Highlights of FDA Activities – 12/1/14 – 12/31/14

**FDA Drug Safety Communications & Drug Information Updates:**

**FDA Issues Final Rule on Changes to Pregnancy & Lactation Labeling Information for Prescription Drug & Biologic Products – Drug Information Update**

12/3/14

The FDA published a final rule setting new standards for how information on medication use in pregnancy and breastfeeding is presented in prescribing information. Three sections labeled “Pregnancy,” “Lactation” and “Females and Males of Reproductive Potential” will be included in the prescribing information for all prescription drug and biologic products. The current letter categories for pregnancy risk (A, B, C, D and X) will be replaced with three detailed subsections that describe the risks in terms relating to providing clinical care for pregnant women: “risk summary,” “clinical considerations” and “data.” The “Lactation” section will include the same three subsections. Drugs and biologic product applications approved as of June 30, 2015 will be required to use the new format, which will be phased in gradually for previously approved products.

**Heart Sync Inc. Multi-function Defibrillation Electrodes: Device Correction – Connector Incompatibility with Philips FR3 and FRx Defibrillator Units**

12/3/14

Certain Multi-function Defibrillation Electrodes will not connect with the Philips FR3 and FRx Defibrillator Units. The manufacturer is in the process of revising the labeling to clarify the use of these electrodes. All consumers were notified on 11/11/14 by letter.

**CONMED Corporation, PadPro and R2 Multi-Function Defibrillation Electrodes Will Not Work with Philips FR3 and FRx AEDs (Class I Recall)**

12/3/14

Since the connector design of the Philips FR3 and FRx AEDs have changed, the CONMED electrodes will no longer work with these AEDs. The FRx AED requires electrode pads be connected to the device before use. The FR3 doesn’t require electrode pads to be pre-connected. A delay in the delivering the electrical therapy, leading to serious injury or death, can result if the users don’t know that the pads do not work in the FR3 AED. The manufacturer do not recommend the use of the affected electrodes with these 2 AEDs.

**Dietary Supplements Containing Live Bacteria or Yeast in Immunocompromised Persons: Warning – Risk of Invasive Fungal Disease**

12/9/14

Following last month’s reporting of the death of a premature infant administered a dietary supplement as part of an inpatient treatment, and subsequent recall of ABC Dophilus Powder contaminated with Rhizopus oryzae mold, the FDA reminds health professionals that dietary supplements, including those containing live bacteria or yeast, are not generally regulated by the FDA. These products should particularly be used with caution in patients who are immunocompromised. Practitioners wishing to use these products as drugs, to treat, mitigate, cure or prevent a disease or condition, are invited to submit an Investigational New Drug Application (IND) for FDA review. The IND process includes an assessment of the quality of manufacturing and testing. Information on IND submission can be found on the FDA website at [http://www.fda.gov/BiologicsBloodVaccines/DevelopmentApprovalProcess/InvestigationalNewDrugINDorDeviceExemptionDEProcess/default.htm](http://www.fda.gov/BiologicsBloodVaccines/DevelopmentApprovalProcess/InvestigationalNewDrugINDorDeviceExemptionDEProcess/default.htm)

**Ziprasidone Drug Safety Communication – Rare But Potentially Fatal Skin Reactions**

12/11/14

Labeling for ziprasidone (Geodon and generics) has been updated to include a new warning regarding the occurrence of Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS). DRESS may start as a rash and progress to include fever, swollen lymph nodes, and inflammation of the liver, kidney, lungs, heart or pancreas; as well as eosinophilia and potentially death. The FDA has received reports of six patients developing DRESS within 11 and 30 days of initiation of ziprasidone therapy; none of the cases were fatal. Patients should be advised to seek urgent care if they develop fever with rash and/or swollen lymph glands. Health care professionals should immediately discontinue treatment if DRESS is suspected.
IV Solutions from Wallcur of San Diego: CDER Statement – FDA Warns Health Care Professionals Not to Administer These IV Training Products

The FDA alerted health care professionals not to administered IV training products from Wallcur of San Diego in human or animal patients. These products are for training purposes only; serious adverse events have been associated with administration of PractiIV Solution Bags, which are labeled “for clinical simulation.”

Major Product Recalls Announced Through MedWatch:

Siemens Healthcare Diagnostics, Rapid Gram Negative Combo Panels – May Produce Incorrect Results (Class I Recall)

This recall includes the Rapid Neg NP Combo Panel Type 3 and Rapid Neg Urine Combo Panel Type 1. These devices, used to identify certain gram negative bacteria and how the bacteria respond to antibiotics in the lab. The recall was issues because incorrect results may occur with aztreonam, cefotaxime, cefazidime, and ceftriaxone; such as reporting the bacteria is sensitive when it is resistant to the bacteria, leading to ineffective treatment. The manufacturer recommends all consumers to stop using the device and follow recall instructions.

Philips/ Children’s Medical Ventures, Gel-E Donut and Squishon 2 – Possibility of Mold (Class I Recall)

This device is used in hospitals, under the supervision of a caregiver, to support and cradle an infant’s head and/or body. Since the manufacturer’s (Philips Health Care) recall in May 2014, there were new complaints of mold leading to injury. Two different types of molds has been identified and are known to cause serious infections, including skin, eye, sinus, and brain infections. There is a potential that the mold can be transferred to the NICU and PICU. Using this product may cause serious adverse health consequences, including death. The manufacturer recommends all consumers to stop using the device even if there is no visible mold and follow recall instructions.

0.9% Sodium Chloride Injection USP in 100 mL Mini-Bag Plus Container by Baxter: Recall – Particulate Matter

Baxter has recalled two lots (P317842 and P317891) of 0.9% Sodium Chloride Injection USP in 100 mL Mini-Bag Plus containers due to complaints of particulate matter identified as a fragment from the vial adapter.

Mitoxantrone (Hospira): Recall – Subpotency and Out of Specification

Hospira is recalling to the user level 10 lots of mitoxantrone injection distributed for human and veterinary use due to confirmed subpotency and elevated impurity levels. Affected lots were distributed from February 2103 through November 2014; a complete list of affected products can be found in a link on the FDA MedWatch site.

Nellcor Puritan Bennett 980 Ventilator System by Covidien: Class I Recall – Component Failure May Cause Display Failure and Burning Odor

Circuit board in the affected units may have cracks resulting in the display to dim and give off a burning odor. There is no risk of fire, but the part needs to be replaced so that information on the display is visible.

KimVent Microcuff Subglottic Suctioning Endotracheal Tubes by Halyard Health: Class I Recall – Component May Detach During Use

Cuff inflation line on certain endotracheal tubes may detach from the tube during use, which may result in reduced air reaching the lungs. The recall affects units manufactured from 11/15/13 to 10/21/14 and distributed from 12/20/13 to 10/30/14.
**Dietary Supplement Recalls & Public Notifications**

In December, the FDA issued notifications to the public regarding undeclared active ingredients in the following products. Patients are advised not to purchase or use these products.

<table>
<thead>
<tr>
<th>Product</th>
<th>Promoted Use</th>
<th>Hidden/Undeclared Drug Ingredient(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>B-Lipo Capsules*</td>
<td>Weight loss</td>
<td>Lorcaserin</td>
</tr>
<tr>
<td>SLIM-K Capsules*</td>
<td>Weight loss</td>
<td>Sibutramine, desmethylsibutramine, &amp; phenolphthalein</td>
</tr>
<tr>
<td>Triple PowerZEN Gold</td>
<td>Sexual enhancement</td>
<td>Sildenafil</td>
</tr>
<tr>
<td>Zhansheng Weige Chaoyue Xilishi</td>
<td>Sexual enhancement</td>
<td>Sildenafil</td>
</tr>
<tr>
<td>Samurai-X</td>
<td>Sexual enhancement</td>
<td>Sildenafil</td>
</tr>
</tbody>
</table>

*Recalled

**New Drug Shortages Reported by the FDA:**

<table>
<thead>
<tr>
<th>Product</th>
<th>Date Initially Posted</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methylphenidate HCl Tablets (Concerta, Janssen)</td>
<td>12/04/14</td>
</tr>
<tr>
<td>Phentolamine mesylate Injection, 5 mg (West-Ward)</td>
<td>12/18/14</td>
</tr>
<tr>
<td>Quazepam (Doral, Sciecure Pharma) 15 mg – see note below under discontinuations</td>
<td>12/23/14</td>
</tr>
</tbody>
</table>

**Product Discontinuations/Withdrawals**

<table>
<thead>
<tr>
<th>Product</th>
<th>Date Initially Posted</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gentamicin sulfate injection USP 1.6 mg/mL, 50 mL premix from Hospira</td>
<td>12/02/14</td>
</tr>
<tr>
<td>Aripiprazole (Abilify) 1 mg/mL oral solution (NDC 59148-013-15), 10 mg and 15 mg Discmelt orally disintegrating tablets (NDCs 59148-640-23 &amp; 59148-641-23), and 9.75 mg/1.3 mL intramuscular injection (NDC 59148-016-65). Product availability is anticipated through May to November 2015; other Abilify formulations remain available. Quazepam (Doral) 15 mg tablets / bottle of 100 Meda/Questcor discontinuing production. Generics remain available and Sciecure is planning to bring Doral back to market.</td>
<td>12/17/14</td>
</tr>
</tbody>
</table>

**New Drug Approvals:**

<table>
<thead>
<tr>
<th>Product</th>
<th>Description</th>
<th>Date Approved</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blinatumomab / Blincyto / Amgen Inc.</td>
<td>See attached drug summary</td>
<td>12/3/14</td>
</tr>
<tr>
<td>Human papillomavirus 9-valent vaccine, recombinant / Gardasil 9 / Merck</td>
<td>HPV vaccine for prevention of 9 types of HPV, compared with the 4 types covered in the current Gardasil product</td>
<td>12/10/14</td>
</tr>
<tr>
<td>Finafloxacin otic suspension / Xtoro / Alcon</td>
<td>See attached drug summary</td>
<td>12/17/14</td>
</tr>
<tr>
<td>Olaparib / Lynparza / AstraZeneca</td>
<td>See attached drug summary</td>
<td>12/19/14</td>
</tr>
<tr>
<td>Ombitasvir, paritaprevir &amp; ritonavir tablets plus dasabuvir tablets / Viekira Pak / AbbVie</td>
<td>See attached drug summary</td>
<td>12/19/14</td>
</tr>
<tr>
<td>Ceftolozane-tazobactam / Zerbaxa / Cubist</td>
<td>See attached drug summary</td>
<td>12/19/14</td>
</tr>
<tr>
<td>Peramivir / Rapivab / Biocryst</td>
<td>See attached drug summary</td>
<td>12/19/14</td>
</tr>
<tr>
<td>Nivolumab / Opdivo / Bristol-Myers Squibb</td>
<td>See attached drug summary</td>
<td>12/22/14</td>
</tr>
</tbody>
</table>

**New Indications:**

<table>
<thead>
<tr>
<th>Product</th>
<th>Description</th>
<th>Date Approved</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ruxolitinib / Jakafi / Incyte Corporation</td>
<td>Polycythemia vera in patients who have had an inadequate response to or are intolerant of hydroxyurea</td>
<td>12/4/14</td>
</tr>
</tbody>
</table>
**New Indications continued:**

<table>
<thead>
<tr>
<th>Drug/Cytokine</th>
<th>Description</th>
<th>Date Approved</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aripiprazole / Abilify / Otsuka Pharmaceutical</td>
<td>Tourette’s disorder in pediatric patients</td>
<td>12/12/14</td>
</tr>
<tr>
<td>Denosumab injection 70 mg/mL / Xgeva / Amgen</td>
<td>Hypercalcemia of malignancy refractory to bisphosphonate therapy</td>
<td>12/5/14</td>
</tr>
<tr>
<td>Ramucirumab / Cyramza / Eli Lilly</td>
<td>Use in combination with docetaxel in patients with metastatic non-small cell lung cancer whose disease has progressed during or following treatment with platinum-based chemotherapy</td>
<td>12/17/14</td>
</tr>
<tr>
<td>Beclomethasone dipropionate nasal aerosol / Qnasl / Teva</td>
<td>Indication for treatment of nasal symptoms of seasonal and perennial allergic rhinitis expanded to include use in patients 4 through 11 years of age</td>
<td>12/17/14</td>
</tr>
<tr>
<td>Elvitegravir + cobicistat + emtricitabine + tenofovir / Stribild / Gilead</td>
<td>For use in HIV-1 infected patients who are virologically suppressed (HIV-1 RNA &lt; 50 copies/mL) on a stable antiretroviral regimen for at least 6 months with no history of treatment failure, to replace their current regimen</td>
<td>12/17/14</td>
</tr>
<tr>
<td>Gadobutol / Gadavist / Bayer</td>
<td>Use in adults and pediatric patients, including term neonates, for detection and visualization of area with disrupted blood brain barrier and/or abnormal vascularity of the central nervous system</td>
<td>12/29/14</td>
</tr>
<tr>
<td>Ivacaftor / Kalydeco / Vertex</td>
<td>Indication expanded to include use in patients with an R117H mutation in the cystic fibrosis transmembrane conductance regulator gene</td>
<td>12/29/14</td>
</tr>
<tr>
<td>Spinosad / Natroba / Parapro</td>
<td>Indication expanded to include use for head lice infestations in patients 6 months of age and older</td>
<td>12/30/14</td>
</tr>
</tbody>
</table>

**New Dosage Form or Formulation:**

<table>
<thead>
<tr>
<th>Drug/Cytokine</th>
<th>Description</th>
<th>Date Approved</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tobramycin inhalation solution (300 mg/5 mL ampule) + PARI LC PLUS Reusable Nebulizer / Kitabis Pak / Pulmoflow Inc.</td>
<td>Management of cystic fibrosis in adults and pediatric patients 6 years of age and older with <em>Pseudomonas aeruginosa</em></td>
<td>12/2/14</td>
</tr>
<tr>
<td>Influenza intradermal quadrivalent vaccine / Fluzone Quadrivalent / Sanofi Pasteur</td>
<td>An intradermal formulation of the quadrivalent vaccine for use in active immunization of persons 18 through 64 years of age for prevention of influenza caused by the influenza A and influenza B viruses containing in the vaccine</td>
<td>12/11/14</td>
</tr>
<tr>
<td>Pasireotide injectable suspension / Signifor LAR / Novartis</td>
<td>Treatment of acromegaly in adults for whom surgery is not an option</td>
<td>12/15/14</td>
</tr>
<tr>
<td>Lanreotide injection / Somatuline Depot / Ipsen Pharmaceuticals</td>
<td>Treatment of gastroenteropancreatic neuroendocrine tumors in adults with unresectable, well or moderately differentiated, locally advanced or metastatic disease</td>
<td>12/16/14</td>
</tr>
<tr>
<td>Ivermectin 1% cream / Soolantra / Galderma</td>
<td>Once-daily topical for the treatment of inflammatory lesions of rosacea; see attached drug summary</td>
<td>12/19/14</td>
</tr>
<tr>
<td>Liraglutide 3 mg / Saxenda / Novo Nordisk</td>
<td>Once daily injection for chronic weight management in addition to a reduced-calorie diet and exercise; see attached drug summary</td>
<td>12/23/14</td>
</tr>
<tr>
<td>Diclofenac sodium injection / Dyloject / Javelin Pharms</td>
<td>For the management of mild to moderate pain and management of moderate to severe pain alone or in combination with opioid analgesics; see attached drug summary</td>
<td>12/23/14</td>
</tr>
</tbody>
</table>

FDA Activity Newsletter | WSU Drug Information Center | December 2014
**New Dosage Form or Formulation:**
Memantine HCl extended release + donepezil HCl / Namzaric / Forest Labs

**Description:**
For the treatment of moderate to severe Alzheimer’s type dementia in patients stabilized on memantine and donepezil

**Date Approved:**
12/23/14

---

**Compiled by:**
Terri Levien, Pharm.D.
Ross Bindler, Pharm.D., PGY1 Drug Information Resident
Anne Kim, Pharm.D., PGY1 Drug Information Resident
Elaine Cen, Pharm.D. Candidate 2015
Wing-Chung Wong, Pharm.D. Candidate 2015

**Blinatumomab/ Blincyto / Amgen Inc.**

<table>
<thead>
<tr>
<th>Generic Name / Brand Name / Company</th>
<th>Blinatumomab/ Blincyto / Amgen Inc.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Date of approval</strong></td>
<td>12/3/2014</td>
</tr>
</tbody>
</table>

**Drug Class (Mechanism of Action if novel agent):**
A bispecific CD19-directed CD3 T-cell engager that activates endogenous T cells when bound to the CD19-expressing target cell on benign and malignant B cells. The drug mediates the formation of a synapse between the T cell and the tumor cell, upregulation of cell adhesion molecules, production of cytolytic proteins, release of inflammatory cytokines, and proliferation of T-cells, resulting in redirected lysis of CD19+ cells.

**Indication:**
Philadelphia chromosome-negative relapsed or refractory B-cell precursor acute lymphoblastic leukemia (R/R ALL)

**Comparative agent – Therapeutic interchange?**
None

**Dosage forms/strengths. Common Dose/sig:**
Single-use vial: 35 mcg of lyophilized powder for reconstitution
One treatment cycle: 4 weeks of continuous IV infusion followed by a 2-week treatment-free interval
Patients ≥45 kg: 9 mcg/day on days 1-7 and 28 mcg/day on days 8-28 of the first 42-day cycle. 28 mcg/day on days 1-28 in subsequent cycles. Allow for a minimum of 2 weeks treatment-free between cycles
For induction, treatment course is up to 2 cycles
For consolidation treatment, 3 additional cycles following induction

**DEA Schedule:**
Not applicable

**Date of market availability:**
Available

**Similar Medications (Look-Alike Sound-Alike):**
None

---

**CLINICAL USE EVALUATION**

**Common Adverse Effects:**
Pyrexia, headache, peripheral edema, febrile neutropenia, nausea, hypokalemia, tremor, rash, and constipation

**Severe Adverse Effects:**
Neurologic toxicity, seizures, cytokine release syndrome, febrile neutropenia, pyrexia, pneumonia, sepsis, neutropenia, device-related infection, tremor, encephalopathy, infection, overdose, confusion, Staphylococcal bacteremia, and headache.

**Severe Drug-Drug Interactions:**
CYP450 substrates with a narrow therapeutic index

**Severe Drug-Food Interactions:**
Not reported

**Important Labs Values to assess prior to order entry or at point of clinical follow up.**
WBC, ANC, AST, ALT, GGT, total bilirubin

**Used in Pediatric Areas:**
Limited experience

**Renal or Hepatic Dosing:**
No formal pharmacokinetic studies in renal or hepatic impairment.
No dose adjustments needed for CrCl > 30 mL/min

**Critical Issues (i.e., contraindications, warnings, etc) that should be emphasized**

- Boxed warning: cytokine release syndrome and neurological toxicities
- Contraindications: known hypersensitivity to blinatumomab or any component of the product formulation
- Monitor patients for signs or symptoms of infection, cytokine release syndrome, infusion reactions, neurological toxicity, and tumor lysis syndrome.
- Precautions: infections, tumor lysis syndrome, neutropenia and febrile neutropenia, leukoencephalopathy, and neurologic events such as seizures
- Effects on ability to drive and use machines

**Special administration technique or considerations**

- Follow instructions for preparation and administration to prevent errors
- Hospitalization is recommended for the first 9 days of the 1st cycle and first 2 days of the 2nd cycle
- Premedicate with dexamethasone 20 mg IV 1 hour prior to the 1st dose of blinatumomab of each cycle, prior to a step dose (i.e. cycle 1 day 8), or when restarting an infusion after ≥ 4 hours of interruption
- Infuse 240 mL blinatumomab IV bag over 24 or 48 hours through a dedicated lumen
- Do not flush the infusion line, this can increase the dose

**Finafloxacin Otic Suspension / Xtoro / Alcon Labs**

<table>
<thead>
<tr>
<th>Generic Name / Brand Name / Company</th>
<th>Finafloxacin otic suspension 0.3% / Xtoro / Alcon Labs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Date of approval</td>
<td>December 17, 2014</td>
</tr>
<tr>
<td>Drug Class (Mechanism of Action if novel agent)</td>
<td>Otic Antibiotics; fluoroquinolone</td>
</tr>
<tr>
<td>Indication</td>
<td>Treatment of acute otitis externa caused by <em>Pseudomonas aeruginosa</em> and <em>Staphylococcus aureus</em></td>
</tr>
<tr>
<td>Comparative agent – Therapeutic interchange?</td>
<td>Otic ciprofloxacin, otic ofloxacin</td>
</tr>
<tr>
<td>Dosage forms/strengths. Common Dose/sig</td>
<td>Otic suspension, 0.3% Instill 4 drops in the affected ear(s) twice daily for 7 days.</td>
</tr>
<tr>
<td>DEA Schedule</td>
<td>Not applicable</td>
</tr>
<tr>
<td>Date of market availability</td>
<td>Not reported</td>
</tr>
<tr>
<td>Similar Medications (Look-Alike Sound-Alike)</td>
<td>Xtandi, ciprofloxacin otic, ofloxacin otic</td>
</tr>
</tbody>
</table>

**CLINICAL USE EVALUATION**

<table>
<thead>
<tr>
<th>Common Adverse Effects</th>
<th>Ear pruritus, nausea</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severe Adverse Effects</td>
<td>None reported</td>
</tr>
<tr>
<td>Severe Drug-Drug Interactions</td>
<td>None reported</td>
</tr>
<tr>
<td>Severe Drug-Food Interactions</td>
<td>None reported</td>
</tr>
<tr>
<td>Important Labs Values to assess prior to order entry</td>
<td>None</td>
</tr>
<tr>
<td>Used in Pediatric Areas</td>
<td>Approved for use in patients 1 year and older; same dose as adults</td>
</tr>
<tr>
<td>Renal or Hepatic Dosing</td>
<td>No dosage adjustments necessary</td>
</tr>
</tbody>
</table>

**Critical Issues (i.e., contraindications, warnings, etc) that should be emphasized**

- Allergic reactions may occur in patients allergic to finafloxacin, other product ingredients, or other quinolones
- Prolonged use could lead to fungal overgrowth

**Special administration technique or considerations**

- Warm suspension in hand for 1-2 minutes before instilling
- Shake bottle well before use
- Lie with affected ear up, instill drops, and maintain position for 60 seconds; repeat in other ear if necessary

**Prepared by**

Elaine Cen, Doctor of Pharmacy student, class of 2015

Terri Levien, Pharm.D.
<table>
<thead>
<tr>
<th><strong>Olaparib / Lynparza / AstraZeneca</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Generic Name / Brand Name / Company</strong></td>
</tr>
<tr>
<td><strong>Date of approval</strong></td>
</tr>
<tr>
<td><strong>Drug Class (Mechanism of Action if novel agent)</strong></td>
</tr>
<tr>
<td><strong>Indication</strong></td>
</tr>
<tr>
<td><strong>Comparative agent – Therapeutic interchange?</strong></td>
</tr>
</tbody>
</table>
| **Dosage forms/strengths. Common Dose/sig** | Capsules: 50 mg  
Dose: 400 mg twice daily (i.e., eight 50 mg capsules twice daily)  
Dose may be decreased to 400 mg per day to diminish adverse events:  
200 mg twice daily (i.e., four 50 mg capsules twice daily). It may be further reduced, if necessary, to 200 mg per day: 100 mg twice daily (i.e., two 50 mg capsules twice daily). |
| **DEA Schedule** | Not applicable |
| **Date of market availability** | Not reported |
| **Similar Medications (Look-Alike Sound-Alike)** | None |

**CLINICAL USE EVALUATION**

**Common Adverse Effects**
- Anemia, nausea, fatigue, asthenia, vomiting, diarrhea, dysgeusia, dyspepsia, headache, decreased appetite, nasopharyngitis/pharyngitis/URI, cough, arthralgia/musculoskeletal pain, myalgia, back pain, dermatitis/rash, and abdominal pain/discomfort commonly occurred in 20% or more of study patients.

**Severe Adverse Effects**
- Myelodysplastic syndrome, acute myeloid leukemia, and pneumonitis were rare, but serious, adverse events reported in study patients.

**Severe Drug-Drug Interactions**
- Concomitant use with other myelosuppressive anticancer agents increase the possible risk and duration of myelosuppressive toxicity.  
- Concomitant use with strong CYP3A inhibitors increase olaparib levels by 2.7-fold and with moderate CYP3A inhibitors increases levels by 2-fold.  
- Concomitant use with strong CYP3A inducers decrease olaparib levels by 87%. Moderate CYP3A inducers are predicted to decrease olaparib levels by 50-60%.

**Severe Drug-Food Interactions**
- Grapefruit and Seville oranges should be avoided.

**Important Labs Values to assess prior to order entry or at point of clinical follow up. (Need Pop Up?)**
- CBC

**Used in Pediatric Areas**
- Safety and effectiveness not established

**Renal or Hepatic Dosing**
- No dose adjustment required for impaired renal function, however patients should be closely monitored for toxicity. No data available for impaired hepatic function as patients with impaired liver function were excluded from study.

**Critical Issues (i.e., contraindications, warnings, etc) that should be emphasized**
- The majority of Myelodysplastic Syndrome/Acute Myeloid Leukemia cases were fatal. Monitor CBC at baseline and every month thereafter. Do not administer drug until patient reaches hematological stability (grade 1 or less) after previous chemotherapy. Interrupt therapy in patients with prolonged hematological toxicity.  
- Fatal pneumonitis may occur. Monitor for dyspnea, fever, cough, wheezing, or radiological abnormality. Interrupt therapy to investigate and discontinue drug upon positive confirmation of pneumonitis.
Avoid use in pregnant women. Olaparib may cause fetal toxicity, as animal studies showed olaparib is teratogenic.

Swallow capsules whole; do not chew, dissolve or open capsules. Do not take capsules which appear deformed or show evidence of leakage.

Prepared by
Anne Kim, PharmD, MPH, MIT

### Peramivir / Rapivab / Biocryst

<table>
<thead>
<tr>
<th>Generic Name / Brand Name / Company</th>
<th>Peramivir injection / Rapivab / Biocryst</th>
</tr>
</thead>
<tbody>
<tr>
<td>Date of approval</td>
<td>December 19, 2014</td>
</tr>
<tr>
<td>Drug Class (Mechanism of Action if novel agent)</td>
<td>Influenza virus neuraminidase inhibitor</td>
</tr>
<tr>
<td>Indication</td>
<td>Treatment of acute uncomplicated influenza in adults who have been symptomatic for no more than 2 days.</td>
</tr>
<tr>
<td>Comparative agent – Therapeutic interchange?</td>
<td>Oseltamivir oral, zanamivir inhalation</td>
</tr>
<tr>
<td>Dosage forms/strengths. Common Dose/sig</td>
<td>Injection: 200 mg in 20 mL (10 mg/mL)</td>
</tr>
<tr>
<td></td>
<td>Dose: 600 mg as an IV infusion over 15 to 30 minutes</td>
</tr>
<tr>
<td>DEA Schedule</td>
<td>Not applicable</td>
</tr>
<tr>
<td>Date of market availability</td>
<td>Available</td>
</tr>
<tr>
<td>Similar Medications (Look-Alike Sound-Alike)</td>
<td>Perampanel, simeprevir</td>
</tr>
</tbody>
</table>

### CLINICAL USE EVALUATION

**Common Adverse Effects**
Diarrhea

**Severe Adverse Effects**
Serious skin and hypersensitivity reactions, neuropsychiatric reactions

**Severe Drug-Drug Interactions**
May diminish efficacy of live attenuated influenza vaccine

**Severe Drug-Food Interactions**
None reported

**Important Labs Values to assess prior to order entry or at point of clinical follow up. (Need Pop Up?)**
Creatine clearance – to determine renal dosing

**Used in Pediatric Areas**
Safety and effectiveness have not been established

**Renal or Hepatic Dosing**
Renal: 200 mg if CrCl 30-49 mL/min, 100 mg if CrCl 10-29 mL/min; in patients on hemodialysis, administered dose after dialysis at dose based on renal function
Hepatic: no dosage adjustments necessary

**Critical Issues (i.e., contraindications, warnings, etc) that should be emphasized**
- Efficacy has not been established in patients with serious influenza requiring hospitalization.
- Monitor for signs of abnormal behavior, hallucinations, delirium.
- Rare cases of serious skin reactions including Stevens-Johnson syndrome and erythema multiforme have been reported with peramivir

**Special administration technique or considerations**
- Administer as IV infusion over 15 to 30 minutes
- Compatible with 0.9% or 0.45% sodium chloride, 5% dextrose, or lactated Ringer’s; do not dilute or co-infuse with other medications

Prepared by
Terri Levien, Pharm.D.

### Ombitasvir/Paritaprevir/Ritonavir tablets + Dasabuvir tablets / Viekira Pak / AbbVie

<table>
<thead>
<tr>
<th>Generic Name / Brand Name / Company</th>
<th>Ombitasvir, paritaprevir, and ritonavir tablets, dasabuvir tablets / Viekira Pak / AbbVie</th>
</tr>
</thead>
<tbody>
<tr>
<td>Date of approval</td>
<td>December 19, 2014</td>
</tr>
<tr>
<td>Drug Class (Mechanism of Action if novel agent)</td>
<td>Combination product containing ombitasvir, a hepatitis C virus NS5A inhibitor, paritaprevir, a hepatitis C virus NS3/4A protease inhibitor, ritonavir, a CYP3A inhibitor, and dasabuvir, a hepatitis C virus non-nucleoside NS5B palm polymerase inhibitor</td>
</tr>
<tr>
<td>Indication</td>
<td>For use with or without ribavirin for the treatment of patients with genotype 1 chronic hepatitis C virus infection, including patients with compensated cirrhosis. Administered with ribavirin if genotype 1a with or</td>
</tr>
</tbody>
</table>
### Comparative agent – Therapeutic interchange?
Ledipasvir/sofosbuvir (Harvoni, Gilead)

### Dosage forms/strengths. Common Dose/sig
- **Tablets:** ombitasvir 12.5 mg, paritaprevir 75 mg, ritonavir 50 mg
- **Tablets:** dasabuvir 250 mg
- **Dose:** 2 ombitasvir/paritaprevir/ritonavir tablets once daily (in the morning) and one dasabuvir tablet twice daily (morning and evening) with a meal; duration is 12 weeks if genotype 1a or 1b without cirrhosis or genotype 1b with cirrhosis; 24 weeks if genotype 1a with cirrhosis.

### DEA Schedule
Not applicable

### Date of market availability
Available

### Similar Medications (Look-Alike Sound-Alike)
Viagra

### CLINICAL USE EVALUATION

#### Common Adverse Effects
- With ribavirin, greater than 10%: fatigue, nausea, pruritus, other skin reactions, insomnia, asthenia
- Without ribavirin, 5% or greater: nausea, pruritus, insomnia

#### Severe Adverse Effects
ALT elevations

#### Severe Drug-Drug Interactions
Contraindicated with drugs strongly dependent on CYP3A for clearance, strong inducers of CYP3A and CYP2C8, and strong inhibitors of CYP2C8

#### Severe Drug-Food Interactions
Absorption increased when administered with food

#### Important Labs Values to assess prior to order entry or at point of clinical follow up. (Need Pop Up?)
Liver function tests should be assessed prior to, during the first 4 weeks of therapy, and as clinically indicated thereafter

#### Used in Pediatric Areas
Safety and effectiveness not established

#### Renal or Hepatic Dosing
- **Hepatic:** no dosage adjustment in mild impairment (Child-Pugh A); not recommended in moderate impairment (Child-Pugh B); contraindicated in severe impairment (Child-Pugh C).
- **Renal:** no dosage adjustment necessary

#### Critical Issues (i.e., contraindications, warnings, etc) that should be emphasized
- Consider ribavirin contraindications, warnings, and precautions if coadministration is necessary
- Contraindicated in severe hepatic impairment
- Numerous severe drug-drug interactions – consult prescribing information for full list of medications contraindicated with the regimen and requiring use with caution
- Contraindicated in patients with known hypersensitivity to ritonavir
- ALT elevations were observed in clinical trials and were observed more frequently in female subjects using ethinyl estradiol containing medications. Such medications must be discontinued prior to starting therapy.

#### Special administration technique or considerations
- Tablets should be taken with a meal, without regard to fat or calorie count

#### Prepared by
Terri Levien, Pharm.D.

### Ceftolozane + Tazobactam / Zerbaxa / Cubist

| Generic Name / Brand Name / Company | Ceftolozane/tazobactam for injection / Zerbaxa / Cubist |
| Date of approval | December 19, 2014 |
| Drug Class (Mechanism of Action if novel agent) | Combination of a cephalosporin antibacterial and a beta-lactamase inhibitor; demonstrated clinical activity in infections caused by Enterobacter cloacae, Escherichia coli, Klebsiella oxytoca, Klebsiella pneumoniae, Proteus mirabilis, Pseudomonas aeruginosa, Bacteroides fragilis, Streptococcus anginosus, Streptococcus constellatus, and Streptococcus salivarius. |
### Indication
- Treatment of complicated intra-abdominal infections in combination with metronidazole
- Treatment of complicated urinary tract infections including pyelonephritis

### Comparative agent – Therapeutic interchange?
Meropenem

### Dosage forms/strengths. Common Dose/sig
- **Injection (powder for reconstitution):** ceftolozane 1 g/tazobactam 0.5 g
- **Dose:** 1.5 g (ceftolozane 1 g/tazobactam 0.5) every 8 hours by IV infusion over 1 hour; treatment duration is 4-14 days in intra-abdominal infections and 7 days in UTIs

### DEA Schedule
Not applicable

### Date of market availability
Available

### Similar Medications (Look-Alike Sound-Alike)
None

### CLINICAL USE EVALUATION

#### Common Adverse Effects
- 5% or greater: nausea, diarrhea, headache, pyrexia

#### Severe Adverse Effects
- Serious hypersensitivity reactions/anaphylaxis; *Clostridium difficile*-associated diarrhea

#### Severe Drug-Drug Interactions
None reported

#### Severe Drug-Food Interactions
None reported

#### Important Labs Values to assess prior to order entry or at point of clinical follow up. (Need Pop Up?)
- Creatinine clearance to determine if renal dosing is required; monitor daily in patients with changing renal function

#### Used in Pediatric Areas
Safety and effectiveness not established

#### Renal or Hepatic Dosing
- **Renal:** CrCl 30-50 mL/min administer 750 mg (500 mg/250 mg) IV every 8 hours; CrCl 15-29 mL/min administer 375 mg (250 mg/125 mg) IV every 8 hours; ESRD on hemodialysis administer 750 mg loading dose followed by 150 mg (100 mg/50 mg) maintenance dose IV every 8 hours
- **Hepatic:** no dosage adjustment necessary

#### Critical Issues (i.e., contraindications, warnings, etc) that should be emphasized
- Contraindicated in patients with known serious hypersensitivity to the agent, piperacillin/tazobactam, or other beta-lactam agents
- Decreased efficacy in patients with baseline CrCl 30-50 mL/min; monitor renal function and adjust doses as recommended

#### Special administration technique or considerations
- Administer in conjunction with metronidazole 500 mg IV every 8 hours in treatment of complicated intra-abdominal infections.
- Do not mix with other drugs or IV solutions containing other drugs
- Vials should be stored refrigerated (2°-8°C, 36°-46°F)

#### Prepared by
Terri Levien, Pharm.D.

### Nivolumab / Opdivo / Bristol-Myers Squibb

<table>
<thead>
<tr>
<th>Generic Name / Brand Name / Company</th>
<th>Nivolumab / Opdivo / Bristol-Myers Squibb</th>
</tr>
</thead>
<tbody>
<tr>
<td>Date of approval</td>
<td>December 22, 2014</td>
</tr>
<tr>
<td>Drug Class (Mechanism of Action if novel agent)</td>
<td>Programmed death receptor-1 (PD-1) blocking monoclonal antibody</td>
</tr>
<tr>
<td>Indication</td>
<td>Treatment of unresectable or metastatic melanoma with disease progression after the use of ipilimumab (Yervoy®) and, if BRAF V600 mutation positive, a BRAF inhibitor</td>
</tr>
<tr>
<td>Comparative agent – Therapeutic interchange?</td>
<td>Pembrolizumab (Keytruda®)</td>
</tr>
</tbody>
</table>
| Dosage forms/strengths. Common Dose/sig | Available as a 4 mL (40 mg total) and 10 mL (100 mg total) single use vial at a concentration of 10 mg/mL
Dose: 3 mg/kg via intravenous infusion over 60 minutes every two weeks until melanoma progression or unacceptable toxicity |
| DEA Schedule                        | Not applicable                           |
| Date of market availability         | Early 2015                               |
| Similar Medications (Look-Alike Sound-Alike) | Nabilone, nebivolol, nepafenac, NephPlex®, Optivite* |

### CLINICAL USE EVALUATION

**FDA Activity Newsletter**

**WSU Drug Information Center**

**December 2014**
### Common Adverse Effects
Rash (21%), pruritus (19%), cough (17%), upper respiratory tract infections (11%), peripheral edema (10%)

### Severe Adverse Effects
Immune-mediated pneumonitis; immune-mediated colitis; immune-mediated hepatitis; immune-mediated nephritis and renal dysfunction; immune-mediated hypo- and hyperthyroidism; others (pancreatitis, uveitis, demyelination, adrenal insufficiency, hypophysitis, diabetic ketoacidosis, hypopituitarism, Guillain-Barre syndrome, myasthenic syndrome and facial and abducens nerve paresis)

### Severe Drug-Drug Interactions
None tested

### Severe Drug-Food Interactions
None tested

### Important Labs Values to assess prior to order entry or at point of clinical follow up.
AST, ALT, total bilirubin, serum creatinine, thyroid function tests

### Safety and efficacy not established

### Renal or Hepatic Dosing
Based on population pharmacokinetic analysis, no adjust will be necessary in adult patients with renal impairment

There is no adjustment required in adult patients with mild hepatic impairment based on Child-Pugh score, but has not been studied in adult patients with moderate or severe hepatic impairment

### Critical Issues (i.e., contraindications, warnings, etc) that should be emphasized
- Immune mediated conditions – pneumonitis, colitis, hepatitis, nephritis, hypo- and hyperthyroidism; treat with corticosteroids based on severity of reaction; withhold or discontinue for severe reactions
- Embryofetal toxicity – use contraception while on nivolumab and for at least 5 months after the last dose

### Special administration technique or considerations
- Administer over 60 minutes through an intravenous line with a sterile, non-pyrogenic, low protein binding in-line filter of 0.2 to 1.2 micrometers in size
- Do not coadminister with other medications
- Flush the line after the infusion is complete

### Prepared by
Ross Bindler, PharmD

---

### Liraglutide / Saxenda / Novo Nordisk

<table>
<thead>
<tr>
<th>Generic Name / Brand Name / Company</th>
<th>Liraglutide / Saxenda / Novo Nordisk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Date of approval</td>
<td>December 23, 2014</td>
</tr>
<tr>
<td>Drug Class (Mechanism of Action if novel agent)</td>
<td>Glucagon-like peptide-1 (GLP-1) receptor agonist</td>
</tr>
<tr>
<td>Indication</td>
<td>For use as an adjunct to a reduced-calorie diet and an increase in physical activity for chronic weight management in adult patients with a body max index (BMI) of:</td>
</tr>
<tr>
<td></td>
<td>30 kg/m² or greater, or</td>
</tr>
<tr>
<td></td>
<td>27 kg/m² with at least one weight related comorbid condition</td>
</tr>
<tr>
<td>Comparative agent – Therapeutic interchange?</td>
<td>None; not interchangeable with liraglutide for type 2 diabetes (Victoza)</td>
</tr>
<tr>
<td>Dosage forms/strengths. Common Dose/sig</td>
<td>Solution for subcutaneous injection in pre-filled, multi-dose pen delivering doses of 0.6, 1.2, 1.8, 2.4, or 3 mg</td>
</tr>
<tr>
<td></td>
<td>Saxenda should be started at 0.6 mg subcutaneously daily for one week, then increased to 1.2 mg daily for one week, then again increased to 1.8 mg daily for one week, once again increased to 2.4 mg daily for one week and 3 mg daily there-after.</td>
</tr>
<tr>
<td>DEA Schedule</td>
<td>Not applicable</td>
</tr>
<tr>
<td>Date of market availability</td>
<td>First quarter of 2015</td>
</tr>
<tr>
<td>Similar Medications (Look-Alike Sound-Alike)</td>
<td>Sugammadex, liarozole, Lioresal, liraglutide (Victoza)</td>
</tr>
</tbody>
</table>

---

### CLINICAL USE EVALUATION
<table>
<thead>
<tr>
<th>Common Adverse Effects</th>
<th>Nausea, hypoglycemia, diarrhea, constipation, vomiting, headache, decreased appetite, dyspepsia, fatigue, dizziness, abdominal pain, and elevations in lipase</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severe Adverse Effects</td>
<td>Hypoglycemia, allergic reactions (anaphylactoid and angioedema), papillary thyroid cancer, colorectal neoplasms, heart conduction disorders, hypotension, abnormalities of various laboratory values including liver enzymes, serum calcitonin, serum lipase and amylase</td>
</tr>
<tr>
<td>Severe Drug-Drug Interactions</td>
<td>Liraglutide delays gastric emptying and could impact the absorption of concomitantly administered oral medications. Clinically relevant effects weren’t observed in the approval trials; however, caution is advised. Do not use any GLP-1 receptor agonist in combination with Saxenda.</td>
</tr>
<tr>
<td>Severe Drug-Food Interactions</td>
<td>None reported</td>
</tr>
<tr>
<td>Important Labs Values to assess prior to order entry or at point of clinical follow up. (Need Pop Up?)</td>
<td>Blood glucose and HbA1c in patients with type 2 diabetes, serum creatinine</td>
</tr>
<tr>
<td>Used in Pediatric Areas</td>
<td>Safety and effectiveness not established</td>
</tr>
<tr>
<td>Renal or Hepatic Dosing</td>
<td>Use with caution in patients with mild, moderate or severe renal impairment; there are postmarketing reports of acute renal failure and worsening chronic renal failure with liraglutide. Limited experience with use in patients with mild, moderate or severe hepatic impairment; use with caution.</td>
</tr>
</tbody>
</table>
| Critical Issues (i.e., contraindications, warnings, etc) that should be emphasized | • Risk of thyroid and C-cell tumors  
• Acute pancreatitis  
• Acute gallbladder disease  
• Hypoglycemia with the use of concomitant anti-diabetic agents  
• Increases in heart rate  
• Acute renal impairment  
• Hypersensitivity reactions  
• Suicidal behavior and ideation |
| Special administration technique or considerations | • New, unused pens should be stored in the refrigerator at 36 to 46 degrees Fahrenheit.  
• The pen in use can be stored for 30 days at room temperature.  
• Remove the cover from the pen and make sure the solution is colorless.  
• Take a new needle and twist on to the pen until it is tight.  
• Twist the end of the pen to dial up the correct dose.  
• Remove the protective cap from the needle and insert into the top layer of the skin.  
• Press and hold the top button with the dose counter says 0; there may noise or feeling of a click.  
• Keep the needle in the skin to the count of 6 and then remove the needle from the skin. |
| Prepared by | Ross Bindler PharmD |

---

**Ivermectin 1% cream / Soolantra / Galderma**

<table>
<thead>
<tr>
<th>Generic Name / Brand Name / Company</th>
<th>Ivermectin 1% cream / Soolantra / Galderma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Date of approval</td>
<td>December 19, 2014</td>
</tr>
<tr>
<td>Drug Class (Mechanism of Action if novel agent)</td>
<td>Cream; Avermectin macrocyclic lactone</td>
</tr>
<tr>
<td>Indication</td>
<td>Treatment of inflammatory lesions of rosacea</td>
</tr>
<tr>
<td>Comparative agent – Therapeutic interchange?</td>
<td>Metronidazole cream</td>
</tr>
</tbody>
</table>
| Dosage forms/strengths. Common Dose/sig | Topical cream, 1%, supplied in 30 g, 45 g, and 60 g tubes  
Apply a pea-size amount to affected areas of the face once daily. |
| DEA Schedule | Not applicable |

---

FDA Activity Newsletter | WSU Drug Information Center | December 2014
### Ivermectin Lotion 0.5%

**Date of market availability**  
Early 2015

**Similar Medications (Look-Alike Sound-Alike)**  
Ivermectin lotion 0.5%

**CLINICAL USE EVALUATION**

<table>
<thead>
<tr>
<th>Common Adverse Effects</th>
<th>Skin burning sensation, skin irritation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severe Adverse Effects</td>
<td>None</td>
</tr>
<tr>
<td>Severe Drug-Drug Interactions</td>
<td>None</td>
</tr>
<tr>
<td>Severe Drug-Food Interactions</td>
<td>None</td>
</tr>
<tr>
<td>Important Labs Values to assess prior to order entry or at point of clinical follow up. (Need Pop Up?)</td>
<td>None</td>
</tr>
<tr>
<td>Used in Pediatric Areas</td>
<td>Safety and effectiveness not established for this indication.</td>
</tr>
<tr>
<td>Renal or Hepatic Dosing</td>
<td>None</td>
</tr>
</tbody>
</table>

**Critical Issues (i.e., contraindications, warnings, etc) that should be emphasized**
- Pregnancy Category C
- Ivermectin is excreted in human milk in low concentrations after oral administration; excretion in human milk is unknown after topical administration.

**Special administration technique or considerations**
- Place pea-size amount on affected area (forehead, chin, nose, and/or each cheek) and then spread as a thin layer, avoiding eyes and lips.

**Prepared by**  
Anne Kim, PharmD, MPH, MIT

---

### Diclofenac Sodium Injection / Dyloject / Javelin Pharms

**Generic Name / Brand Name / Company**  
Diclofenac sodium / Dyloject / Javelin Pharms

**Date of approval**  
December 23, 2014

**Drug Class (Mechanism of Action if novel agent)**  
NSAID

**Indication**  
Management of mild to moderate pain; management of moderate to severe pain alone or with opioid analgesics

**Comparative agent – Therapeutic interchange?**  
Ketorolac injection, Ibuprofen injection

**Dosage forms/strengths. Common Dose/sig**  
37.5 mg/mL single-dose vial  
Inject 37.5 mg via intravenous bolus injection over 15 seconds every 6 hours as needed – not to exceed 150 mg/day.

**DEA Schedule**  
Not applicable

**Date of market availability**  
Not reported

**Similar Medications (Look-Alike Sound-Alike)**  
Dolgic, Dylix, Dilex

**CLINICAL USE EVALUATION**

<table>
<thead>
<tr>
<th>Common Adverse Effects</th>
<th>Gastrointestinal reactions (abdominal pain, constipation, diarrhea, dyspepsia, flatulence, gross bleeding/perforation, heartburn, nausea, Gl ulcers, vomiting), abnormal renal function, headache, infusion site pain, dizziness, insomnia, pruritus, hypotension</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severe Adverse Effects</td>
<td>Anaphylaxis, hypersensitivity reactions, severe skin reactions (Stevens-Johnson Syndrome, toxic epidermal necrolysis, exfoliative dermatitis)</td>
</tr>
</tbody>
</table>
| Severe Drug-Drug Interactions | Concomitant administration with:  
  - aspirin decreases the protein binding of diclofenac.  
  - anticoagulants (e.g., warfarin) increases risk of gastrointestinal bleeding.  
  - ACE inhibitors decreases the antihypertensive effect of ACE inhibitors.  
  - cyclosporine increases risk of cyclosporine nephrotoxicity.  
  - diuretics decreases natriuretic effect of furosemide and thiazides.  
  - lithium increases risk of lithium toxicity due to decreased renal clearance of lithium.  
  - methotrexate increases risk of methotrexate toxicity.  
  - CYP2C9 inhibitors increases diclofenac levels. |

---

**FDA Activity Newsletter**  
WSU Drug Information Center  
December 2014
- CYP2C9 inducers decreases diclofenac levels.

<table>
<thead>
<tr>
<th>Severe Drug-Food Interactions</th>
<th>None reported</th>
</tr>
</thead>
<tbody>
<tr>
<td>Important Labs Values to assess prior to order entry or at point of clinical follow up. (Need Pop Up?)</td>
<td>Monitor for signs or symptoms of gastrointestinal bleeding. Monitor CBC, liver enzymes, and basic chemistry panel</td>
</tr>
<tr>
<td>Used in Pediatric Areas</td>
<td>Safety and effectiveness not established</td>
</tr>
<tr>
<td>Renal or Hepatic Dosing</td>
<td>No dose adjustment required for mild hepatic impairment or mild to moderate renal impairment. Use in patients with moderate to severe hepatic impairment is not recommended, and use in moderate to severe or severe renal impairment should be avoided.</td>
</tr>
</tbody>
</table>

Critical Issues (i.e., contraindications, warnings, etc) that should be emphasized

- Gastrointestinal – inflammation, bleeding, ulceration, perforation of gastrointestinal tract
- Hepatic – elevated liver enzymes, hepatotoxicity, jaundice, liver necrosis, liver failure
- Hematological – anemia, increased bleeding time from inhibition of platelet aggregation
- Hypertension – increased risk of new onset or worsening of pre-existing hypertension
- Renal – avoid use in patients with moderate to severe renal insufficiency
- Anaphylaxis – avoid use in patients with known hypersensitivity to diclofenac
- Cardiovascular – avoid use in patients with perioperative pain in the setting of coronary artery bypass graft surgery to avoid increased risk of cardiovascular thrombotic events, myocardial infarction, or stroke
- Asthma – avoid use in aspirin-sensitive asthma patients, use with caution in patients with pre-existing asthma
- Pre-existing congestive heart failure/edema – use with caution because drug may increase fluid retention and edema
- Masking inflammation/fever – infections may not be detected since diclofenac decreases signs of fever and inflammation
- Wound healing – caution with post-operative use because drug may deter wound healing
- Pregnancy Category C prior to 30 weeks gestation; Category D starting at 30 weeks gestation – avoid use at 30 weeks gestation and beyond to prevent premature closure of the fetal ductus arteriosus

| Special administration technique or considerations | Patient should be well-hydrated prior to drug administration. |
| Prepared by | Anne Kim, PharmD, MPH, MIT |