Highlights of FDA Activities – 2/1/16 – 2/29/16

FDA Drug Safety Communications & Drug Information Updates:

Drug Information Update: Over-the-Counter "Chelation" Product 2/1/16

The FDA reminded consumers to be wary of "chelation" products marketed over-the-counter (OTC) to prevent or treat diseases such as lead poisoning. No chelation products have been FDA approved for OTC use. The products currently available OTC have not been reviewed by the FDA and are illegally marketed. FDA approved chelation products require a prescription because safe chelation therapy requires supervision by a health care provider.

Drug Information Update: Sweeping Review of FDA Opioid Policies 2/4/16

FDA Deputy Commissioner for Medical Products and Tobacco, Dr. Robert Califf, announced an action plan to reassess the FDA's approach to opioids. The FDA will:

- Re-examine the risks and benefits of opioids and ensure that the agency considers their wider public health effects;
- Changes to immediate-release opioid labeling, adding warnings and safety information that incorporate elements similar to those required for the extended-release/long-acting opioid analgesics labeling;
- Update Risk Evaluation and Mitigation Strategy requirements for opioids after considering advisory committee recommendations and review of existing requirements;
- Encourage the development of abuse-deterrent formulations;
- Improve access to naloxone and medication-assisted treatment options for patients with opioid use disorders; and
- Support better pain management options, including alternative treatments.

The agency is seeking guidance from outside experts in the field of pain management and drug abuse, and will convene independent advisory committees when considering approval of any new opioids that do not contain abuse-deterrent properties and any pediatric opioid labeling. Additional post-marketing data will be required of manufacturers to assess long term impact of use of extended-release and long-acting opioids.

Major Product Recalls Announced Through MedWatch:

Fagron Syrspend SF and Syrspend SF Grape Suspending Agents: Recall Due to Contamination 02/10/16

Fagron, Inc. recalled several lots of two compounding agents, SyrSpend SF and SyrSpend SF Grape, due to microbial contamination with yeast (*Candida galli*). Recalled lots of SyrSpend SF are: 15I21-U01-026920; 15J26-U05-027457; 15J26-U05-027473; 15I21-U01-027370; and 15J19-U05-027406. Recalled lots of SyrSpend SF Grape are: 15G29-U03-025975; 15A05-U03-022765; and 15A05-U06-023277

Pharmakon Pharmaceuticals Morphine Sulfate 0.5 mg/mL: Recall Due to Potency Issues 02/16/16

Pharmakon Pharmaceuticals recalled one lot of 0.5 mg/mL morphine sulfate preservative free in 0.9% sodium chloride 1 mL syringe (NDC 45183-0322-78; Lot E52418EV11C, Expiration: 03/19/2016) at the manufacturer level. The recall was issued after laboratory tests conducted by the manufacturer showed the product to be super potent.

Baxter 0.9% Sodium Chloride for Irrigation: Recall Due to Presence of Particulate Matter 02/17/16

Baxter International Inc. recalled one lot of irrigation solution at the hospital/user level. The recall is in response to a customer complaint of particulate matter, identified as an insect. The recalled product is 0.9% Sodium Chloride Irrigation, USP, 500 mL plastic pour bottle (NDC 0338-0048-03; Lot G120162, Expiration: 11/30/2018)

Dietary Supplement Recalls & Public Notifications

In February, 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)*
Boss Number #Six	Sexual Enhancement	Tadalafil
Bull	Sexual Enhancement	Sildenafil
Bull's Genital	Sexual Enhancement	Sildenafil
Ginseng Power-X	Sexual Enhancement	Sildenafil and Sulfoaildenafil
Golden Night	Sexual Enhancement	Sildenafil and Hydroxythiohomosildenafil
Mamba is Hero	Sexual Enhancement	Sildenafil, Demethyl carbodenafil, and Dapoxetine
Neophase Natural Sex Enhancer	Sexual Enhancement	Hydroxyacetildenafil
Ninja-X	Sexual Enhancement	Sildenafil and Thiosildenafil
Weekend Prince	Sexual Enhancement	Sildenafil
Zhong Hua Niu Bian	Sexual Enhancement	Sildenafil

New Product Shortages Reported by the FDA:	*Date Initially Posted*
Potassium Acetate Injection, USP (2 mEq/mL; 20 and 50 mL vials)	02/03/16
Sodium Acetate Injection, USP (2 mEq/mL; 20, 50, and 100 mL vials)	02/03/16
Sodium Bicarbonate Injection, USP (4%, 5 mL vial; 4.2%, 10 mL syringe; 7.5%, 50 mL syringe; 8.4%, 10 mL vial, 50 mL vial, 50 mL syringe, 10 mL syringe)	02/04/16
Tretinoin Capsules (10 mg)	02/19/16

Product Discontinuations/Withdrawals	*Date Posted*
Memantine hydrochloride unit dose XR capsules (Namenda, Forest Laboratories, Inc.) Namenda XR 14 mg (NDC 0456-3414-63) and Namenda XR 28 mg (NDC 0456-3428-63) discontinued Namenda XR 7 mg and 21 mg capsules are still available	02/12/16
Valsartan tablets (Sandoz) Valsartan 40 mg (NDC 0781-5607-31), 80 mg (NDC 0781-5608-92), 160 mg (NDC 0781-5618-92), and 320 mg (NDC 0781-5619-92) discontinued Remains available from other generic manufacturers	02/16/16
Valsartan and Hydrochlorothiazide tablets, film coated (Sandoz) Valsartan 80/12.5 mg (NDC 0781-5948-92), 160/12.5 mg (NDC 0781-5949-92), 160/25 mg (NDC 0781-5950-92), 320/12.5 mg (NDC 0781-5951-92), and 320/25 mg (NDC 0781-5952-92) discontinued Remains available from other generic manufacturers	02/16/16

New Drug Approvals:	*Description*	*Date Approved*
Brivaracetam / Briviact / UCB, Inc.	See attached drug summary	02/18/16

New Indications:	***Description***	***Date Approved***
Palbociclib / Ibrance / Pfizer	Treatment of HR-positive, HER2-negative advanced or metastatic breast cancer, in combination with: ▪ Letrozole as initial endocrine based therapy in postmenopausal women, or ▪ Fulvestrant in women with disease progression following endocrine therapy	02/19/16
Everolimus / Afinitor / Novartis	Treatment of progressive, well-differentiated non-functional, neuroendocrine tumors (NET) of gastrointestinal or lung origin, with unresectable, locally advanced or metastatic disease	02/26/16
Obinutuzumab / Gazyva / Genentech, Inc.	Treatment of follicular lymphoma (FL), in combination with bendamustine, in patients that relapsed/refractory to a rituximab-containing regimen ▪ Obinutuzumab and bendamustine combination to follow obinutuzumab monotherapy	02/26/16

New Dosage Forms or Formulation:	***Description***	***Date Approved***
Betamethasone dipropionate spray 0.5% / Sernivo / Promius Pharma	Spray for the treatment of mild to moderate psoriasis in adults.	2/5/16
Tofacitinib / Xeljanz XR /	Extended-release dosage form indicated for RA	2/24/16

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Brivaracetam / Briviact / UCB, Inc.	
Generic Name / Brand Name / Company	Brivaracetam / Briviact / UCB, Inc.
Date of approval	02/18/16
Drug Class (Mechanism of Action if novel agent)	Exact mechanism of action is unknown. Selective, high-affinity, ligand for synaptic vesicle protein 2A in the brain, which may confer anticonvulsant activity
Indication	Add-on treatment for partial onset seizures in patients 16 years and older with epilepsy
Comparative agent – Therapeutic interchange?	Levetiracetam analog
Dosage forms/strengths. Common Dose/sig	Recommended starting dose is 50 mg twice daily, and does *not* require gradual dose escalation Tablets: 10 mg, 25 mg, 50 mg, 75 mg, and 100 mg ▪ Do not crush or chew; swallow table whole (with fluids) Oral Solution: 10 mg/mL Injection: 50 mg/5 mL single-dose vial ▪ Administer IV over 2 to 15 minutes; vial for single use only
DEA Schedule	To be determined
Date of market availability	Second quarter of 2016
Similar Medications (Look-Alike Sound-Alike)	Levetiracetam

CLINICAL USE EVALUATION	
Common Adverse Effects	Drowsiness, dizziness, fatigue, nausea and vomiting, constipation
Severe Adverse Effects	Suicidal thoughts or behavior, agitation, new or worsening depression, aggression, and panic attacks; bronchospasm; angioedema; rare incidence of leukopenia and neutropenia reported; coordination disorder, including balance/gait disturbance, ataxia, nystagmus
Severe Drug-Drug Interactions	Rifampin: decreased brivaracetam plasma concentrations due to CYP2C19 induction -- recommendation to double dose in patients on rifampin Carbamazepine: increased exposure to active metabolite of carbamazepine -- recommendation to decrease carbamazepine dose Phenytoin: increased plasma concentration of phenytoin -- recommendation to monitor phenytoin levels when initiating or discontinuing concomitant brivaracetam Levetiracetam: considered duplicate therapy, without added benefit
Severe Drug-Food Interactions	None listed
Important Labs Values to assess prior to order entry or at point of clinical follow up.	None listed
Used in Pediatric Areas	Safety and efficacy not established in patients less than 16 years of age
Renal or Hepatic Dosing	Renal: No dose adjustments required for renal impairment; no data in patients with end-stage renal disease/dialysis; use *not* recommended in these patients Hepatic: A 50% dose reduction recommended for *all* stages of hepatic impairment; starting dose is 25 mg twice daily (50 mg/day); maximum dose 75 mg twice daily (150 mg/day)
Critical Issues (i.e., contraindications, warnings, etc.) that should be emphasized	Contraindications: ▪ Hypersensitivity (angioedema or bronchospasm) to the active and inactive ingredients; discontinue use in patients that develop hypersensitivity reactions Warnings and Precautions: ▪ Increased risk of suicidal thoughts/behavior, which may manifest within one week of treatment initiation ▪ Psychiatric adverse reactions (eg: irritability, anxiety, nervousness, aggression, belligerence, anger, agitation, restlessness, depression, mood swings) and psychotic adverse reactions (eg: hallucinations, paranoia, or acute psychosis) were reported in 13% of patients ▪ Increased risk of neurologic adverse reactions such as somnolence, fatigue, dizziness, and gait disturbance Avoid abrupt discontinuation to reduce risk of increased seizure frequency or status epilepticus
Special administration technique or considerations	May be initiated with either intravenous or oral administration Tablets and oral solution may be taken with or without food Oral Solution: ▪ Use a calibrated measuring device to measure and administer dose; household teaspoon/tablespoon is not recommended ▪ May be administered via a nasogastric or gastronomy tube ▪ Discard any unused oral solution after 5 months of opening bottle Injection: ▪ May be administered IV without further dilution, or mixed with the following diluents: 0.9% Sodium Chloride injection, USP; Lactated Ringer's injection; 5% Dextrose injection, USP ▪ Diluted solution is stable for 4 hours at room temperature
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