Thursday, July 11, 2019
7:15 a.m. to 8:30 a.m.
Cannon Health Building
Room 125

**Board Members Present:**
Kumar Shah, MSc, PEng, Board Chair
Eric Cannon, PharmD, FAMCP
Jennifer Brinton, MD
Judith Turner, DVM, PharmD
Katherine Smith, PharmD
Neal Catalano, PharmD
Sharon Weinstein, MD

**Board Members Excused:**
Susan Siegfied, MD
Michelle Hoffman, MD

**Dept. of Health/Div. of Health Care Financing Staff Present:**
Jennifer Strohecker, PharmD
Bryan Larson, PharmD
Joe Busby, RPh, MBA
Kelby Kuhn, PharmD
Andrea Rico, CPhT, CPC
Dana Bui, CPhT
Spencer Miller, CPhT
Lotao Tavui, CPhT

**University of Utah Drug Regimen Review Center Staff Presenter:**
Joann LaFleur, PharmD

**Other Individuals Present:**
Jason Bott, Eli Lilly
Joanita Lake, U of U
Michelle Bice, Gilead
Lisa Wilson, Biogen
Kaysen Bala, Biogen
Matthew Call, U of U Health Plans
Dr. Russell Butterfield, U of U
Michelle Puyear, Gilead
Valerie Gonzales, U of U
Kara Clawson, Sarepta
Joan Schindler, Sarepta
Lauren Heath, U of U
Vicky Frydrych, U of U
Lori Howarth, Bayer
Rob Booth, Allergan

**Meeting conducted by:** Kumar Shah

1) **Welcome & Housekeeping:** Kumar Shah opened the meeting, announced a quorum and reminded everyone to sign the rosters. Jennifer Strohecker introduced new clinical pharmacist Kelby Kuhn, as well as several new pharmacy technicians Koa, Dana, Spencer that will support the pharmacy operations in the Bureau of Coverage and Reimbursement Policy.

2) **Review and Approval of Choose an item Minutes:** Eric Cannon made a motion to Approve the minutes from June. Neal Catalano seconded the motion. All in favor, motion passed. Sharon Weinstein was not present for the vote.
3) **P&T Committee Update:** Bryan Larson presenting a brief overview of the agenda that was presented during the June 2019 P&T Committee including: ACO’s presented their methodologies for the preferred drug lists Laura Britton (Healthy U), Shea Wilson (Molina), Cody Ball (SelectHealth), and Robyn Seely (Steward Health Choice). Additional items discussed were ADHD Stimulants, Sedative Hypnotics with a motion to refer to Hetlioz to the DURB for review.

4) **Spinal Muscular Atrophy:**
   a. **Information:** Jennifer Strohecker introduced guest speaker Dr. Russell Butterfield who is an expert in Spinal Muscular Atrophy and intimately involved with the clinical trials research for both therapies for Spinal Muscular Atrophy. Dr. Butterfield was invited to share his experience with both medications available to treat this devastating condition and give about a fifteen minute presentation and will then open up to board discussion and review of the draft prior authorization criteria of Zolgensma and current prior authorization criteria of Spinraza.

Dr. Butterfield runs the neuromuscular program at the University of Utah. He is involved with clinical trials and by way of disclosure for both nusinersen and aveaxis gene therapies. He has also worked as an advisor for both companies. Dr. Butterfield presented information on gene therapy. Both medications are genetic therapies however, are very different in their approach, nusinersen is a genetic trick. The severity of SMA is controlled by the leaky transcription out of the SMN2 gene, which is a broken copy of the SMN1 gene and it’s a way to turn the volume up on the transcription out of the that gene. Use a small piece of DNA, small piece of RNA and binds down and covers up a splicing inhibitor and in turn gets better splicing.

Zolgensma is single dose of a viral vector to deliver a gene transfer, new copy of SMN1. Vehicle delivers a new gene into the neurons, that vehicle is a virus called AAV9. Adeno associated virus may be a little bit of a misconception it is not adenovirus that we might get sick from, that maybe a person has today. Adenovirus causes cough, cold and flu symptoms. Adeno associated virus can cause similar symptoms only if you have an active adenovirus infection in nature it doesn’t contain enough genes to replicate itself and borrows genes from adenovirus. There is a history with adenovirus vectors back in the late 90’s that created models about ethical thinking and research with the Jesse Gelsinger case, which shut down gene therapies for several years. Adeno associated virus vectors are really pretty handy vectors. They contain a small amount of DNA, which means a small gene may fit in there easily, a large gene may be a little harder to deliver and there are lots of different types of AAV and target different tissues. AAV9 serotype used in Zolgensma targets neurons in muscle very well, it also goes to liver and lots of other tissues. What is does it what viruses do, it delivers its DNA into the cell. That DNA quickly becomes a circular piece of DNA, which
doesn’t integrate into a chromosome it just sits there in the nucleus and produces whatever gene it was engineered to produce. It is not exactly a natural SMN1 gene, rather a highly engineered copy of SMN1 designed to make lots of SMN protein. In essence it’s delivering an equivalent to a new SMN gene to the individual. The therapy is only delivered one time. As far as it is known, the neurons are very stable they don’t replicate. There is one example using an AAV vector in a Duchene Muscular Dystrophy model in a dog that persisted for at least eight years. When they sacrificed that dog they found that gene in almost every muscle. With the single dose idea we should be careful, not to think of it as a cure, this is not exactly a cure, rather a single time dose. Once the dose is administered you become immune to the virus, thereby immune to the vector. If a patient were to receive a second dose it would inactive the virus. The patient probably wouldn’t notice anything, you just wouldn’t deliver the transgene into the cell like you thought you did. Immunity to AAV is prevalent in the community, approximately 10-15% of people are immune. Patient population that is being treated would be lower just because of age. For example we test any patient that we consider delivering this therapy to for antibodies to AAV9. If a patient has the AAV9 antibody, they cannot receive the therapy.

There are a number of other issues in comparison to Spinraza. There are safety issues with Zolgensma that aren’t relevant to Spinraza. Spinraza is administered via lumbar puncture four times in the first two months of treatment and then every four months thereafter. There are very few side effects related to the Spinraza treatment, it is very clean. Most of the issues that arise with Spinraza are related to the complexity of the spinal tap.

Zolgensma, there are lots of risks, mostly with the liver. Patients are treated with high doses of steroids to limit the effect on the liver. Patient will present to clinic for dose of prednisone prior to infusion and will stay on prednisone for about a month if the liver function tests return to normal the patient will begin to taper the steroid over another month. So far, that has protected most patients.

Dr. Butterfield stated he knows of one case in Colorado, a six month old patient went into acute liver failure. Patient had been receiving Spinraza for about 5-6 months and then received a dose of gene therapy under an early access program. The patient had pre-existing elevated LFT’s, had a GI consult that felt like it was ok to proceed, proceeded with gene therapy, they steroid was tapered a little early and about six weeks they had a spike in liver enzymes and coagulopathy and pretty typical acute liver failure. The steroid was restarted and the patient recovered without any issues. That is the data as of week of July 1, 2019. Dr. Butterfield stated this is the only case he is aware of where a patient had a severe reaction to the drug.
Dr. Butterfield stated there is a real concern and risk with the use of Zolgensma. From an efficacy standpoint Dr. Butterfield states this product works beautifully and very well. One published study that was submitted to the FDA for approval 15 children three at a lower dose and 12 at a higher dose, which is the dose that is currently being delivered. 12 kids were treated around two to three months old and most of them did very well with the treatment.

Dr. Butterfield stated there is no direct comparison with Spinraza mostly due to the ages at which the patients were treated were pretty different between the clinical trials. There is no way to say if one therapy is better than the other. There are some poorly designed studies going around that may suggest the gene therapy is better, or might be better. Families are more interested in it mostly due to the single dose and not having to return for multiple spinal taps.

There are currently three unpublished studies. One consists of 25 children that are predicted type I SMA kids, presymptomatic, just finished enrollment and will be a pivotal study because these are the kids that they are mostly targeting before symptoms arise. Any of these drugs are far more efficacious before symptoms arise. Anticipating data in about one year. There is another study in type I infants that finished enrollment in the fall of 2018 with about 25 kids, anticipating data winter of 2019. Preliminary data looks about like the first study. Patient’s motor function and motor development continue to do very well, not quite on a normal trajectory. A third study in older children, in predicted type II SMA and type III SMA patients with three or four copies do the SMN2 gene. This study is a different creature, therapy is administered intrathecally and is designed to assess what the gene therapy would look like in older individuals. The study fully enrolled in February 2019 and Dr. Butterfield has treated three patients in that study, and they are opening up a second cohort. Anticipating data on this study in spring 2020. Dr. Butterfield states the patients he knows are doing amazing.

b. Board Discussion: Jennifer Strohecker inquired about the newborn screening and asked the board if any anyone was aware of this. Dr. Butterfield responded stating Utah is the first state to do newborn screening for SMA. It began in January 2018, it was clear very early that earlier treatment had better outcomes with Spinraza. With SMA once you lose a motor neuron it is gone, it will not recover. In a symptomatic patient we are stopping the progression of the disease but most patients with SMA are born without symptoms. Even a type I SMA patient who’s almost completely paralyzed at two months of age is at two weeks of age almost normal. The newborn screening is a simple process, genetic test which 95% of patient have the same genetic mutation. The technology already existed in the state lab. The cost was $3 difference in the kit fee, for about $150,000 every patient in Utah is tested. Through this test, they have identified about 4 patients which is a little short of the expectation. The test is administered before the patient leave the hospital, it takes about two days to get from the baby to the state
lab and then reported to Dr. Butterfield around day six or seven. The notification goes to the primary care physician and then to Dr. Butterfield with the intent that Dr. Butterfield will connect with the primary care physician and arrange a follow-up in the next day. Depending on circumstances the goal is to initiate treatment within one to two weeks after the follow-up, within 21 days of age. For the most part, they are meeting that goal. Most recent positive came at the end of May and was dosed this week with gene therapy and the child was predicted type II SMA so they didn’t push hard for timing.

Joe Busby inquired about continuation of treatment and the board at the University that reviews these patients. Dr. Butterfield responded stating that initially with the medications Exondys and Spinraza they established a neurology therapy board/committee within the University to assess from a medical standpoint the appropriateness of treatment with some of these therapies. Not necessarily a board with neuromuscular experts because Dr. Butterfield is the only neuromuscular expert but he is not part of the board, rather he is presenting to the board. The board consists of two pediatric neurologists, an adult neurologist, a pulmonologist, an ethics committee member. Dr. Butterfield present a clinical picture of the patient and why the therapy is appropriate. They have started looking at re-approvals and why the patient is appropriate to continue therapy. Jennifer Strohecker inquired as to whether or not this board would been within 21 days. Dr. Butterfield stated they meet monthly and ad-hoc as needed.

Joann LaFleur inquired about the potential for false positives with the genetic tests. Dr. Butterfield responded stating there is very little risk for false positives. In the history of the screening the very first case was a false positive. There was some fine tuning of the test and have not had any issues since. Dr. Butterfield stated there are more states implementing the newborn screening test with the genetic test for SMA.

Jennifer Brinton inquired about how it is determined whether the patient receives the gene therapy or the plasma therapy. Dr. Butterfield’s response is there are a few factors but the one real definitive factor is if the patient has AAV antibodies which makes the patient ineligible for gene therapy. Beyond that is parent choice and risk levels, and the tradeoffs with the risk to the liver versus the ongoing spinal taps.

Bryan Larson asked what Dr. Butterfield’s thoughts were on the treatment of type III and type IV SMA. Dr. Butterfield stated newborn screening has changed the thinking in these types of SMA. The types of SMA do not fit the clinical situations presented. In practice, there are presymptomatic kids for the most part, but now we are talking about those kids that two, three or four copy number for SMN2 and those are predictive pretty well but not 100%. Usually if a patient
violates the rule that we would expect a type III to have four copies, the patient’s condition is milder, and working a little but under probabilities. Most patients with type III become symptomatic in childhood but can become symptomatic well after that. If they become symptomatic well into adulthood they are considered type IV. Regardless of the type of SMA, it is all SMA with different levels of severity. Dr. Butterfield believes every patient with SMA should be treated with some therapy. Treatment as is transformative for the symptomatic type III patients. Type III patients are just followed clinically until there is a need for treatment.

Jennifer Brinton asked about the diagnoses information “Spinraza requiring SMA I or SMA II and on Zolgensma it talks about 5q SMA homozygous gene mutation or homozygous gene deletion of SMN1 and fewer than four copies of SMN2”, she asked Dr. Butterfield if this excludes the type III patients that could benefit from treatment. Dr. Butterfield states that it would and needs some fine tuning. He also stated some of the criteria should match on both prior authorizations for example assessment of motor function, laboratory testing and baseline etc. He also suggested changing the language about the type of SMA to be more copy number driven. He advocates to include four copies. Jennifer Strohecker clarified that it should not state fewer than, Dr. Butterfield agreed. Dr. Butterfield stated nine kilos was the beginning number but the weight and other elements should match the label.

Jennifer Strohecker requested input from Dr. Butterfield on treating patients with Zolgensma after using Spinraza. Dr. Butterfield doesn’t believe that there would be any Medicaid recipients affected by this. Jennifer Brinton wanted to clarify if the patient received the plasma therapy, they are not eligible to receive the gene therapy. Dr. Butterfield stated that there is no reason the patient couldn’t receive both treatments, rather they shouldn’t. He stated to leave the criteria that if you have received Zolgensma, you shouldn’t receive Spinraza.

c. **Board Action:** Jennifer Brinton motioned to approve the prior authorization criteria, Sharon Weinstein seconded, unanimous approval as follows:
   i. Zolgensma
      1. Diagnosis change the language of fewer than to include less than or equal to four copies
      2. Change weight to match the label, 13kg
      3. Change the language for “motor assessment…” to age appropriate assessment of motor function
   ii. Spinraza criteria:
      1. Diagnosis change the language of fewer than to include less than or equal to four copies
      2. Change the language for “motor assessment…” to age appropriate assessment of motor function
d. **Public Comment:** Kaysen Bala, Medical Liaison for Biogen presented clinical information on Spinraza.

5) **U of U Retrospective DUR work, 2018:**

e. **Information:** Joann LaFleur presented a comprehensive slide deck on the Drug Regimen Review Center at the University of Utah’s retro DUR work for 2018 with in depth information and data to show patient reviews, DUR Board Reviews and P&T Committee Reviews. The DRRC has worked with Utah Medicaid since 2001 to provide robust support to the program for its DUR Board and P&T activities, including the following:

i. Conducting retrospective, patient-level drug utilization review of the drug therapy of Utah Medicaid patients who meet criteria for high risk or utilization;  

ii. Supporting the Medicaid Drug Utilization Review (DUR) Board’s requirement to conduct retrospective and prospective drug utilization review by providing reports of patient-level utilization and evidence-based recommendations for minimizing risks of future drug therapy problems (DTPs); and  

iii. Supporting the Utah Medicaid Pharmacy and Therapeutics (P&T) Committee by providing systematic reviews of the evidence for comparative safety and efficacy for medications under consideration for inclusion on Medicaid’s preferred drug list (PDL).

f. **Public Comment:** none

g. **Board Discussion:** Eric Cannon commented on ROI

h. **Board Action:** none

6) **Pharmacy Policy Changes:**

i. **Information:** July 1, 2019 policy updates- high dose MME threshold reduced from 180 MED to 150 MED; implementation of an opioid-benzodiazepine edit for concurrent use of long-acting opioids with a benzodiazepine medication; implementation of and edit that restricts the use of opioids to 7 days or less in pediatrics without a PA or cancer diagnosis. Truvada prior authorization criteria removed.

j. **Public Comment**

k. **Board Discussion**

l. **Board Action**

7) **Public Meeting Adjourned:** Neal Catalano motioned to close the meeting. Eric Cannon seconded the motion. Unanimous Approval.

8) **The next meeting scheduled for** Thursday, August 08, 2019 Pharmacy Quality Measures.

Audio recordings of DUR meetings are available online at:  