2014
Vol. 27, No. 1

DUR DIGEST

The Bulletin of Medicaid Drug Utilization Review in Iowa

Long-Acting Opioid Use in Opioid-Naïve Patients

Long-acting opioids can be useful medications when trying to control a patient's pain allowing for better pain control due to their longer duration of action. Use of long-acting opioids in patients who are opioid naïve can be a cause for concern since it is a leading cause of death from respiratory depression in these patients. It is estimated, in 2010, that respiratory depression is the cause of death in about 16,000 opioid-related mortalities in the United States. While the use of any long-acting opioid in these patients can lead to death, fentanyl transdermal patch is the medication most likely to cause death from respiratory depression.

Several case reports have been published regarding use of fentanyl patch in opioid naïve patients. Use of fentanyl transdermal patch in opioid naïve patients often times results in death. Patients being treated for post-operative pain are those that seem to be the most susceptible. Death does not always occur when fentanyl transdermal patches are used improperly. Unfortunately, these deaths could have been avoided if proper prescribing practices were followed. Respiratory depression and risk of death seen in opioid naïve patients is increased when the patient has preexisting respiratory compromise, such as COPD and sleep apnea.

The FDA has issued multiple warnings and has taken several actions since 2005 to combat the use of long-acting opioids in opioid naïve patients. These actions include adding these medications to its risk evaluation and mitigation strategies (REMS) program in April 2011. A black box warning has been issued to be included on the packaging of all long-acting opioids about the risk of respiratory depression and death that can result from the misuse of these medications. Long-acting opioids are intended to be used in opioid tolerant patients. To be considered opioid tolerant, the patient must have been taking an opioid dose of 60mg morphine equivalents or more per day for a minimum of one week.

In September 2013, the FDA announced that they would require long-acting opioids to state that the use of these medications are indicated for severe pain management that is inadequately controlled with other treatment options and requires long-term, daily, around-the-clock opioid therapy. Very low doses of some long-acting opioids may be used successfully in opioid naïve patients without major adverse effects, but fentanyl transdermal patches and extended-release hydromorphone are contraindicated in these patients and should never be used due to the higher risk of respiratory depression associated with their use.

Prescribers should keep in mind a few simple guidelines when prescribing long-acting opioids for patients to protect themselves and adequately control the patients' pain.

- It is important to keep the whole picture of the patient in mind, as well as the adverse effects associated with these medications to avoid any unnecessary risk.
-

- When a patient is determined to be an appropriate candidate for opioid therapy, initiation of the medication should be done at the lowest dose and titrated upward to the lowest effective dose for each patient.
- Duration of use should be considered when reevaluating the patient's pain to ensure these medications are not used longer than necessary.

To obtain more guidance on safe prescribing of long-acting opioids the FDA has issued its Blueprint for Prescriber Education for Extended-Release and Long-Acting Opioid Analgesics which can be found at http://www.fda.gov/downloads/drugs/drugsafety/informationbydrugclass/ucm277916.pdf

Patient safety should be at the forefront of all prescribing practices, including when prescribing long-acting opioids. These medications can be valuable tools in controlling pain in patients who suffer from chronic pain issues. Prescribing and patient safety issues come into play when long-acting opioids are improperly used in patients whom the medications were not intended, including the opioid naïve and those with acute or post-operative pain. The main adverse effect of concern with use of these medications is respiratory depression that can lead to death. These outcomes could be avoided by following the warnings and guidance put in place by the FDA to maintain patient safety at all times.

Currently, non-preferred long-acting opioids are subject to prior authorization criteria as follows:

Prior authorization is required for all non-preferred long-acting narcotics. Payment will be considered under the following conditions:

1. There is documentation of previous trials and therapy failures with two (2) chemically distinct preferred long-acting narcotics (such as extended-release morphine sulfate, Opana ER and methadone) at therapeutic doses, and
2. A trial and therapy failure with fentanyl patch at maximum tolerated doses, and
3. A signed chronic opioid therapy management plan between the prescriber and patient must be included with the prior authorization, and
4. The prescriber must review the patient's use of controlled substances on the Iowa Prescription Monitoring Program website at https://pmp.iowa.gov/IAPMPWebCenter/ prior to requesting prior authorization.
5. Requests for long-acting narcotics will only be considered for FDA approved dosing.

The required trials may be overridden when documented evidence is provided that use of these agents would be medically

References

1. Jones CM, Mack KA, Paulozzi LJ. Pharmaceutical overdose deaths, United States, 2010. JAMA. 2013 Feb 20;309(7):657-9.
2. 2. Grissinger M. Inappropriate prescribing of fentanyl patches is still causing alarming safety problems. P T. Dec 2010; 35(12): 653–654.
3. 3. US Food and Drug Administration. FDA Blueprint for Prescriber Education for Extended-Release and Long-Acting Opioid Analgesics. US Food and Drug Administration Web site. Available at http://www.fda.gov/downloads/ drugs/drugsafety/informationbydrugclass/ucm277916.pdf. Accessed February 14, 2014.
4. 4. US Food and Drug Administration. FDA announces safety labeling changes and postmarket study requirements for extended-release and long-acting opioid analgesics. US Food and Drug Administration Web site. Available at http://www.fda.gov/newsevents/newsroom/pressannouncements/ ucm367726.htm. Accessed February 14, 2014.
5. 5. Gregory TB. How to safely prescribe long-acting opioids. J Fam Pract. 2013 Dec;62(12 Suppl 1):S12-8.

FDA Updates

The FDA is requiring a Boxed Warning for lidocaine topical 2% (viscous) solution alerting health care providers and caregivers against its use in treating teething pain in infants and children, which may cause serious harm, including death. When too much viscous lidocaine is given to infants and young children, or if they accidentally swallow too much, seizures, severe brain injury, and cardiac problems may result.

Reports of serious adverse events (including death) in infants and young children 5 months to 3.5 years of age given lidocaine 2% viscous solution for mouth pain (including pain due to teething and stomatitis), or with accidental ingestion, have been reviewed by the FDA.

The American Academy of Pediatrics recommends managing teething pain with a chilled (not frozen) teething ring or gently rubbing/massaging with the caregiver's finger. The FDA recommends against using topical OTC medications for teething pain as some products may cause harm.

Further information can be found at:
http://www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm402790.htm?source=govdelivery&utm_medium=email&utm_source=govdelivery

The FDA is warning that certain OTC topical acne products marketed under various brand names may cause rare but serious and potentially life-threatening allergic reactions or severe irritation. Consumers should seek immediate emergency medical attention if they experience hypersensitivity reactions such as throat tightness, difficulty breathing, faintness, or swelling of the eyes, face, lips, or tongue, and should also stop using topical acne products if they develop hives or itching. These serious reactions may occur within minutes to a day or longer after product use and differ from the local skin irritation (redness, burning, dryness, itching, peeling, or slight swelling) that may occur at the application site. It has not been determined if the serious hypersensitivity reactions are triggered by the products' active ingredients (benzoyl peroxide or salicylic acid), inactive ingredients, or by a combination of both. The FDA is monitoring and evaluating this safety issue. At first use, consumers should apply a small amount of any OTC topical acne product to 1 or 2 small affected areas for 3 days to make sure they do not develop hypersensitivity symptoms.

http://www.fda.gov/Drugs/DrugSafety/ucm400923.htm

New and Updated Drug Prior Authorization Criteria

Antidepressants (combines existing criteria for vilazodone (Viibryd) and desvenlafaxine (Pristiq) and applies to all non-preferred antidepressants subject to clinical criteria): Prior authorization is required for *non-preferred antidepressants subject to clinical criteria.* Requests for doses above the manufacturer recommended dose will not be considered. Payment will be considered for patients when the following criteria are met:

1. The patient has a diagnosis of Major Depressive Disorder (MDD) and is 18 years of age or older; and
2. Documentation of a previous trial and therapy failure at a therapeutic dose with *two* preferred generic SSRIs; and
3. Documentation of a previous trial and therapy failure at a therapeutic dose with one preferred generic SNRI; and
4. Documentation of a previous trial and therapy failure at a therapeutic dose with one *non-SSRI/SNRI* generic antidepressant.
5. *If the request is for an isomer, prodrug or metabolite of a medication indicated for MDD, one of the trials must be with the preferred parent drug of the same chemical entity that resulted in a partial response with a documented intolerance.*

The required trials may be overridden when documented evidence is provided that the use of these agents would be medically contraindicated.

DUR Activities

Medicaid Statistics for Prescription Claims

from April 1, 2014 to June 31, 2014*

Number of claims paid: 1,066,054

Total dollars paid: $67,703,983

Percent generic prescriptions: 83%

Average amount paid per claim: $63.51

Average amount paid per claim, brand: $278.87

Average Amount paid per claim, generic: $19.51

Top Drugs by Number of Prescriptions	Top Drugs by Dollars Spent	Top Therapeutic Class by Dollars Spent
Hydrocodone/APAP 5-325mg $14.42/RX	*Abilify* 20mg $1,499,335 $572.48/RX	Antipsychotics – Atypicals $6.9 million
Loratadine 10mg $9.24/RX	*Lantus* Injection 100/ml $1,695,903 $279.25/RX	Stimulants – Amphetamines – Long Acting $4.7 million
Ventolin HFA $53.17/RX	Methylphenidate ER 36mg $1,085,296 $171.10/RX	Anticonvulsants $4.1 million
Tramadol 50mg $10.71/RX	*Abilify 30*mg $1,062,305 $581.77/RX	Stimulants- Methylphenidate-Long Acting $3.1 million
Amoxicillin 400mg/5ml $11.01/RX	*Cymbalta* 60mg $1,245,326 $233.43/RX	Antidepressants – Selected SSRIs $2.5 million

*All dollars reported are pre-rebate