



STATE MEDICAID DUR BOARD MEETING  
 THURSDAY, September 11, 2008  
 7:00 a.m. to 8:30 a.m.  
 Cannon Health Building  
 Room 125



## MINUTES

**Board Members Present:**

**Mark Balk, PharmD.**  
**Wilhelm Lehmann, M.D.**  
**Joseph Miner, M.D.**  
**Dominic DeRose, R.Ph.**  
**Bradford Hare, M.D.**

**Peter Knudson, D.D.S.**  
**Derek Christensen, R.Ph.**  
**Bradley Pace, PA-C**  
**Colin VanOrman, M.D.**

**Board Members Excused:**

**Neal Catalano, R.Ph.**  
**Joseph Yau, M.D.**

**Tony Dalpiaz, PharmD.**

**Dept. of Health/Div. of Health Care Financing Staff Present:**

**Jennifer Zeleny**  
**Lisa Hulbert**  
**Carol Runia**

**Tim Morley**  
**Duane Parke**

**Other Individuals Present:**

**John Stockton, Genentech**  
**Felicia Fuller, Bigen Idec**  
**Emily Trone**  
**Steve Hill, SP**  
**Jeff Buel, Johnson & Johnson**

**Ben Focht, Amylin**  
**David Young, U of U**  
**Ben Campbell, DRRC**  
**Ron Robinson, Pfizer**  
**Don McNaul, Elan**

**Bob Halter, Amylin**  
**Ann Lingard**  
**Cody Wardell**  
**Sabrina Aery, BMS**  
**Alan Bailey, Pfizer**

Meeting conducted by: Colin VanOrman, M.D.

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1. Minutes for August 14, 2008 were reviewed, corrected and approved. The motion to approve the minutes was made by Mark Balk and seconded by Dr. Miner. The minutes were unanimously approved by Dr. Miner, Dr. VanOrman, Derek Christensen, Dr. Hare, Mark Balk, and Dr. Knudsen.
  2. Introduction of New Member: Dr. Peter Knudson will be serving as the dentist on the DUR Board.
  3. Hyper-Sal vs Pulmozyme - Step Therapy PA: Dr. Young from the University of Utah addressed the Board. He provided a handout from the CF Foundation that has evidence-based guidelines for maintaining lung health in CF patients. They listed chronic medications,

ranked the evidence, and analyzed the type of evidence available on lung health. Hypertonic Saline is an interesting therapy for CF. Salt water is not a new concept. It came from Australia. The CF centers noticed that some of their patients were doing better than others, and discovered that they were surfers. They thought that the salt water they were inhaling was perhaps helping them and constructed a trial. There is not a lot of evidence on hypertonic saline, but it does have an evidence grade of B. The Cochrane review is dated, and does not show the best trial, which was from 2006 and conducted by the Australians. This largest trial had n=164, which is quite large for a CF study. All of the other trials preceding this were done over a 2 or 12 week period. This trial was done over 48 weeks. They found that there was a significant 6% increase in FEV1 by the end of the trial. There are 4 main therapies used in CF. Hypertonic saline is one, dornase alpha (Pulmozyme) is another, Tobi is another, and azithromycin is another. Those are the "big 4" in CF care. The Elkin study also had a significant 56% reduction in exacerbation for CF. The standard hospital admission for a CF patient is 14 days, so a 56% reduction in exacerbations is significant. They also had a 47 day exacerbation-free period, keeping patients out of the hospital longer. They had 39 fewer antibiotic days. There was a 17 day difference between the hypertonic saline group and the normal saline group for missed days of work and school.

Hypertonic saline does not work like Pulmozyme. None of the trials on hypertonic saline discontinued Pulmozyme. It would probably be unethical to do that, since Pulmozyme is considered standard therapy. It was used in addition to Pulmozyme. The patients in the trials were on both, and they still saw striking benefits. Pulmozyme and hypertonic saline are different pharmacologically. Their underlying mechanisms are totally different. They both target mucolysis, but they do it in totally different ways. Pulmozyme does it by breaking up the DNA bonds in the mucous. Research shows that hypertonic saline actually builds up the apical layer of water in the lungs, and increases the mucociliary clearance of mucous. At this point, they are additive to each other.

The reason that products like Hyper-sal are used rather than having patients mix their own concentrations is because they are safer. They come in unit-dosed ampules. This is preferable to having patients mix their own hypertonic saline because patients can contaminate their products.

Tim asked if the products are supposed to be used together or as a step therapy. Dr. Young stated that there are no guidelines on which product to start first or whether to start them together. The University has some patients on one, some patients on the other, and some patients on both. Some patients that tolerate one will not tolerate the other. The University has patients try it in the clinic and follows up with spirometry to see the level of benefit that the therapy is providing and that they are handling it well.

Tim asked if any nebulizer works. Any nebulizer can be used to administer Hyper-sal.

Tim stated that the dilemma for Medicaid is that Hyper-sal is listed by the FDA as a medical device. As such, it is not eligible for a rebate. If Medicaid were to pay for it, all State funds would need to be used. Medicaid is currently researching if there is a possibility for a federal match. At this point, it does not look like there is a possibility for a federal match.

Medicaid has tried to identify the level of usage of Hyper-sal. At this point, it does not look like it is being dispensed very much through the pharmacy POS system. Utilization data for Pulmozyme has been included for the Board's information.

Dr. Young stated that utilization of Hyper-sal, on a national level, is trending upward. The good news is that Hyper-sal is the cheapest of all of the chronic drugs given for CF. The cash price for Hyper-sal is approximately \$60. The cash price for Pulmozyme would be close to \$3,500 and Tobi would be \$4,000.

Duane asked if there is a reduction in Pulmozyme when Hyper-sal is used. This doesn't tend to happen, since they are not meant to replace one another and work by a totally different mechanism. There is an additive benefit from doing both together.

The Board asked how long this drug has been out. Hyper-sal, as a brand, is relatively new. Studies for hypertonic saline go way back. There are abstracts that are quite old. In the past, people shied away from hypertonic saline due to the bronchospams that could occur. This is why therapy is initiated in clinic, and bronchodilators are provided to patients prior to initiating therapy. Use didn't start ramping up until this study from 2006. It was also difficult to teach patients how to mix the saline.

The Board asked if there is evidence of a reduction in healthcare costs for patients receiving hypertonic saline. There is evidence that this reduces exacerbations by 56%, which can mean that a significant number of patients is kept out of the hospital. They also had fewer antibiotic days, and that includes in and outpatient antibiotics.

The Board asked Tim what the options were. He stated that the Board can choose to cover it with all State funds, control the use through a PA, or restrict the use to a physician's office. Dr. Young's testimony seems to indicate that it is intended for use in the home, so that may not be a rational approach either. In order to take advantage of a therapeutic benefit, Medicaid would likely need to cover it with all State funds.

Dr. Knudson asked about the budget impact of covering Hyper-sal with all State funds. Medicaid is not allowed, by law, to discuss cost until the deliberations about PA are completed.

Dr. Young stated that the order of therapy is important as well. First, the bronchodilator is given, then Hyper-sal, then Pulmozyme, and then an antibiotic. This is listed on the handout. It does not mean the order in which the therapy is initiated; it means that this is the order in which the patient is meant to administer the medications. Hypertonic is listed before Pulmozyme because it seems to give more benefit by rehydrating the bronchial tree first before using the Pulmozyme.

Derek moved to cover Hyper-sal with no PA and covered with all State funds. Dominic seconded the motion. The motion was unanimously approved by Dr. Miner, Dr. VanOrman, Derek Christensen, Dr. Hare, Mark Balk, and Dr. Knudsen, Dr. Lehmann, and Dr. Hare.

Now that the motion was passed, Tim provided financial information about Hyper-sal. Tim stated that in the last fiscal year, Medicaid has expended approximately \$482 for Hyper-sal and \$1million for Pulmozyme alone.

Medicaid thanked the University for making a presentation to the DUR Board. It had been suggested to Medicaid that Hyper-sal could be a replacement for Pulmozyme, which is clearly not the case. By counting prescriptions, it looks like the same number of prescriptions as were filled for Pulmozyme during the last fiscal year would have cost the

state approximately \$200,000. That may not be a good conversion, but it's a rough figure to consider as a potential liability to the state on a yearly basis.

Duane suggested that Medicaid could track the utilization of these agents against the rate of hospitalization for the CF population. The amount of expenditures on the Hyper-sal could easily be saved by preventing a small number of hospitalizations.

4. Zyvox PA: Dr. Pearl addressed the Board. Dr. Pearl is a pulmonary critical care physician who works at LDS Hospital, an adjunct professor at the University in pulmonary critical care. He has been in Utah working for the University for 34 years, and working for LDS Hospital for 30 years of that time. He has the opportunity to see a lot of patients in whom MRSA and VRE are becoming very serious problems. There are 4 types of MRSA: USA 100, 200, 300, and 400. 100 is a common outpatient bacteria, which is now responsible for a high number of outpatient cellulitis, skin abscesses, and wound abscesses. 200 is less of a problem, but a much more highly resistant bacteria that is not susceptible to Septra. 300 and 400 are nasty bugs that come in the hospital. They are highly resistant. Fortunately, in this country, there are only a few cases of Vancomycin-resistant MRSAs, but they are coming. There have been a number of cases in Chicago and some other big cities. They are really nasty bugs, and may be prevalent in the Orient, although there is no good data on that. VRE is a really common bug for people who have been hospitalized for any period of time. Vancomycin-resistant enterococci come in two types, both of which are pretty difficult to deal with. Vancomycin-resistant enterococci are fairly sticky, so it has a tendency to stick to prosthetic limbs and heart valves, and is very difficult to eradicate. Once somebody is colonized by that, they are prone to get infections and systemic disease from it. Zyvox is one of a couple of antibiotics that is available for these highly resistant and nasty organisms. There are Wall Street Journal lead articles on MRSA. Several years ago, there was an outbreak of MRSA in an NFL team's locker room. Five team members were hospitalized, and they are strong and tough guys. He has never been aware of any misuse of this antibiotic. It has an advantage in that it can be given IV to a patient that is very sick, and then converted to oral. Orally, it has good penetration and tissue penetration. This year he has had 6 cases of community acquired MRSA pneumonia. 3 years ago, he never had any, so it is becoming a big problem. These were all ventilated ICU patients, and all came in with that particular bug. Without that antibiotic to treat it, there will be a higher mortality and longer hospital stays. Comparing its price to Vancomycin, which works for most MRSAs, it is less expensive. It can also be given orally, so there are no issues with IV access or maintaining a PICC line. Prescribers do not have to deal with the issues of ototoxicity and renal toxicity and having to adjust levels, so it is a very useful drug with high penetration into skin, lung tissue, and organs, and it works very well. There have been a number of studies that demonstrate that Zyvox is more cost effective as an outpatient drug than Vancomycin. He is not aware of any clinical misuse of Zyvox.

Tim Morley stated that one of the major concerns is the development of resistance. Dr. Pearl stated that so far there has been no resistance reported with MRSA. It has a mechanism that actually kills the staph in two different ways. The staph has not, to date, been able to develop resistance. In VRE, there is a small amount of resistance that has developed, probably around 2% nationwide. There has not been a case in Utah, to his knowledge. Zyvox will be used outside the Medicaid population, so on a global basis one needs to think about whether or not managing utilization in a minuscule number of patients will have an effect on global resistance patterns.

Tim asked if it is standard therapy to test for the nature of the organism prior to initiating therapy on Zyvox. Dr. Pearl stated that in pneumonia, if someone comes in and is not particularly sick, they will receive the typical community program, which is Rocephin and azythromycin. If someone very sick comes in, and they have been in a nursing home or been hospitalized, they would get Zyvox immediately. The data is impressive that an appropriate first choice of antibiotics saves lives, reduces hospital stays, reduces ICU stays, and reduces intubation times. If someone comes in and is not particularly sick, they would not receive Zyvox until there was culture data to support it.

Dr. Miner asked if the question is whether or not to require PA. Dr. Miner asked if it was possible to require a PA if the prescriber was not an intensivist, critical care, pulmonary, or infectious disease specialist. He is concerned about it being handed out too freely in local clinics, without properly identifying the organism.

Dr. Pearl stated that getting good culture data in the community is difficult. If someone has progressive cellulitis, it is difficult to tell whether it is a resistant organism. Dr. Miner responded that much of the community acquired MRSA is sensitive to clindamycin, which is a much less expensive antibiotic. Dr. Pearl stated that it would be appropriate to ask for a failure on clindamycin or Septra out in the community prior to initiating Zyvox. However, he did not feel that there was evidence of inappropriate utilization in the community.

Tim Morley stated that utilization in the hospital is not under the purview of the DUR Board, since inpatient drugs are covered under a DRG, or diagnosis related group. Hospitals also have protocols to ensure appropriate utilization. The DUR Board mostly deals with the patients that are out in the community. Does the DUR Board have a responsibility to appropriately utilize this drug and not be using it in a way that results in the selection of resistant organisms. Should Medicaid have wide open access to Zyvox, or should Medicaid require something else first, out of the gate.

Mark Balk asked if it was possible that patients being treated in the community are receiving a continuation of therapy that was initiated in the hospital. Tim stated that the PA nurses would know if a drug was being given as a continuation of therapy that was initiated in the hospital. There are several other drugs that require PA, where a PA is given as a continuation of therapy initiated in the hospital.

Dr. Pearl stated that it creates problems and frustrations to have to get a PA on a weekend for a patient that needs to be discharged. Tim stated that these patients are the exception and not the rule. There are mechanisms to address these situations, and Medicaid will work with the pharmacies to get the drug paid on a Monday if they made a decision to dispense a drug given the circumstances.

The Board asked if Medicaid is seeing the 4-day work week impact the PA process. Tim stated that the PA nurses have their work schedule in statute and work 5 days per week from 8-5.

Dr. Lehmann stated that, from the primary care perspective, the trend had been that new antibiotics would surge to the top of utilization almost immediately and resistance would be seen shortly after that. It seems that the word got out to not use Zyvox indiscriminately and to reserve it only for special cases. This probably has something to do with why there has not been much resistance seen to date. Dr. Pearl added that this probably also has something to

do with bacteriologic mechanism of action.

Dr. Pearl asked if Medicaid has seen high utilization of this antibiotic. Tim stated that 117 patients have used it with 403 prescriptions in the last year. Use appears to be increasing, possibly due to the increase in MRSA.

Dr. Miner stated that Utah Valley Regional Medical Center had to institute internal controls for utilizing Zyvox due to concerns that it was being over utilized. Dr. Pearl stated that he had seen internal controls at LDS, but they were dropped because there seemed to be no over utilization.

The Board asked if Zyvox was being promoted more heavily. It does not appear to be promoted very heavily. Dr. Pearl stated that he has only ever seen it being promoted for highly select cases.

Dr. Hare stated that the discussion seems to indicate that the antibiotic is almost too good to be true. He was concerned that opinions may change to “why not use it?”. Dr. Pearl stated that this is a very narrow spectrum antibiotic, so it is not a good choice to treat an infection without knowing what is being treated. A new strategy is to try to identify the infection being treated as soon as possible and de-escalate therapy as quickly as possible after the infection is identified.

Tim asked if it makes sense to export this strategy into the community. Dr. Pearl hasn't had a perception that there is inappropriate use. He asked Tim if there was a sense that inappropriate use is increasing. There is only a sense that utilization is increasing, but there is no way to tell whether it is appropriate utilization.

Dr. Hare suggested that perhaps utilization could be monitored for 3-6 months. If utilization seems to be increasing sharply, it could be brought back to the DUR Board for further consideration. Dr. Miner seconded the motion.

Mark Balk suggested that Medicaid could return with utilization data broken out by which type of specialist is prescribing the medication, to see if it is a type of specialist that is likely to use it correctly.

Duane suggested that perhaps a 3 day course could be left open without a PA to give physicians an opportunity to culture the infection. The Board felt that this would not be helpful, since many patients who do well on Zyvox do not have a positive culture. It is also impractical to culture all patients who receive antibiotics in the community.

The Board voted unanimously to monitor utilization, as per Dr. Hare's original motion, for a 6 month time period. The motion was unanimously approved by Dr. Miner, Dr. VanOrman, Derek Christensen, Dr. Hare, Mark Balk, and Dr. Knudsen, Dr. Lehmann, and Dr. Hare.

5. Byetta - PA Review: Rob Halter, PharmD., with Amylin Pharmaceuticals addressed the Board. He is requesting that Byetta, a novel therapy for patients with Type II diabetes mellitus, be added to the Utah Medicaid PDL. Byetta has been available in the US market for 3 years. It is approved for use with a combination of the most commonly used generic agents, metformin and sulfonoureas, and also TZDs. Byetta has powerful efficacy, as evidenced by long term clinical trials, a favorable safety profile, and is easy to use without

additional management. Clinical trials with Byetta 10mcg bid demonstrate powerful A1C reduction with weight loss, and in a recent 30 week pivotal trial there was a 1.5% A1C reduction as compared to active comparator, and a weight loss of 8lbs. The majority of patients have A1C benefit at 3 years, 78% have an A1C reduction at 3 years, and 84% have weight loss. Byetta has similar efficacy in comparison with insulin glargine in randomized controlled clinical trials, ranging between 1-1.4% reduction in A1C. Additionally, Byetta reduced the weight, while insulin glargine caused weight gain. Up to 4 times as many patients reach goal of 7 or below with Byetta. Durability - diabetes is a progressive disease, and Byetta has shown sustained A1C control. Significant reductions were seen by week 12, and sustained over a 3 year period. An increased risk of hypoglycemia has not been seen in combination with metformin or TZDs; less hypoglycemia than insulin glargine in a crossover study. In addition, Byetta did not increase cardiovascular risk factors. In fact, it increased HDLs, lowered triglycerides, and lowered systolic and diastolic blood pressure in clinical trials at 82 weeks. The label was updated in October 2007, in regards to pancreatitis. This information contained within the label is not new to Amylin, and is currently bolded under the precautions sections of the label. An independent analysis of claims shows that when Byetta is available without restriction, it is being appropriately utilized by physicians for patients with diabetes, and after failure of cheaper oral agents. Byetta is simple to use, comes in a fixed-dose pen injected twice daily before meals. Overweight and obesity rates are helping to fuel the diabetes epidemic. A1C reduction and weight loss are important to diabetes management. Byetta can help patients in the state of Utah powerfully and safely lower A1C and lower weight.

Tim Morley clarified that PDL issues are not being considered at this meeting. The Prior Authorization requirements for both Byetta and Symlin are under review. Both drugs are currently under PA, and the Board is doing the required review to determine whether or not they should remain under PA or if the PA requirements need to be changed. Tim clarified that Byetta is not indicated for weight loss, but it does cause weight loss. Medicaid is not able to pay for drugs for weight loss. It also not to be used as a first-line treatment for diabetes, and meant to be used as an adjunct therapy with sulfonoureas, metformin, or TZDs. Dr. Halter clarified that there is an application with the FDA pending for Byetta to be used as monotherapy.

Tim Morley stated that the Byetta PA seems to be working. He was in the home of a neighbor who stated that her doctor had put her on Byetta for weight loss. She is not a Medicaid client and not diabetic, so it is an indication that the use is out there.

The Board was provided with a packet that contains the current PA. Mark Balk asked if there is a pediatric indication. There is no pediatric indication, but there is a study that has been conducted down to age 17. There are some kinetic studies in 12-16 year olds, but no safety and efficacy data in that age group.

Duane Parke asked about the deaths that have been reported in some of the Byetta studies, and asked if there will be a change in labeling as a result. Dr. Halter stated that the deaths did not occur in any of the studies. They occurred in the post-marketing surveillance of the drug. Pancreatitis has been in the Byetta label ever since the drug came out in 2005. In 2007, Amilyn actually updated the label to bold the pancreatitis in the warning section of the label. This is not because pancreatitis is caused by Byetta, but because some of the side-effects of Byetta are nausea and vomiting. The way that pancreatitis presents is with nausea, vomiting, and abdominal cramping. Amilyn wants to make sure that the true cases of

pancreatitis are not being missed and attributed to Byetta's side effects. Since 2005, there were 2 cases of pancreatitis-related deaths. All that is known is that these were patients who had pancreatitis and were on Byetta. One individual was a 400lb man. The three main causes of pancreatitis are gallstones, a history of alcohol abuse, and a history of high triglycerides. This person, upon autopsy, was shown to have gallstones. The other individual had concomitant disease states and had stopped their Byetta two months prior to entering the hospital for pancreatitis. Byetta's rates of pancreatitis are 0.34 events per 1,000 patient years. The incidence rate for type II diabetes alone, in non Byetta users, ranges from 0.33 to 0.44. Even at the lower end of Type II diabetes in general, Byetta is in line with the rates. Amilyn is very confident in the safety of this drug.

The Board asked if Amilyn recommends additional monitoring. There are no specific recommendations that he knows of that are being discussed with the FDA.

The Board questioned the wording of the criteria point that states that Byetta is not meant to be used as a replacement for insulin. Tim stated that the statement is meant to convey that this is not meant to be used for Type I diabetes instead of insulin. Mark Balk stated that this was probably put in there because this was one of the first injectable drugs to come out for the treatment of Type II diabetes specifically, and there were concerns about provider confusion.

Mark suggested that the current PA criteria could be cleaned up. He suggested removing the repetitive statements that it is not being used instead of insulin by stating that it is to be used for Type II diabetics. He also suggested cleaning up the language that states what Byetta should be used with by stating that it is to be used as an adjunct therapy with sulfonourea, metformin, or TZD or a combination of these all in one sentence. He also suggested that the last bullet point stating that information showing lack of glycemic control as indicated by an  $A1C > 7$  be cleaned up. If there was someone with an  $A1C < 7$  who as on Byetta and an oral agent and was showing good glycemic control, it wouldn't be prudent to take them off Byetta because they were under control. Dr. Miner stated that it is appropriate to require an  $A1C > 7$  at initiation, but if a patient drops below 7 on the therapy that is the goal. The criteria should be changed to reflect that the  $A1C$  of 7 or greater is required at initiation of therapy. Some other professional groups suggest a lower  $A1C$  level of 6.5 as indicative of a lack of glycemic control. The Board felt that 7 was an appropriate level.

Tim Morley stated that Byetta is not indicated for use with insulin. Therefore, the exclusion of concomitant use with insulin should be kept in the criteria. It was suggested that perhaps only the point about not using Byetta as a substitute for insulin be removed for clarity and cleanliness of the criteria.

Dr. Halter asked if a monotherapy indication would be added to the criteria if it were to be approved. If this indication comes out, the DUR Board will re-address the matter.

Mark Balk moved to accept the criteria as amended. Dr. Miner seconded the motion. The motion was unanimously approved by Dr. Miner, Dr. VanOrman, Derek Christensen, Dr. Hare, Mark Balk, and Dr. Knudsen, Dr. Lehmann, and Dr. Hare.

Symmlin discussion was postponed due to lack of time.

Meeting adjourned.

The DUR Board Prior Approval Subcommittee did not consider any petitions this month.

Minutes prepared by Jennifer Zeleny