent Vaccine, Recombinant) injectable suspension, for intramuscular use. Prescribing information. Merck Sharp & Dohme Corp.; 2021. Accessed October 3, 2022. Available at https://www.merck.com/product/usa/pi_circulars/g/gardasil_9/gardasil_9_pi.pdf.

33. Recombivax HB Hepatitis B Vaccine (Recombinant) injectable suspension, for intramuscular use. Prescribing information. Merck Sharp & Dohme Corp.; 2020. Accessed October 3, 2022. Available at https://www.merck.com/product/usa/pi_circulars/r/recombivax_hb/recombivax_pi.pdf.

34. Engerix-B Hepatitis B Vaccine (Recombinant) injectable suspension, for intramuscular use. Prescribing information. GlaxoSmithKline Biologicals; 2021. Accessed October 3, 2022. Available at https://gskpro.com/content/dam/global/hcpportal/en_US/Prescribing_Information/Engerix-B/pdf/ENGERIX-B.PDF.

35. Genital Herpes - CDC Detailed Fact Sheet. Fact sheet. CDC.gov. July 22, 2021. Accessed October 7, 2022. Available at https://www.cdc.gov/std/herpes/stdfact-herpes-detailed.htm.

36. McQuillan G, Kruszon-Moran D, Flagg EW, Paulose-Ram R. Prevalence of Herpes Simplex Virus Type 1 and Type 2 in Persons Aged 14-49: United States, 2015-2016. NCHS Data Brief. 2018, (304):1-8. .

37. Albrecht M. Treatment of genital herpes simplex virus infection. UpToDate.com; 2022. Last Updated May 25, 2022. Accessed October 7, 2022. Available at https://www.uptodate.com/contents/treatment-of-genital-herpes-simplex-virus-infection.

38. Permethrin (Lexi-Drugs): Dosing: Pediatric. Lexicomp.com; 2022. Last Updated September 19, 2022. Accessed October 7, 2022. Available at http://online.lexi.com.

39. Pyrethrins and Piperonyl Butoxide (Lexi-Drugs): Dosing: Pediatric. Lexicomp.com; 2022. Last Updated September 19, 2022. Accessed October 7, 2022. Available at http://online.lexi.com.

40. About Pubic "Crab" Lice - Frequently Asked Questions (FAQs). Fact sheet. CDC.gov. September 17, 2020. Accessed October 7, 2022. Available at https://www.cdc.gov/parasites/lice/pubic/gen_info/faqs.html.

41. Treatment - Pubic "Crab" Lice. Fact sheet. CDC.gov. September 12, 2019. Accessed October 7, 2022. Available at https://www.cdc.gov/parasites/lice/pubic/treatment.html.

42. Scabies - Biology. Fact sheet. CDC.gov. November 2, 2010. Accessed October 7, 2022. Available at https://www.cdc.gov/parasites/scabies/biology.html.

43. About Scabies - Frequently Asked Questions (FAQs). Fact sheet. CDC.gov. September 1, 2020. Accessed October 7, 2022. Available at https://www.cdc.gov/parasites/scabies/gen_info/faqs.html.

44. Trichomoniasis - CDC Basic Fact Sheet. Fact sheet. CDC.gov. April 25, 2022. Accessed October 7, 2022. Available at https://www.cdc.gov/std/trichomonas/stdfact-trichomoniasis.htm.

45. Paromomycin (Lexi-Drugs): Product Availability. Lexicomp.com; 2022. Last Updated September 19, 2022. Accessed October 10, 2022. Available at http://online.lexi.com.

46. Vaginal Candidiasis. Fact sheet. CDC.gov. July 13, 2022. Accessed October 10, 2022. Available at https://www.cdc.gov/fungal/diseases/candidiasis/genital/index.html.

47. Utah Department of Health and Human Services. Preferred Drug List. Medicaid.Utah.gov. 2022. Last Updated October 1, 2022. Accessed October 10, 2022. Available at https://medicaid.utah.gov/pharmacy/preferred-drug-list/.

48. Hepatitis C Questions and Answers for Health Professionals. Fact sheet. CDC.gov. August 7, 2020. Accessed October 4, 2022. Available at https://www.cdc.gov/hepatitis/hcv/hcvfaq.htm.

49. Jin F, Matthews GV, Grulich AE. Sexual transmission of hepatitis C virus among gay and bisexual men: a systematic review. Sex Health. 2017;14(1):28-41. doi:10.1071/sh16141.

50. Body fluids that transmit HIV. Fact sheet. CDC.gov. April 21, 2021. Accessed October 4, 2022. Available at https://www.cdc.gov/hiv/basics/hiv-transmission/body-fluids.html.

51. Ways HIV can be transmitted. Fact sheet. CDC.gov. March 4, 2022. Accessed October 4, 2022. Available at https://www.cdc.gov/hiv/basics/hiv-transmission/ways-people-get-hiv.html.

52. About HIV. Fact sheet. CDC.gov. June 30, 2022. Accessed October 4, 2022. Available at https://www.cdc.gov/hiv/basics/whatishiv.html.

APPENDIX A – SUPPLEMENTARY DRUG REGIMEN TABLES

Appendix A, Table 1. Medications Used in Treatment Regimens for Bacterial STIs

Medication (Route of Administration)	Bacterial STI (Indicated Population or Drug Formulation)											
	BV	Cervicitis	Chancroid	Chlamydia	Epididymitis	Gonorrhea	Granuloma Inguinale	LGV	NGU	PID	Proctitis	Syphilis
Amoxicillin (PO)				AR (PG)								
Ampicillin-sulbactam (IV)										AR		
Aqueous crystalline penicillin G (IV)												RR[a]
Azithromycin (PO)		AR	RR	RR (PG, INF, CHD [≥45 kg]); AR (AD, ADO; INF with CP)		AR (AD and ADO)	RR	AR	RR (MS *M. genitalium*); AR			
Benzathine penicillin G (IM)												RR (AD, INF, CHD, NEO)
Cefixime (PO)						AR (AD and ADO)						
Cefotaxime (IV, IM)						RR (NEO); AR (AD and ADO)				RR		
Cefotetan (IV)										RR		
Cefoxitin (IV, IM)										RR		
Ceftizoxime (IV, IM)						AR[b]				RR (IM)		
Ceftriaxone[c] (IM, IV)			RR		RR	RR (AD, ADO, NEO, INF, CHD)				RR	RR	

Abbreviations: AD, adults; ADO, adolescents; AR, alternative regimen; BV, bacterial vaginosis; CH, children; CP, chlamydial pneumonia; EB, erythromycin base; EES, erythromycin ethyl succinate; IM, intramuscularly; INF, infants; IVA, intravaginally; IV, intravenously; LGV, lymphogranuloma venereum; MR, macrolide resistant; MS, macrolide sensitive; NEO, neonates; NGU, nongonococcal urethritis; PG, pregnancy; PID, pelvic inflammatory disease; PO, orally; RR, recommended regimen; STI, sexually transmitted infection

Appendix A, Table 1. Medications Used in Treatment Regimens for Bacterial STIs

Medication (Route of Administration)	Bacterial STI (Indicated Population or Drug Formulation)											
	BV	Cervicitis	Chancroid	Chlamydia	Epididymitis	Gonorrhea	Granuloma Inguinale	LGV	NGU	PID	Proctitis	Syphilis
Ciprofloxacin (PO)			RR									
Clindamycin (IVA, PO, IV)	RR (IVA); AR (PO, IVA)									AR (IV)		
Doxycycline[c] (PO or IV)		RR (PO)		RR (PO; AD, ADO, and CHD [≥8 years of age])	RR (PO)		AR (PO)	RR (PO)	RR (PO); AR (PO)	RR (PO, IV); AR (PO, IV)	RR (PO)	
Erythromycin (ethyl succinate/base; PO, ointment; topical)			RR (EB only)	RR (NEO; INF with CP; INF and CHD [<45 kg]; EES and EB)		P (topical ointment[d], NEO)	AR (EB only)	AR (EB only)				
Gentamicin (IV, IM)						AR (IM)				AR (IV or IM)		
Levofloxacin (PO)				AR (AD and ADO)	RR							
Metronidazole[c] (PO, IVA, IV)	RR (PO, IVA)								RR (PO; *T. vaginalis*)	RR (PO, IV)		
Moxifloxacin (PO)									RR (MR *M. genitalium*)[e]			
Probenecid (PO)										RR		AR (AD)[f]
Procaine penicillin G (IM)												RR (NEO); AR (AD)[f]

Abbreviations: AD, adults; ADO, adolescents; AR, alternative regimen; BV, bacterial vaginosis; CH, children; CP, chlamydial pneumonia; EB, erythromycin base; EES, erythromycin ethyl succinate; IM, intramuscularly; INF, infants; IVA, intravaginally; IV, intravenously; LGV, lymphogranuloma venereum; MR, macrolide resistant; MS, macrolide sensitive; NEO, neonates; NGU, nongonococcal urethritis; PG, pregnancy; PID, pelvic inflammatory disease; PO, orally; RR, recommended regimen; STI, sexually transmitted infection

Appendix A, Table 1. Medications Used in Treatment Regimens for Bacterial STIs

Medication (Route of Administration)	Bacterial STI (Indicated Population or Drug Formulation)											
	BV	Cervicitis	Chancroid	Chlamydia	Epididymitis	Gonorrhea	Granuloma Inguinale	LGV	NGU	PID	Proctitis	Syphilis
Secnidazole (PO)	AR											
Tinidazole (PO)	AR								RR (*T. vaginalis*)			
Trimethoprim-sulfamethoxazole (PO)							AR					

*Grey color indicates that the antibiotic is part of a **recommended** regimen. Blue color indicates that the antibiotic is part of an **alternative** regimen. Red color indicates that it should be used as **prophylaxis.** Agents that are included in alternative and recommended regimens (RR/AR) are differentiated based on the formulation of the agent or indicated population. Recommended regimens should be used primarily for the majority of patients unless contraindicated on the basis of allergy or medical conditions. Alternative regimens are considered inferior and may have disadvantages compared to recommended regimens, but can be considered when a recommended regimen is unable to be used. Alternative regimens are not provided for all STIs, in which case, consulting with an infectious disease specialist is recommended. For dosing recommendations, please refer to **Table 2** (recommended regimens only) or the specific STI section in the body of the report. The alternative regimens reported in the table do not include regimens that are suggested based on limited evidence for certain patient populations (ie, non-pregnant adults, women at low-risk for acquiring gonorrhea).*

[a] *Recommend regimen for adults with neurosyphilis, otosyphilis, or ocular syphilis, and neonates, infants, and children with congenital syphilis*

[b] *A preferred administration route for ceftizoxime is not provided in the CDC guideline, but other resources that claim to be in alignment with the 2021 guideline recommend ceftizoxime should be administered IV.*[23]

[c] *Also a recommended agent to be used in adult and adolescent sexual assault survivors (oral metronidazole is only recommended in females)*

[d] *Erythromycin 0.5% ophthalmic ointment is the only recommended prophylactic agent for gonorrhea ophthalmia neonatorum*

[e] *Also part of a recommended regimen if M. genitalium resistance testing is unavailable*

[f] *For the treatment of neurosyphilis, otosyphilis, or ocular syphilis*

Abbreviations: AD, adults; ADO, adolescents; AR, alternative regimen; BV, bacterial vaginosis; CH, children; CP, chlamydial pneumonia; EB, erythromycin base; EES, erythromycin ethyl succinate; IM, intramuscularly; INF, infants; IVA, intravaginally; IV, intravenously; LGV, lymphogranuloma venereum; MR, macrolide resistant; MS, macrolide sensitive; NEO, neonates; NGU, nongonococcal urethritis; PG, pregnancy; PID, pelvic inflammatory disease; PO, orally; RR, recommended regimen; STI, sexually transmitted infection

Appendix A, Table 2. Medications Used in Treatment Regimens for Viral STI-Related Sequelae

Medication (Route of Administration)	Viral STI (Related Sequelae)				
	HPV (Genital Warts)[a]		HSV (Genital Herpes)		
	External anogenital warts	*Vaginal, cervical, and intra-anal warts*	*First episode*	*Suppressive*[b]	*Episodic*
Acyclovir (PO)			RR	RR	RR
BCA[c] (topical)	RR	RR			
Famciclovir (PO)			RR	RR	RR
Imiquimod[d] (topical)	RR				
Podofilox[d] (topical)	RR				
Sinecatechins[d] (topical)	RR				
TCA[c] (topical)	RR	RR			
Valacyclovir (PO)			RR	RR	RR

Grey color *indicates that the antibiotic is part of a* ***recommended*** *regimen. Recommended regimens should be used primarily for the majority of patients unless contraindicated on the basis of allergy or medical conditions. Alternative regimens are considered inferior and may have disadvantages compared to recommended regimens, but can be considered when a recommended regimen is unable to be used. No formal guideline-recommended alternative regimens were provided for the treatment of viral STI-related sequelae. For dosing recommendations, please refer to* ***Table 4*** *(recommended regimens only) or the specific STI section in the body of the report.*

Abbreviations: BCA, bichloroacetic acid; HPV, human papillomavirus; HSV, herpes simplex virus; PO, orally; RR, recommended regimen; STI, sexually transmitted infection; TCA, trichloroacetic acid

[a] *The use of cryotherapy, cryoprobe, and surgical excision were excluded from the table since these are not treatment methods that are considered to be drugs. Therefore, warts within the urethral meatus were not addressed since only those excluded interventions are recommended for this indication.*

[b] *Pregnant women taking suppressive therapy for recurrent genital herpes should only receive either acyclovir or valacyclovir*

[c] *Should be administered in a health care setting by the provider*

[d] *Applied by the patient*

Appendix A, Table 3. Medications Used in Treatment Regimens for Parasitic STIs

Medication (Route of Administration)	Parasitic STI		
	Pediculosis Pubis	**Scabies**	**Trichomoniasis[a]**
Permethrin (topical)	RR (1% cream rinse)	RR (5% cream)[b]	
Pyrethrin and piperonyl butoxide (topical)	RR		
Malathion (topical)	AR (0.5% lotion)		
Ivermectin (PO or topical)	AR (PO)	RR (1% lotion or PO)	
Lindane[c] (topical)		AR (1% lotion or cream)	
Metronidazole (PO)			RR (adult men and women)
Tinidazole (PO)			RR; AR (adult men and women [non-pregnant])

*Grey color indicates that the antibiotic is part of a **recommended** regimen. Blue color indicates that the antibiotic is part of an **alternative** regimen. Recommended regimens should be used primarily for the majority of patients unless contraindicated on the basis of allergy or medical conditions. Alternative regimens are considered inferior and may have disadvantages compared to recommended regimens, but can be considered when a recommended regimen is unable to be used. For dosing recommendations, please refer to **Table 5** (recommended regimens only) or the specific STI section in the body of the report.*

Abbreviations: AR, alternative regimen; PO, orally; RR, recommended regimen; STI, sexually transmitted infection

[a] Does not include additional agents that may be used intravaginally for in vitro nitroimidazole-resistant trichomoniasis since a stepped approach with standard agents is preferred.

[b] For the treatment of scabies, permethrin 5% cream is preferred to ivermectin for infants and children (<5 years) who weigh <15 kg, and for treatment during pregnancy

[c] Lindane should not be used in pregnant or lactating women, infants and children <10 years of age, and individuals with severe dermatitis or crusted scabies

APPENDIX B – VIRAL HEPATITIS AND HIV SUPPLEMENTARY INFORMATION

Hepatitis A Virus

Hepatitis A virus (HAV) may be acquired via sexual contact, most likely via fecal-oral exposure or by consuming contaminated water or food.[1] Bloodborne transmission of HAV is rare. HAV reproduces in the liver and is shed in the feces from 2–3 weeks prior to 1 week following symptom onset, with an estimated 28-day incubation period (ie, time from initial exposure to symptom onset).[1]

Postexposure Prophylaxis: Upon exposure to HAV, an unvaccinated individual should receive a monovalent hepatitis A vaccine or immunoglobulin (IG) (0.1 mL/kg) within 2 weeks after exposure or whenever feasible.[1] Due to the longer duration of protection, ability to induce active immunity, improved tolerability, better access, and ease of administration, the hepatitis A vaccine is preferred compared to IG for postexposure prophylaxis in most individuals. However, IG is recommended for infants <6 months of age, individuals with chronic liver disease, a contraindication to the vaccine (eg, history of an anaphylactic reaction to the vaccine), or who are immunocompromised. IG can also be administered simultaneously with the vaccine at different injection sites. To ensure long-term immunity, the 2-dose vaccine regimen should be completed; however, only one dose is required for postexposure prophylaxis.[1]

Treatment: Infection with HAV is often self-limiting and does not progress to chronic infection, nor does it cause chronic liver disease.[1] Most adults (70%) tend to have a symptomatic infection, whereas pediatrics are generally asymptomatic, suggesting the risk of experiencing symptoms is associated with age.[1]

Acute HAV infections typically require only supportive care, but hospitalization may be required for individuals that are dehydrated or those who experience signs of acute liver failure.[1] However, acute liver failure due to HAV is uncommon. Among individuals with HAV, drugs that are metabolized via the liver or potentially cause liver injury should be used cautiously.[1]

Hepatitis B Virus

The transmission of hepatitis B virus (HBV) occurs upon contact with contaminated blood or body fluids (ie, semen, exudate from wounds, vaginal discharge, saliva) via mucous or percutaneous (eg, needle stick, bite) membrane exposure.[1] The blood contains the highest amount of HBV. HBV has an estimated incubation period that varies between 6 weeks to 6 months. HBV has the potential to be self-limited or chronic, with the highest risk of chronicity among infants and children. About 90% of infants and 30% of children<5 years of age progress to chronic HBV, whereas 2–6% of adults become chronically infected. Infection with chronic HBV increases the risk of premature mortality due to hepatocellular carcinoma or cirrhosis. The highest rates of acute infection have predominately affected high-risk adults (≥30 years) (eg, MSM, injection drug users, individuals in non-monogamous relationships).[1]

Postexposure Prophylaxis: For unvaccinated individuals or individuals that previously lacked an adequate response to the vaccine with a known exposure to hepatitis B surface antigen (HBsAg)

contaminated blood or body fluids, the vaccine and hepatitis B immune globulin (HBIG) (0.06 mL/kg) should be administered simultaneously at different injection sites, preferably within 24 hours of exposure.[1] For individuals exposed to blood or body fluids with an unknown HBsAg status, only the HBV vaccine should be administered as soon as possible, preferably within 24 hours of exposure. Individuals that have not completed the vaccine series should receive HBIG (if a known exposure) and finish the series according to the appropriate schedule and guidance. Individuals with a known exposure that failed to have postvaccination testing after completing the series should have a one-time booster dose, but no further treatment is required for those exposed to an unknown HBsAg source. An occupational-related exposure should be managed according to the ACIP guidelines.[1]

Treatment: Supportive treatment is indicated for individuals with an acute HBV infection.[1] Individuals with a chronic HBV infection should be referred to a hepatologist or gastroenterologist for appropriate treatment with an FDA-approved antiviral (eg, entecavir, tenofovir dipovoxil fumarate) to ensure liver disease remission and maintained reproductive suppression of HBV.[1] For recommended treatment options, please refer to the 2018 chronic hepatitis B guideline by the American Association for the Study of Liver Diseases (AASLD) available at: https://www.aasld.org/practice-guidelines/chronic-hepatitis-b.

Hepatitis C Virus

In the US, chronic hepatitis C virus (HCV) infection affects approximately 2.4 million individuals, making it the most common bloodborne infection.[1] HCV is mainly transmitted parenterally from infected blood, frequently due to sharing needles when injecting drugs.[1] Less commonly, HCV can also be transmitted from an infected mother to a neonate during or near delivery.[1,48] The risk of transmission is higher among mothers with comorbid HIV and if maternal HCV viremia is present at labor.[1] Lactating women with HCV may continue breastfeeding because it does not appear to be a source of transmission.[1] HCV is usually not spread through sexual contact, but evidence suggests that it can happen, especially in MSM living with HIV.[1] The incidence among MSM living with HIV was estimated to be 6.35 per 1,000 person-years, according to a 2017 systematic review.[1,49]

Usually, HCV-infected individuals either have mild symptoms or are asymptomatic.[1] Approximately 75–85% of individuals with an acute HCV infection will develop a chronic infection, and 10–20% of those individuals will progress to cirrhosis within two-to-three decades of active liver disease. Therefore, individuals with HCV should refrain from consuming alcohol and other hepatotoxic agents to prevent additional liver damage.[1]

Postexposure Prophylaxis: Unlike HAV and HBV, there are no vaccines for HCV and IG is ineffective as postexposure prophylaxis.[1] Additionally, it is not recommended to use direct-acting antivirals for prophylaxis. Since no therapy has shown to be effective against HCV as postexposure prophylaxis, prompt diagnosis is crucial to treat the infection early and minimize the transmission to others.[1]

To minimize the chance of transmitting HCV to others, infected individuals should refrain from donating semen or blood and sharing household personal items (eg, razors, toothbrushes).[1] In addition, any sores or cuts should be wrapped.

Treatment: Individuals with HCV should be treated to ensure their personal health and to minimize the potential transmission to others.[1] Regardless of the HCV genotype, HCV is curable in 90% of infected

individuals using an 8–12 week oral regimen.[1] For appropriate treatment of HCV, readers should refer to the website-based guideline recommendations from the AASLD and Infectious Diseases Society of America, in partnership with the International Antiviral Society – USA,[1,48] available at: https://www.hcvguidelines.org/

Human Immunodeficiency Virus

The transmission of HIV occurs upon contact with contaminated blood or body fluids, including genital secretions (eg, semen, pre-seminal fluid) via mucous membranes or injured tissue.[50] Therefore, transmission can occur from sexual contact via vaginal or anal intercourse, or from sharing needles or other drug paraphernalia.[51] HIV can also be transmitted perinatally from an infected mother to her fetus during pregnancy or labor, or upon breastfeeding.[51]

An acute influenza-like retroviral syndrome (eg, pharyngitis, fatigue, fever, general discomfort, arthritis, lymphadenopathy, muscle aches, rash) often manifests in individuals living with HIV within 2–4 weeks after exposure[1,52]; however, some individuals may be asymptomatic.[1] Over time, the acute infection develops into a chronic infection that continues to diminish $CD4^+$ T lymphocytes, negatively impacting the functionality of the immune system.[1] Therefore, untreated HIV can result in a serious, fatal condition called acquired immunodeficiency syndrome (AIDS) at the latest stage of the infection.[1] Although the virus is a life-long infection, prompt treatment can ensure a healthy, near-normal lifespan.[1,52]

Treatment: Antiretroviral therapy (ART) suppresses HIV reproduction causing levels to decrease below detectable thresholds, thereby reducing HIV-related morbidity and mortality, and preventing transmission to non-infected individuals.[1] Sexual transmission is considered no longer a risk once the viral load is consistently <200 copies/mL. Based on the known benefits, treatment guidelines from the International AIDS Society –USA Panel and US Department of Health and Human Services (DHHS) recommend all individuals living with HIV receive ART immediately after diagnosis, irrespective of the $CD4^+$ T cell levels. Recognizing HIV at the acute stage is vital because the infection is highly contagious at this stage due to the elevated viral concentrations located in the plasma and genital secretions. Initiating ART for an acute infection can also improve objective viral markers, decrease infection severity, preserve immune response, and reduce the viral setpoint. In addition, the use of ART during pregnancy and other interventions (eg, cesarean delivery, avoiding breastfeeding) can reduce the transmission risk from the mother-to-baby to <2%, whereas without ART, the risk is 30%.[1] Details about specific recommended ART for adults, and recommendations for the use of ART among pediatrics per DHHS guidelines can be accessed at: https://clinicalinfo.hiv.gov/en/guidelines