Warnings with Methadone
(Visneta Risbood, PharmD, Pain Management Clinical Pharmacist)

• Methadone is considered a high risk pain medication due to its complex pharmacokinetic profile and numerous drug interactions
  ○ Methadone has long been associated with adverse events
    • Respiratory and CNS depression
    • QT prolongation and torsades de pointes
    • Hypotension
  • Between 1999 and 2004, the number of poisoning deaths from methadone increased 390 percent due to unintentional methadone overdoses and drug interactions

Pharmacokinetics
• Methadone’s analgesic duration of action is 2-10 hours, approximately the same as morphine in single dose studies, however methadone’s elimination half-life is much longer and ranges from 8 hours up to 59 hours
• The respiratory depressant effects of methadone occur later and persist longer than its peak analgesic effects
• If methadone is taken too often, if the amount is too high, or if it is taken with certain other medications, it can cause drug accumulation to toxic levels in the body causing an increase risk of adverse events
• When treatment is initiated, methadone’s full analgesic effect is not usually achieved until 3-5 days of dosing
• Cross-tolerance between methadone and other opioids is incomplete, causing a potential for methadone overdose upon transition from another opioid, even in patients receiving high doses of another opioid

Drug Interactions
• Medications that have been shown to cause an increase in methadone levels or effects include, but are not limited to:
  ○ Drugs that inhibit CYP3A4 activity, such as azole antifungal agents (e.g., ketoconazole) and macrolide antibiotics (e.g., erythromycin), may decrease clearance of methadone resulting in increased or prolonged opioid effects
  ○ Drugs that prolong QT interval (quinolone antibiotics, antipsychotics, antidepressants)
• Check Lexicomp Online for a full list of medications with a potential for an interaction with methadone

Recommendations
• Healthcare providers should be aware of all concomitant medications because many drugs can prolong the effects of methadone and lead to serious side effects
• Patients taking methadone should be advised not to suddenly stop or start new medications without first consulting with their healthcare provider
• The pain management clinical pharmacist performs background surveillance of all patients receiving methadone through KPOH pharmacy benefit, checking for drug interactions on a weekly basis and occasionally contacting providers with recommendations to minimize the risk of respiratory depression and/or prolonged QT interval
• Comprehensive Pain Management Services (CPMS), a new pain service is outreaching to members on methadone for pain

• The goal of CPMS is to manage the methadone prescribing across KPOH to enable more proactive monitoring

Overdose
• Deaths have been associated with methadone use in both opioid-naïve patients and in patients who were being converted from other strong opioids to methadone
• Close monitoring of the patient is required when converting, initiating or adjusting dosages of methadone
• Healthcare professionals and patients should be aware of the following signs of methadone overdose
  ○ Difficulty breathing or shallow breathing
  ○ Extreme tiredness or sleepiness
  ○ Blurred vision
  ○ Inability to think, talk or walk normally
  ○ Feeling faint, dizzy or confused
• More information can be found at: http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/DrugSafetyInformationforHealthcareProfessionals/PublicHealthAdvisories/ucm124346.htm

Helping Members “Kick Butt”
Free Federal Employee Smoking Cessation
(Jessica Hendricks, MBA, Marketing and Advertising and Paul Bandfield, PharmD, Formulary Management Services)
• Kaiser Permanente of Ohio (KPOH) is committed to helping all members quit smoking
• As part of this commitment, KPOH has partnered with all Federal Employee groups to provide smoking cessation resources at no charge
• Federal Employees compose the largest KPOH employer group
• Federal Employee groups encompass a range of members who work for U.S. Department of Veterans Affairs, Defense, Homeland Security, Justice, Treasury, and Transportation, as well as NASA and the Social Security Administration
• The following preferred formulary agents are offered at no charge for Federal Employee groups:
  ○ Nicotine replacement therapy (NRT)
  ○ Bupropion Sustained-Release (SR)
• Other Commercial members can receive over-the-counter (OTC) nicotine patches and bupropion SR with a prescription for their generic copy
• Please note that OTC nicotine patches are not eligible for coverage under the Medicare Part D benefit
• In addition to medications, KPOH provides wellness coaching by phone, an interactive online program, a guided imagery audio program, and many other resources at no charge to all Medicare and Commercial members, including Federal Employee groups
• If you encounter a member who is part of a Federal Employee group who smokes, please educate that member about the smoking cessation programs and preferred formulary medications available to them at no charge
• For all members, from those who are thinking about quitting to those who are ready to take the first step, all of KP’s smoking cessation resources and tools are gathered in one convenient place at: http://kp.org/quitsmoking

(Continues on reverse side)
Market Withdrawal Infants' Acetaminophen 80mg/0.8mL
(Paul Bandfield, PharmD, Formulary Management Services)

- Under advisement of the Food and Drug Administration (FDA), manufacturers have agreed to gradually transition from acetaminophen 80mg/0.8mL to the less concentrated 160mg/5mL.
- The recommendation was made by the FDA to reduce the risk of overdose.
- While the transition is occurring, both the “old” 80mg/0.8mL being phased out and the “new” 160mg/5mL strengths will be available from manufacturers.
- With both strengths available at stores and at homes, there exists a potential for dosing errors.

KP Facilities Removed Infants’ Acetaminophen 80mg/0.8mL

- To prevent overdosing and confusion, existing stock of all acetaminophen 80mg/0.8mL products at KP Pharmacies and the medical modules should be removed and are no longer available.
- Only the new less concentrated Infants’ and Children’s Acetaminophen 160mg/5mL formulations will now be available at KP Pharmacies.

Recommendations

- Carefully read the Drug Facts label on the package to identify the concentration of the liquid acetaminophen dosage and directions for use.
- Patients should always use the dosing device provided with the product in order to correctly measure the amount of liquid acetaminophen to be given.
- Always provide directions to patients that specify the concentration and dose of liquid acetaminophen that should be given to a child.
- This should be especially noted if the patient or caregiver is familiar to using the 80mg/0.8mL concentration of liquid acetaminophen.
- More information can be found at: http://www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm284807.htm

FDA Alerts

Aliskiren-containing Medications: Drug Safety Communication - New Warning and Contraindication

Brilliant Blue G Compounded by Franck’s: Recall of Unapproved Drug - Ongoing Investigation of Fungal Endophthalmitis Cases

Certain Compounded Drugs from Franck’s: FDA Issues Second Warning to Physicians

Morphine Sulfate Injection USP, 4 mg/mL (C-II), 1 mL fill in 2.5 mL Carpuject by Hospira, Inc: Recall - May Contain More Than Intended Fill Volume

Altuzan (bevacizumab): Counterfeit Product - Contains no Active Ingredient

Celexa (citalopram hydrobromide) - Drug Safety Communication: Revised Recommendations, Potential Risk of Abnormal Heart Rhythms

Argatroban Injection 30 mg/50 mL (1 mg/mL): Recall - Potential for Visible Particulates

Skin Creams, Soaps and Lotions Marketed as Skin Lighteners and Anti-aging Treatments: May Contain the Toxic Metal, Mercury

Initiatives

Inter-Regional Clinical Pharmacy Services Subcommittee (ICPSS) Initiatives

- Insulin NPH and 70/30 use preferred over Lantus and Levenir.
- Dulera use preferred over Advair and Symbicort.
- Brand Adderall XR capsule preferred ADHD medication.
- OxyContin use discouraged over other long-acting opioids.
- Generic levofloxacin preferred over brand Avelox.
- Skeletal muscle relaxant use discouraged in elderly.
- Hydroxyzine use discouraged in elderly.

Pharmacy Conversion Team Projects

- Vytorin to atorvastatin Therapeutic Interchange.

Current Half-Tab Initiatives

Abilify Celexa Imitrex Lexapro* Paxil Zocor Aricept Crestor Lamictal Lipitor* Propranolol Zoloft Atorvastatin* Escitalopram* Levothyoxyzine Nuvigil Viagra

*Both brand and generic tablet products are half-tab initiatives.

Formulary Changes

The Ohio Regional Pharmacy & Therapeutics Committee approved the following formulary changes:

- The KP Ohio Region Drug Formulary is available by accessing the Lexicomp Online Formulary through the Internet.
- Formulary changes are updated in Lexicomp on their respective effective dates.

Commercial Additions

<table>
<thead>
<tr>
<th>Drug</th>
<th>Effective Date</th>
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<tbody>
<tr>
<td>Axitinib (Inlyta) 1mg, 5mg Tab</td>
<td>5.1.12</td>
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<tr>
<td>Peginterferon A-2a (Pegasys Prolick) Inj</td>
<td>5.9.12</td>
</tr>
<tr>
<td>Ruxolitinib (Jakafi) 5mg, 10mg, 15mg, 20mg, 25mg Tab</td>
<td>5.1.12</td>
</tr>
<tr>
<td>Vismodegib (Erivedge) 150mg Cap</td>
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Medicare Part D Tier Changes

<table>
<thead>
<tr>
<th>Drug</th>
<th>Effective Date-New Tier</th>
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</thead>
<tbody>
<tr>
<td>Abobotulinumtoxin A ( Dysport) 500U, 5000U Inj</td>
<td>1.1.12 - Tier 4</td>
</tr>
<tr>
<td>Asparagus esculenta (Erwinia Inj)</td>
<td>2.7.12 - Tier 5</td>
</tr>
<tr>
<td>Ruxolitinib (Jakafi) 5mg, 10mg, 15mg, 20mg, 25mg Tab</td>
<td>2.7.12 - Tier 5</td>
</tr>
</tbody>
</table>

Criteria Updates

- Attention-Deficit/Hyperactivity Disorder (ADHD) Medications
- Budesonide Inhalation Suspension (Pulmicort Respules)
- Less-Sedating Antihistamines (LSAs)
- Orlistat (Xenical)

Inquiries

Ohio Regional Formulary Management/Drug Information Service
(8:30 a.m. – 5:00 p.m. Mon – Fri, excluding holidays)
E-mail: oh.drug.info@kp.org
Pager for urgent inquiry: (216) 568-3133
References are available upon request.