Highlights of FDA Activities – 6/1/15 – 6/30/15

FDA Drug Safety Communications & Drug Information Updates:

Drug Safety Communication - Potiga (ezogabine): FDA Determines 2013 Labeling Adequate to Manage Risks of Retinal Abnormalities, Potential Vision Loss, and Skin Discoloration 6/16/15

Potiga (ezogabine), an anti-seizure drug, was determined to have potential risks of vision loss due to pigment changes in the retina and of skin discoloration. The FDA has determined that the potential risks of this medication can be adequately managed by the recommendations currently found in the medication labeling. To further explore the potential long-term consequences, the FDA has ordered the manufacturer (GlaxoSmithKline) to conduct a long-term observational study. The REMS will not be modified at this time, as a FDA review of additional safety reports indicate that pigment changes in the retina are a cosmetic effect and do not affect vision. Health care professionals should continue to adhere to the Boxed Warning of the medication, as well as the Warnings & Precautions and Usage sections of the labeling information.

Drug Information Update- New Risk Evaluation and Mitigation Strategies website 6/16/15

The FDA launched a new online resource "REMS@FDA" (http://www.accessdata.fda.gov/scripts/cder/rems/index.cfm) to provide the public with information about currently approved individual and shared system REMS, as well as historical and released REMS.

Drug safety Communication – Daytrana Patch (methylphenidate transdermal system): Permanent Skin Color Changes 6/24/15

Permanent loss of skin color may occur with use of the Daytrana patch (methylphenidate transdermal system) for Attention Deficit Hyperactivity Disorder (ADHD). The FDA added a new warning to the labeling describing the skin condition, which is known as chemical leukoderma. Patients or their caregivers should be advised to watch for new areas of lighter skin, especially under the drug patch, and immediately report these changes to their health care professionals. Areas of skin color loss up to 8 inches in diameter have been reported. Alternative treatments should be considered for patients who experience skin color changes.

Drug Information Update - Drug Supply Chain Security Act (DSCSA) Product Tracing: Enforcement Delay 6/30/15

The FDA notified dispensers, primarily pharmacies, that although the DSCSA was to require product tracing beginning July 1, the FDA does not intend to take enforcement action against dispensers who do not meet the requirements of the act prior to November 1, 2015. The FDA is allowing more time to ensure all parties can receive, capture, and maintain required product-tracing information as required by the law.

Major Product Recalls Announced Through MedWatch:

Vascu-Guard Peripheral Vascular Patch by Baxter: Recall – Difficulty Distinguishing the Smooth from Rough Surface 6/3/15

Baxter has voluntarily recalled its Vascu-Guard Peripheral Vascular Patch. This is due to customer complaints that it is difficult to distinguish between the rough and smooth side of the patch. Incorrect placement of the patch with the rough side toward the bloodstream could potentially increase the risk of vessel thrombosis and/or embolism. Product codes affected by this recall include:

1504026 VASCU-GUARD TS 1x6cm
1504028 VASCU-GUARD TS 0.8x8cm
1504030 VASCU-GUARD TS 1x10cm
1504032 VASCU-GUARD TS 2x9cm

Recall of Gemcitabine injection and methotrexate injection by Mylan 6/8/15

Mylan has voluntarily recalled various lots of Gemcitabine for injection and Methotrexate Injection (25mg/mL) due to the presence of visible foreign particulate matter in tested retention samples.
The recalled products are:

NDC #	Product & Strength	Lot #	Exp. Date
0069-3857-10	Gemcitabine for Injection, USP 200 mg	7801084	07/2015
0069-3857-10	Gemcitabine for Injection, USP 200 mg	7801110	08/2015
67457-463-02	Gemcitabine for Injection, USP 2 g	7801221	03/2016
67457-464-20	Gemcitabine for Injection, USP 200 mg	7801398	08/2016
67457-464-20	Gemcitabine for Injection, USP 200 mg	7801406	08/2016
67457-464-20	Gemcitabine for Injection, USP 200 mg	7801427	09/2016
67457-462-01	Gemcitabine for Injection, USP 1 g	7801284	05/2016
67457-467-99	Methotrexate Injection, USP 50 mg/2 mL (25 mg/mL)	7801421	09/2016

HeartWare Ventricular Assist System (VAS): Recall – Damaged to Alignment Guides, Connector Pins or Driveline Connector May Cause Pump to Stop; Battery Failure May Prevent Alarm from Sounding 6/16/15 & 6/22/15

Multiple issues have been identified which may result in failure of the VAS used to deliver blood from the heart to the rest of the body in patients awaiting heart transplant. Damage to the alignment guides, connector pins, or driveline connector may result in interruption of the electrical connection and pump stoppage, which can result in serious patient harm and/or death. Battery failure may prevent an alert that external power source has been disconnected. Patients currently supported by the HeartWare System should be identified and notified directly. Patient devices should be inspected as soon as possible to investigate for damage, and controllers replaced if necessary. The recall includes product codes 1101 and 1103 and the serial numbers for all Heartware systems currently in use.

M/L Taper with Kinectiv Technology Prosthesis by Zimmer: Recall – Higher than expected levels of manufacturing residues 6/19/15

A process monitoring failure led to higher than expected amounts of manufacturing residues left on the Zimmer M/L Taper with Kinectiv Technology Femoral Stems and Necks, Tivanium allow implants used for hip replacements. These residues can cause serious adverse health issues including allergic reactions, pain, infections, or death. Use of these products may require the need for a revision surgery to replace the affected implant. Manufacturing and distribution dates: March 31, 2015 through April 20, 2015. A completed list of affected products can be found on the MedWatch site (http://www.fda.gov/MedicalDevices/Safety/ListofRecalls/ucm451936.htm)

Covidien Shiley Neonatal and Pediatric Tracheostomy Tube by Medtronic: Recall 6/24/15

Medtronic is voluntarily recalling Covidien Shiley tracheostomy tubes from eight product lines that were manufactured after November 29, 2012 following complaints of 12 serious patient injuries including breathing difficulties that impacted oxygen levels immediately upon tube placement or discomfort. The tracheotomy tubes were found to have a wider-angle bend than standard. A complete list of recalled lots can be found on the MedWatch site (http://www.fda.gov/Safety/Recalls/ucm452490.htm)

Dietary Supplement Recalls & Public Notifications

In June, 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.

Product	***Promoted Use***	***Hidden/Undeclared Drug Ingredient(s)***
Smart Lipo*	Weight loss	Sibutramine, desmethylsibutramine, and phenolphthalein
Pyrola Advanced Joint Formula*	Joint pain	Diclofenac, chlorpheniramine

*Recalled

New Product Shortages Reported by the FDA:	***Date Initially Posted***
Nimodipine (Nymalize) Oral Solution	6/2/15
Ethiodized oil (Lipiodol) Injection	6/24/15
Aprepitant (Emend) Capsules	6/26/15

Product Discontinuations/Withdrawals	***Date Posted***
Ezetimibe / Atorvastatin (Liptruzet) Merck Sharp & Dohme has discontinued all strengths and presentations of Liptruzet. Both components remain available as individual agents.	6/2/15
Metoprolol Tartrate (Lopressor) Injection Novartis has discontinued Lopressor ampules; metoprolol tartrate injection remains available from other manufacturers.	6/9/15

New Drug Approvals:	***Description***	***Date Approved***
Cangrelor/Kengreal/Medicines Company	See attached drug summary	6/22/15

New Indications:	***Description***	***Date Approved***
Eltrombopag / Promacta / Novartis	Pediatric patients 6 years and older included as part of the current approved indication	6/12/15
Zolmitriptan / Zomig / AstraZeneca	Treatment of migraine with or without aura in adolescents 12 to 17 years old	6/12/15
Perampanel / Fycompa / Eisai Inc	Adjunctive therapy for primary generalized tonic-clonic seizures in patients 12 years and older with epilepsy	6/22/15

New Dosage Forms or Formulation:	***Description***	***Date Approved***
Metaxalone/ Skelaxin HB/ Corepharma	New tablet strength of 640 mg	6/1/15
Albenza/ Albenzazole / Amedra	New dosage form (chewable tablets)	6/11/15

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Cangrelor / Kengreal / Medicines Company	
Generic Name / Brand Name / Company	Cangrelor / Kengreal / Medicines Company
Date of approval	6/22/15
Drug Class (Mechanism of Action if novel agent)	Direct-acting $P2Y_{12}$ platelet receptor inhibitor
Indication	Adjunct to percutaneous coronary intervention (PCI) to reduce risk of periprocedural myocardial infarction, repeat coronary revascularization, and stent thrombosis in patients who have not been treated with a $P2Y_{12}$ platelet inhibitor and are not receiving a glycoprotein IIb/IIIa inhibitor
Comparative agent – Therapeutic interchange?	Ticagrelor, prasugrel, clopidogrel
Dosage forms/strengths. Common Dose/sig	Injection: lyophilized powder for solution 50 mg/10 mL Dose: 30 mcg/kg IV bolus prior to PCI followed immediately by a 4 mcg/kg/min IV infusion for at least 2 hours or the duration of the procedure, whichever is longer.
DEA Schedule	Not applicable
Date of market availability	Anticipated July 2015
Similar Medications (Look-Alike Sound-Alike)	
CLINICAL USE EVALUATION	
Common Adverse Effects	Bleeding (15.5%), worsening renal function in patients with severe renal impairment (3.2%), dyspnea (1.3%)
Severe Adverse Effects	Bleeding, hypersensitivity reactions
Severe Drug-Drug Interactions	Thienopyridines (Clopidogrel & Prasugrel): avoid concomitant use. Initiate therapy immediately after discontinuation of the cangrelor infusion.
Severe Drug-Food Interactions	Not applicable
Important Labs Values to assess prior to order entry or at point of clinical follow up. (Need Pop Up?)	None
Used in Pediatric Areas	Safety and efficacy have not been established in this population
Renal or Hepatic Dosing	No dosage adjustment required
Critical Issues (i.e., contraindications, warnings, etc) that should be emphasized	• Contraindications: o Hypersensitivity to cangrelor or formulation components o Significant active bleeding • An oral $P2Y_{12}$ platelet inhibitor should be administered to maintain platelet inhibition following discontinuation of the cangrelor infusion. Therapy should be initiated with one of the following: o Ticagrelor 180 mg at any time during the infusion or immediately after discontinuation o Prasugrel 60 mg immediately after discontinuation of the infusion o Clopidogrel 600 mg immediately after discontinuation of the infusion
Special administration technique or considerations	• Do not use without dilution with normal saline or 5% Dextrose injection USP. • Administer via a dedicated IV line. • Administer bolus dose rapidly (less than 1 minute) from the diluted bag via manual IV push or pump.
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