

# Wyoming Drug Utilization Review

## Neonatal Abstinence Syndrome

*Muriah Kayser, 2016 PharmD Candidate*

Neonatal Abstinence Syndrome (NAS) is a clinical diagnosis, and is the result of abrupt discontinuation of chronic fetal exposure to substances that were abused or misused during pregnancy.<sup>2</sup> NAS is characterized by hyperirritability of the central nervous system (CNS) and dysfunction in the autonomic nervous system (ANS), gastrointestinal tract (GIT), and

respiratory system.<sup>1</sup> When left untreated, NAS has the potential to cause serious illness (e.g., diarrhea, feeding difficulties, weight loss, and seizures) and death.<sup>1</sup> The incidence of NAS continues to increase as mothers use opioids during pregnancy.<sup>2</sup> Heroin abuse remains stable, but is more common among mothers who are unmarried, unemployed, less educated, and less insured.<sup>2</sup>

Methadone has become the standard of care for mothers with opioid addiction during pregnancy and has shown to decrease illicit drug use, improve fetal outcomes, and optimize obstetric care.<sup>2</sup> Buprenorphine, has been found to be equally effective and as safe as methadone in the treatment of opioid addiction in pregnant women.<sup>2</sup> In addition to

opioids being used during pregnancy, psychotropic medications to control depression and anxiety have increased over the last decade, along with the use of methamphetamines and inhalants.<sup>2</sup> Prior to the 1970's, NAS was considered secondary to either morphine or heroin use, but now, NAS may be secondary to morphine, heroin, methadone, buprenorphine, prescription opioid analgesics, antidepressants, anxiolytics, and/or other substances.<sup>2</sup> An article from the Indian Journal of Pediatrics studied the effects of substance misuse in pregnant mothers and the impact it had on their newborns.<sup>3</sup> The study found the higher the dose of methadone (greater than 20mg/day), the more likely the infant was to suffer with NAS.<sup>3</sup> Also, if infants did not exhibit signs of NAS within 72 hours, it was very unlikely that they would develop NAS requiring treatment and could be discharged home safely.<sup>3</sup>

Treating neonates with NAS requires careful monitoring and diligent efforts by the medical team.<sup>2</sup> Every four hours while the infant is awake and after the infant is fed, the Finnegan scoring system should be used for opioid and non-opioid withdrawal assessment.<sup>2</sup> Nonpharmacologic options to treat these neonates should be considered first-line.<sup>2</sup> Management includes gentle handling, demand feeding, and careful avoidance of waking the sleeping infant.<sup>2</sup> Breastfeeding has been shown to be associated with increasing mother-infant bonding, enhancing maternal confidence, and encouraging maternal participation.<sup>2</sup> Ultimately, active maternal participation is the best nonpharmacologic care.<sup>2</sup>

Pharmacologic treatment of these neonates include morphine, methadone, buprenorphine or phenobarbital.<sup>2</sup> Morphine decreases the incidence of feeding, eliminates diarrhea, decreases agitation, and can control severe symptoms.<sup>2</sup> Morphine may prolong

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## P & T Committee Meeting Update

The P&T Committee met for its quarterly business meeting on February 11, 2016.

Highlights of this meeting include:

CMS is requiring states to have an Access Monitoring Plan to ensure that policies are not limiting access to providers. Currently, Wyoming has nearly 100% of eligible pharmacies enrolled.

Praluent and Repatha will be approved for patients who are intolerant to statin therapy or are not at goal with a maximum dose statin for patients with heterozygous familial hypercholesterolemia. It will be approved for patients with homozygous familial hypercholesterolemia.

Brilinta will be approved for up to two years based on its new indication.

Intuniv and Kapvay will be approved for children with tics, without a trial of stimulant. Other clinical criteria and trial and failure of a short-acting agent still apply.

Movantik will be allowed for patients with cancer or in palliative care without a trial of Amitiza.

Viberzi will be approved for patients with IBS-D.

Rexulti will be non-preferred, requiring a 30-day trial of two preferred antipsychotics prior to approval.

The proposed prior authorization criteria will be posted for public comment at [www.uwyo.edu/DUR](http://www.uwyo.edu/DUR). Comments may be sent by email to [alewis13@uwyo.edu](mailto:alewis13@uwyo.edu) or by mail to: Wyoming Drug Utilization Review Board, Dept. 3375, 1000 E. University Avenue, Laramie, WY 82071. Comments should be received prior to April 1, 2016 for prior authorization criteria.

The next P&T Committee meeting will be held Wednesday, May 11, 2016 in Cheyenne. An agenda will be posted approximately two weeks prior to the meeting.

### *Neonatal Abstinence Syndrome, continued*

an infant's hospital stay because it needs to be given regularly and then weaned gradually.<sup>2</sup> Methadone is an alternative agent to morphine and due to its long half-life, titration may be difficult.<sup>2</sup> Buprenorphine is a new option that is given sublingually, but research is still lacking on support of this medication being used.<sup>2</sup> Phenobarbital is the drug of choice in nonopioid NAS and often used in combination with morphine, methadone, or in infants suffering from polydrug abuse.<sup>2</sup>

The New England Journal of Medicine, *Neonatal Abstinence Syndrome after Methadone or Buprenorphine Exposure*, examined which pharmacologic option used during pregnancy would lead to possible better outcomes with infants suffering with NAS. The study found that buprenorphine could be considered an alternative to methadone for the

treatment of opioid dependence during pregnancy.<sup>1</sup> The benefits of buprenorphine in reducing the severity of NAS in neonates suggest that it could be considered first line, but it is important for clinicians to think about the possibility of reduced adherence and the ceiling effect of buprenorphine compared to methadone.<sup>1</sup>

#### References:

1. Jones H, Kaltenbach K, Heil S, et al.. Neonatal Abstinence Syndrome after Methadone or Buprenorphine Exposure. *N Engl J Med*. 2010 Dec 9 [cited 2015 Oct 6]; 363:2320-31.
2. Kocherlakota P. Neonatal Abstinence Syndrome. *Pediatrics*. 2014 Aug [cited 2015 Oct 6]; 134 (2): e547-556.
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# Naloxegol for the Treatment of Opioid-Induced Constipation

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Opioid-induced constipation (OIC) is an ongoing problem in patients being treated for chronic noncancer pain with opioids. Counseling patients on bowel regimens are essential and will greatly increase their overall quality of life. When counseling patients on opioids for more than a few days on a bowel regimen, starting with an over-the-counter osmotic laxative, such as polyethylene glycol (Miralax®) is important.<sup>1</sup> These are well tolerated with less cramping than stimulants and safe to use for patients on chronic opioids.<sup>1</sup> If needed, the patient may switch or add a stimulant laxative (bisacodyl) to their treatment.<sup>1</sup> Adding a stool softener to a patient's regimen may not help the OIC, and it may just lead to "all mush, no push," since it does not increase GI mobility.<sup>1</sup> If these over-the-counter medications do not help enough, the suggestion would be to switch to an opioid antagonist, such as naloxegol or methylnaltrexone, and to continue incorporating lifestyle changes into their diet; fluids, fiber, prunes, or physical activity.<sup>1</sup>

Naloxegol (Movantik®) is a new medication approved in September 2014 for the treatment of OIC, chronic non-cancer pain.<sup>2</sup> This new medication is more cost effective and the preferable route of administration compared to other opioid antagonists for the treatment of OIC. A 30-day supply of naloxegol is about \$300 currently and may differ depending on insurance coverages.<sup>2</sup> This medication is a mu-opioid receptor antagonist derivative of naloxone that is specific to peripheral tissues (GI tract) due to pegylation that decreases passive permeability and CNS penetration at recommended doses. A recommended dose of 25mg orally once daily in the morning or 12.5mg orally once daily, only if the higher dose is not tolerated by the patient.<sup>2</sup> Patients with renal impairment (CrCl less than 60mL/min) or are taking other CYP3A4 inhibitors, such as clarithromycin or ketoconazole, should reduce the dose to 12.5mg once daily.<sup>2</sup> Taking this medication with a high-fat meal will increase oral absorption of this drug.<sup>1</sup> Therefore, it is important to take this medication one hour before or two hours prior after first meal of the day.<sup>2</sup> Prior to initiating

naloxegol, patients are to discontinue maintenance laxatives and only resume them on an as-needed basis after three days if necessary.<sup>2</sup> Discontinuation of therapy will occur when opioid analgesics are discontinued.<sup>2</sup> *Naloxegol for OIC in Patients with Noncancer Pain* article found that the use of rescue laxatives were least likely to be used in patients taking a 25mg daily dose than those taking 12.5mg daily.<sup>3</sup> A shorter time to the first post-dose spontaneous bowel movement and a higher mean number of days per week with one or more spontaneous bowel movements were observed with 25mg of naloxegol versus placebo in both studies (p<0.001).<sup>3</sup>

Some common adverse effects reported included abdominal pain (12-21%), diarrhea (6-12.9%), flatulence (3-6.9%), nausea (7-9.4%), vomiting (3-5%), arthralgia (6.2%), and headache (4-9%).<sup>2</sup> Patients who are contraindicated from using this medication includes those with known or suspected gastrointestinal obstruction or at an increased risk for recurrent obstruction, concomitant use with strong CYP3A4 inhibitors, or any hypersensitivity to naloxegol or any ingredients.<sup>2</sup> When talking to patients regarding the efficacy of their medication, it is important to ask about the relief of their constipation and if they are experiencing any severe or worsening abdominal pain.<sup>2</sup> It is also important to ask about any signs of withdrawal, especially if these patients have blood-brain barrier disruptions, such as patients with meningitis, epilepsy, or Alzheimer's disease.<sup>2</sup> Possible withdrawal symptoms include sweating, chills, diarrhea, abdominal pain, anxiety, irritability, and yawning.<sup>2</sup> Symptoms of withdrawal are more likely in patients who misuse their medication and take more than directed.<sup>2</sup> Within trials, the signs and symptoms of withdrawal were very rare and unlikely to occur.<sup>3</sup>

#### References:

1. PL Detail-Document, Treatment of Constipation in Adults. *Pharmacist's Letter/Prescriber's Letter*. June 2015.
2. Naloxegol: Micromedex [database on the Internet]. Ann Arbor (MI): Truven Health Analytics; 2105 [cited 2015 Oct 8].
3. Chey W, Webster L, Sostek M, Lappalainen J, Barker P, Tack J. Naloxegol for Opioid-Induced Constipation in Patients with Noncancer Pain. *N Engl J Med*. 2014 Jun 19 [cited 2015 Oct 8]; 370:2387-96.

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*March 2016*

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