

Highlights of FDA Activities – 8/1/2016 – 8/31/2016

FDA Drug Safety Communications & Drug Information Updates:

Drug Information Update: FDA Approves First Generic Tamiflu (oseltamivir phosphate) 8/3/16

The FDA has approved the first generic version of Tamiflu (oseltamivir phosphate) for the treatment of influenza A and B in patients two weeks of age and older who have had flu symptoms for no more than 48 hours. The generic, manufactured by Natco Pharma, is available as capsules in the same strengths as Tamiflu: 30 mg, 45 mg, and 75 mg.

Drug Information Update: Pharmacy Compounding – Draft Guidance on Insanitary Conditions 8/3/16

The FDA issued a [draft guidance](#) on insanitary conditions at compounding facilities, intended to assist facilities in identifying insanitary conditions in order to take corrective action and assist state regulatory agencies in understanding what the FDA regards as insanitary conditions.

Drug Information Update: Kratom (*Mitragyna speciosa*) 8/4/16

The FDA announced the U.S. Marshals Service seized more than 100 cases of products labeled as kratom, and alleged the seized products are unapproved new drugs and misbranded drugs under the Federal Food, Drug, and Cosmetic Act. Kratom consumption has been associated with respiratory depression, vomiting, nervousness, weight loss, and constipation, as well as withdrawal symptoms including hostility, aggression, excessive tearing, muscle and bone aches, and spasms. It has been associated with both narcotic and stimulant-like effects. In addition, on 8/30/16 the U.S. Drug Enforcement Agency filed a notice of intent to place kratom, and its two primary constituents (mitragynine and 7-hydroxymitragynine) temporarily onto Schedule 1 as of 9/30/16.

Drug Information Update: Drugs Similar to French BIA 10-2474 Do Not Pose Similar Safety Risks 8/12/16

Based on findings regarding investigational drug BIA 10-2474, which was associated with neurologic injuries and a death in a phase 1 study conducted in France, the FDA determined that agent exhibits a unique toxicity that does not extend to other members of the fatty acid amide hydrolase (FAAH) inhibitor class. The FDA is working with sponsors to allow continued investigation of agents in this class in the U.S.

Drug Information Update: Redesigned Orange Book 8/15/16

The FDA announced the launch of an improved web-based version of the Approved Drug Products with Therapeutic Equivalence Evaluations – most commonly known as the “[Orange Book](#).”

Drug Information Update: Import Alert for All Drugs Produced by Laxachem Organics in India 8/16/16

The FDA placed Laxachem Organics Pvt. Ltd., Ahmednagar, Maharashtra, India, on import alert on 8/11/16, for refusing to allow FDA investigators to inspect its facility. The import alert stops all Laxachem pharmaceutical products from entering the United States legally and will remain in effect until the facility has been fully inspected by the FDA and found to meet U.S. standards. Laxachem manufactures active pharmaceutical ingredient (API) for repackagers, labelers, and wholesale drug distributors, some of which sell API to manufacturing facilities in the United States. One of the drugs Laxachem manufactures is Docusate Sodium.

FDA Safety Communication: Programmable Syringe Pumps - Problems With Fluid Flow Continuity at Low Infusion Rates 8/25/2016

The FDA informed health care professionals that when using programmable syringe pumps to infuse therapies at low rates (e.g., less than 5 mL per hour, and especially at flow rates of less than 0.5 mL per hour), a lack of flow continuity (i.e., inconsistent rate of delivery) can result in serious clinical consequences, including delay of therapy, over-infusion or under-infusion. The FDA believes that these concerns may extend to all programmable syringe pumps while infusing at low rates. The FDA currently believes that the overall benefits of programmable syringe pumps outweigh their risks; however, the FDA has requested that manufacturers make labeling changes to their syringe pumps to address flow continuity concerns.

Drug Safety Communication: Serious Risks & Death When Combining Opioids with Benzodiazepines 8/31/16

FDA review has found that the growing combined use of opioids with benzodiazepines or other drugs that depress the central nervous system (CNS) has resulted in serious side effects, including slowed or difficult breathing and deaths. In an effort to decrease the use of opioids and benzodiazepines, or opioids and other CNS depressants, together, Boxed Warnings are being added to the drug labeling of prescription opioid pain and prescription opioid cough medicines, and benzodiazepines. Health care professionals should limit prescribing opioid pain medicines with benzodiazepines or other CNS depressants only to patients for whom alternative treatment options are inadequate. If these medicines are prescribed together, limit the dosages and duration of each drug to the minimum possible while achieving the desired clinical effect. Warn patients and caregivers about the risks of slowed or difficult breathing and/or sedation, and the associated signs and symptoms. Avoid prescribing prescription opioid cough medicines for patients taking benzodiazepines or other CNS depressants, including alcohol.

Major Product Recalls Announced Through MedWatch:**Topical Skin Products by Sage Products: Recall – Product Contamination** 8/1/16 & 8/23/16

Sage Products recalled select lots of impregnated cloth topical skin products at the distributor, healthcare facility, retail, and user levels due to potential product contamination with the bacteria *Burkholderia cepacia*. The recalled products include Comfort Shield® Barrier Cream Cloths, Incontinence Clean-Up Cloth, M-care™ Meatal Cleansing Cloths for the Foley Catheterized Patient, Comfort Bath® Cleansing Washcloths, and 2% Chlorhexidine Gluconate Cloths. A complete list of affected product lots, which were distributed worldwide between August 2014 and August 2016 can be found on the [FDA web site](#).

Amikacin Sulfate Injection USP 500 mg/2 mL (250 mg/mL) and 1 Gram/4 mL (250 mg/mL) Vials by Teva: Recall - Glass Particulate Matter 8/3/16

Teva Pharmaceuticals recalled seven lots of Amikacin Sulfate Injection USP, 500 mg/2mL (250 mg/mL) and 1 gram/4mL (250 mg/mL) vials due to the potential for the presence of glass particulate matter. A complete list of affected product lots can be found on the [FDA web site](#).

0.25% Bupivacaine Hydrochloride Injection, USP by Hospira: Recall- Particulate Matter 8/5/16

Hospira recalled one lot of 0.25% Bupivacaine Hydrochloride injection at hospital/retail level due to the presence of an unknown particulate matter within a single vial. The recall affects NDC number: 0409-1159-02, Lot number: 59-064-DK, expiration 11/1/2017, distributed to wholesalers and hospitals between December 2015 and January 2016.

Liquid Drug and Dietary Supplement Products by PharmaTech: Recall - Product Contamination 8/9/16

PharmaTech, LLC recalled all liquid products due to a potential risk of product contamination with *Burkholderia cepacia*. Drug products recalled: Aller-chlor Antihistamine, Diocto Syrup, Docusate Sodium, Ninjacof, Ninjacof A, Senexion Liquid, Senna Syrup, Sennazon Syrup, Virtrate-2, Virtrate-K. Dietary supplement products recalled: Calcionate Syrup, Cerovite Liquid, CertaVite with Antioxidants, CytoDetox, D3 Vitamin Liquid, D-Vita Drops, Fer-iron Liquid, Ferrous Drops, Ferrous Sulfate Liquid, Liquid Vitamin C, Pedia D-Vite Drops, Pedia Poly-Vite Drops, Pedia Tri-Vite Drops, Poly-Vita Drops, Poly-Vita Drops with Iron, Polyvitamin liquid, Polyvitamin liquid with Iron, Renew HC, Tri-Vita Drops, Tri-Vitamin liquid. This recall affects all liquid products distributed from 10/20/15 through 7/15/16.

Ton Shen Health “DHZC-2” Tablet Recall: Lead Levels 8/12/16 & 8/29/16

Ton Shen Health of Chicago, IL, recalled all lots of “DHZC-2” Tablets and discontinued distribution of all Ton Shen Health/Life Rising products because they have the potential to be contaminated with elevated levels of lead. The recalled “DHZC-2” tablets were mostly sold locally in Chicago area in retail stores and some were distributed to other states through mail order.

Cetylev® (Acetylcysteine) Effervescent Tablets for Oral Solution by Arbor Pharmaceuticals: Recall - Inadequate Seal of the Blister Pack 8/18/16

Arbor Pharmaceuticals, LLC recalled of three lots of Cetylev (acetylcysteine) effervescent tablets for oral solution, 500 mg, due to an inadequate seal of the blister pack. Three lots of the 500 mg strength (Lot Numbers 005C16, 006C16 and 007C16, expiration date 02/2018) with NDC 24338-700-10 are included in the recall.

Oxacillin for Injection, USP, 10 g by Sagent Pharmaceuticals: Recall - Presence of Iron Oxide Particulate Matter 8/19/16

Sagent Pharmaceuticals, Inc. recalled one lot of Oxacillin for Injection, USP, 10 g (NDC 25021-163-99) Lot OXT512 (Exp. Date March 2017) manufactured by Astral SteriTech Private Limited and distributed by Sagent. This recall to the user level was initiated following receipt of a product complaint for a single vial containing small, dark particulate matter found within the solution after reconstitution which was identified as iron oxide.

Eyesaline Eyewash Solution from Honeywell: Recall - Microbial Contamination 8/22/16

Honeywell is recalling one lot (lot# F15091-61) of 32-ounce bottles of Eyesaline Eyewash solution, which is used for emergency eye rinsing after an injury, as a precautionary measure due to a low risk of product contamination with *Klebsiella pneumoniae*. Eyesaline Eyewash is sold through industrial sales distributors.

Lamotrigine Orally Disintegrating Tablet 200 mg by Impax: Recall - Incorrect Labeling of Blister Cards 8/29/16

Impax Laboratories, Inc. recalled one lot of Lamotrigine Orally Disintegrating Tablet (ODT) 200 mg, NDC 0115-1529-08, Lot # 502240 to the retail level due to mislabeling. The affected lot was distributed between 6/13/16 and 8/10/16 to wholesale distributors and retail pharmacies nationwide. Unit-of-use blister packs may contain 100 mg product instead of 200 mg product. Each blister card within the unit-of-use blister pack is properly labeled as 100 mg ODT, however the plastic shell pack containing the 100 mg blister cards is labeled as 200 mg ODT. Shell-packs from the affected lot may contain 100 mg ODT instead of 200 mg ODT, and as a result, it is possible that consumers could take less than their intended lamotrigine dose.

Dietary Supplement Recalls & Public Notifications

In August, 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.

<u>Product</u>	<u>Promoted Use</u>	<u>Hidden/Undeclared Drug Ingredient(s)</u>
Adelgazantes R-II	Weight Loss	Sibutramine ¹
Anaconda Strong Formula	Sexual Enhancement	Sildenafil ²
Boss-Rhino Gold X-tra Strength	Sexual Enhancement	Sildenafil ²
Citrus' Fit	Weight Loss	Sibutramine ¹
De Guo Hei Bei (德国黑倍)	Sexual Enhancement	Sildenafil ²
DHZC-2*	Chinese Herbal Supplement	Elevated Lead Levels
Kopi Jantan Tradisional Natural Herbs Coffee	Natural Coffee	Desmethyl carbodenafil (sildenafil-like) ²
Love4Long	Sexual Enhancement	Sildenafil ²
Master Zone 1500	Sexual Enhancement	Sildenafil and tadalafil ²
Natural Eruption	Weight loss and increasing energy	Sibutramine ¹
One More Knight 1750	Sexual enhancement	Tadalafil ² & Dapoxetine ³
Super Shanghai	Sexual enhancement	Sildenafil ²
The Golden Root	Sexual enhancement	Sildenafil ²
Weili (一炮到天亮 or Yi Pao Dao Tian Liang)	Sexual enhancement	Sildenafil ²

Ziyinzhuangyang Sexual enhancement Sildenafil²

*Recalled

¹Sibutramine: oral anorexiant; risk - increased cardiovascular events; discontinued 2010 [FDA](#)

²Sildenafil, tadalafil: used to treat erectile dysfunction, may interact with nitrates to lower blood pressure to dangerous levels

³Dapoxetine: selective serotonin reuptake inhibitor studied for use in premature ejaculation, but not FDA approved

New Product Shortages Reported by the FDA:

Date Initially Posted

Ceftazidime and avibactam for injection (Avycaz, Cerexa) 2.5 g	8/9/16
Estradiol Valerate (Delestrogen, Par) Injection 10 mg/mL, 5 mL vials; 20 mg/mL, 5 mL vials; 40 mg/mL, 5 mL vials.	8/10/16
Penicillin G Procaine Injection (Pfizer) 1,200,000 Units/2 mL 2 mL syringe; 600,00 Units/1 mL 1 mL syringe	8/24/16

Product Discontinuations/Withdrawals

Date Posted

Reserpine tablets 0.1 mg and 0.25 mg (Sandoz) - No reserpine products remain available in the U.S.	8/30/16
Triamcinolone hexacetonide injectable suspension 20 mg/mL (Aristospan, Sandoz) No alternative triamcinolone hexacetonide formulations are available in the U.S.	8/30/16

New Drug Approvals:

Description

Date Approved

Oxycodone & Naltrexone / Troxyca ER / Pfizer	See attached drug summary	8/19/16
Etanercept-szszs / Erelzi / Sandoz	Biosimilar to Enbrel; products not considered interchangeable. Package sizes differ from Enbrel. Only available as a 25 mg/0.5 mL and 50 mg/1 mL prefilled syringe, or a 50 mg/mL prefilled pen. No available dosage form allows weight based dosing for pediatric patients below 63 kg. Inactive ingredients differ significantly from Enbrel.	8/30/16

New Indications:

Description

Date Approved

Pembrolizumab / Keytruda / Merck Sharp & Dohme Corp.	For the treatment of patients with recurrent or metastatic head and neck squamous cell carcinoma (HNSCC) with disease progression on or after platinum-containing chemotherapy.	8/5/16
Topiramate extended-release / Trokendi XR / Supernus Pharmaceuticals	Monotherapy treatment for partial onset or primary generalized tonic-clonic seizures in patients 6 to 10 years of age	8/18/16
Ofatumumab / Arzerra / Glaxo	Use in combination with fludarabine and cyclophosphamide in relapsed chronic lymphocytic leukemia	8/30/16

<u>New Dosage Forms or Formulation:</u>	<u>Description</u>	<u>Date Approved</u>
Fluticasone furoate spray / Flonase Sensimist / GSK Consumer Healthcare	Rx-to-OTC switch of product formerly available as Veramyst, for treatment of symptoms associated with seasonal and perennial allergies in patients 2 years of age and older	8/2/16
Granisetron / Sustol / Heron Therapeutics	Injection, extended release; 5-HT ₃ antagonist for treatment of nausea/vomiting. See details below.	8/9/16
Influenza vaccine / Afluria Quadrivalent/ Seqirus	Quadrivalent vaccine for use in adults, supplied in single-dose, preservative-free pre-filled syringes.	8/26/16

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Granisetron Extended-Release Injection / Sustol / Heron Therapeutics	
Generic Name / Brand Name / Company	Granisetron / Sustol / Heron Therapeutics
Date of approval	8/9/16
Drug Class (Mechanism of Action if novel agent)	5-HT ₃ Antagonist
Indication	Chemotherapy-induced nausea and vomiting associated with initial/repeat courses of moderately emetogenic chemotherapy, or anthracycline and cyclophosphamide combination therapy
Comparative agent – Therapeutic interchange?	Granisetron, ondansetron, palonosetron
Dosage forms/strengths. Common Dose/sig	Extended-release injection: 10 mg/0.4 mL in single-dose, pre-filled syringe Dose: 10 mg subcutaneously before the start of emetogenic chemotherapy on day 1.
DEA Schedule	Not scheduled
Date of market availability	Unknown
Similar Medications (Look-Alike Sound-Alike)	Granisetron, ondansetron, palonosetron, Sustiva
CLINICAL USE EVALUATION	
Common Adverse Effects	Injection site reactions, constipation, fatigue, headache, diarrhea, abdominal pain, insomnia, dyspepsia, dizziness, asthenia, gastroesophageal reflux
Severe Adverse Effects	Hypersensitivity reactions, serotonin syndrome
Severe Drug-Drug Interactions	Other serotonergic medications
Severe Drug-Food Interactions	None listed
Important Labs Values to assess prior to order entry or at point of clinical follow up. (Need Pop Up?)	Renal function (eGFR or CrCl)
Used in Pediatric Areas	Safety and effectiveness not established in patients under the age of 18
Renal or Hepatic Dosing	Avoiding use in patients with severe renal impairment (CrCl <30 mL/min) and do not administer more than once every 14 days in patients with CrCl 30-59 mL/min. There are no specific recommendations for patients with hepatic impairment.
Critical Issues (i.e., contraindications, warnings, etc) that should be emphasized	<ul style="list-style-type: none"> Do not use in patients with hypersensitivity to granisetron or any component of Sustol Injection site reactions may occur, such as infection, bruising, hematomas, bleeding nodule formation. Pain and tenderness may also occur. Use of granisetron extended-release may mask a progressive ileus and/or gastric obstruction. This should be closely monitored in patients who have had recent abdominal surgery, or those at risk for gastrointestinal obstruction. Serotonin syndrome may occur with use of this product, particularly when used with concomitant serotonergic drugs.
Special administration technique or considerations	Administer via subcutaneous injection into the back of the upper arm, or in the skin of the abdomen at least 1 inch away from the umbilicus. Due to its viscosity, administer as a slow, sustained injection, over 20 to 30 seconds.
Prepared by	Christopher Robinett, Pharm.D. Candidate 2017

Oxycodone & Naltrexone Extended-Release Capsules / Troxyca ER / Pfizer	
Generic Name / Brand Name / Company	Oxycodone & Naltrexone / Troxyca ER / Pfizer
Date of approval	8/19/16
Drug Class (Mechanism of Action if novel agent)	Combination opioid and opioid antagonist; abuse deterrent formulation
Indication	Severe pain
Comparative agent – Therapeutic interchange?	OxyContin
Dosage forms/strengths. Common Dose/sig	Extended release capsules: 10 mg/1.2 mg, 20 mg/2.4 mg, 30 mg/3.6 mg, 40 mg/4.8 mg, 60 mg/7.2 mg, 80 mg/9.6 mg For opioid-naïve or non-tolerant, initiate with one 10 mg/1.2 mg capsule every 12 hours. The 40 mg/4.8 mg, 60 mg/7.2 mg, and 80 mg/9.6 mg strengths are only for use in patients with known opioid tolerance.
DEA Schedule	Schedule II
Date of market availability	TBD
Similar Medications (Look-Alike Sound-Alike)	OxyContin
CLINICAL USE EVALUATION	
Common Adverse Effects	Nausea, constipation, vomiting, headache, somnolence
Severe Adverse Effects	Addiction, respiratory depression, neonatal opioid withdrawal syndrome, adrenal insufficiency, hypotension, seizures, withdrawal, anaphylaxis, myocardial ischemia, ventricular fibrillation
Severe Drug-Drug Interactions	Interactions with CNS depressants, may cause increased CNS depression; interaction with CYP2D6/CYP3A4 inhibitors/inducers, may affect concentration of drug; interaction with serotonergic drugs, may cause serotonin syndrome; interaction with muscle relaxants, may increase degree of respiratory depression; interaction with MAOI, may increase risk of anxiety, confusion, hypotension, respiratory depression, sedation, coma and death; interaction with diuretics, this drug may reduce diuretic efficiency by inducing ADH release; interaction with anticholinergics, may increase risk of urinary retention, severe constipation, and paralytic ileus.
Severe Drug-Food Interactions	None known
Important Labs Values to assess prior to order entry or at point of clinical follow up. (Need Pop Up?)	Renal/hepatic function
Used in Pediatric Areas	Safety and efficacy have not been established in pediatric patients
Renal or Hepatic Dosing	No specific dosing, but recommended to follow a conservative approach when titrating dose.
Critical Issues (i.e., contraindications, warnings, etc) that should be emphasized	<ul style="list-style-type: none"> • Contraindications: significant respiratory depression; acute/severe bronchial asthma in unmonitored setting or in absence of resuscitative equipment; known GI obstruction (including paralytic ileus); hypersensitivity to oxycodone, naltrexone or any components of Troxyca ER. • Warnings: risk for addiction, abuse, and misuse; life-threatening respiratory depression; neonatal withdrawal syndrome; interactions with CYP2D6/CYP3A4 inhibitors/inducers; increased CNS depression when used concomitantly with other CNS depressants; risk for serotonin syndrome when used concomitantly with serotonergic drugs; risk of adrenal insufficiency with long-term use; risk of severe hypotension; risk of GI obstruction; increased risk of seizures; potential withdrawal; do not drive or operate heavy machinery while taking this medication.
Special administration technique or considerations	<ul style="list-style-type: none"> • Do not break, chew, or crush Troxyca ER • Capsule may be opened and the contents (pellets) sprinkled on applesauce – swallow without chewing
Prepared by	Christopher Robinett, Pharm.D. Candidate 2017