# Highlights of Medication-Related FDA Activities – 8/1/15 – 8/31/15

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

**Gilenya (fingolimod): FDA Warns About Cases of Rare Brain Infection** 8/4/15

The FDA is warning that a case of definite progressive multifocal leukoencephalopathy (PML) and a case of probable PML have been reported in patients treated with fingolimod for multiple sclerosis. Unlike earlier cases, these patients had not been previously treated with an immunosuppressant, therefore information about these cases is being added to the product labeling. Patients treated with fingolimod should be advised to contact a health care professional immediately if they experience symptoms such as new or worsening weakness, increased trouble using their arms or legs, or changes in thinking, eyesight, strength, or balance.

**Compounded Drugs Stored in Becton-Dickinson 3 mL and 5 mL Syringes: Do Not Use** 8/18/15

The FDA is alerting health care professionals not to use compounded or repacked medications stored in Becton-Dickinson (BD) 3 ml and 5 ml general purpose syringes unless there are no alternatives. The rubber stopper in the syringe may interact with the medication causing potency loss over time. General purpose syringes are approved for fluid aspiration and injection only, not as closed containers. BD's 10ml, 20ml, and 30ml general purpose syringes may also contain the same rubber stopper material and should not be used as closed containers for compounding or repackaging drugs. FDA-approved prefilled syringes do not carry this warning.

**Picato (ingenol mebutate) Gel: FDA Warns of Severe Adverse Events, Requires Label Changes** 8/21/15

The FDA warns about reports of severe allergic reactions and herpes zoster associated with the use of Picato gel. The reports included cases of severe eye injury and skin reactions. Some reports were related to not following the labeled instructions on the product. FDA is requiring label changes to warn of the additional safety risks, and provide additional instructions on safe and appropriate application of the product. Patients experiencing severe allergic reaction such as throat tightness, difficulty breathing, feeling faint, or swelling of the lips or tongue should discontinue using Picato gel and get immediate medical attention. Patients should also discontinue Picato gel and contact their doctor if they develop severe skin rash, hives, or itching.

**Dipeptidyl peptidase-4 (DPP-4) inhibitor drug class Warning and Precaution update. FDA warns of severe and disabling joint pain.** 8/28/15

The FDA has added a new Warning and Precaution to labels of all DPP-4 medications (sitagliptin, saxagliptin, linagliptin, and alogliptin) used to treat type 2 diabetes, due to reports of potentially severe and disabling joint pain associated with the use of these medications. Joint pain has been reported from 1 day to years after starting a DPP-4 inhibitor, and resolved following discontinuation, usually within a month. Joint pain recurred in some patients upon exposure to the same or another DPP-4 inhibitor.

## *Major Medication/Delivery Device Recalls Announced Through MedWatch:*

**Prolotherapy with Phenol, Injectable by Hartley Medical: Recall – Non-sterility Concerns** 8/18/15

This recall follows an inspection that raised concerns about Hartley's sterility methods and testing procedures specifically for this product. The recall affects 3 lots (RX328690, exp. 12/1/2015; RX323132, exp. 10/6/2015; and RX321608, exp. 11/1/2015) distributed to pain clinics in California and Nevada from 5/15/15 to 7/14/15.

**Refresh Lacri-Lube, Refresh P.M., FML 0.1%, & Blephamide 10%/0.2% by Allergan: Recall - Particulate Matter** 8/24/15

Allergan is conducting recall to the consumer level of Refresh Lacri-Lube 3.5 g and 7 g for dry eye, Refresh P.M. 3.5 g for dry eye, FML (fluorometholone) 0.1% sterile ophthalmic ointment, and Blephamide (sulfacetamide sodium and prednisolone acetate) 10%/0.2% sterile ophthalmic ointment 3.5 g following reports of small black particles

coming off of the cap, due to the unscrewing action of the container, and getting into the preparation. Affected products and lot numbers can be found at: http://www.fda.gov/Safety/Recalls/ucm459485.htm

**Alaris Syringe Pump by CareFusion: Recall – Alarm Error May Cause Interruption of Therapy** 8/27/15
The Alaris Syringe Pump model 8110 has been recalled due to an error that triggers an alarm and prompts the pump to stop the infusion to the patient, even if the error code is cleared. Units displaying error code 351.6740 should be removed from use until repairs are made.

**Alaris Medley Large Volume Pump (LVP) Frame Membrane by Elite Biomedical Solutions LLC: Recall – Potential for Over or Under Delivery of Fluids by an Infusion Pump** 8/27/15
The recall is for the frame member in select Alaris Medley Large Volume Pumps. The membrane is part of the infusion pump that separates internal components from liquid contamination. Use of pumps with the recalled membrane could result in over or under infusion of fluids to the patient. The affected part and lot numbers are: Frame Membrane NOEM, Part # TC10006587 / 10013801 (Lot # 022015502 and 0421151000) and Frame Membrane NOEM Shipped with LVP Bezel Assembly, Part # 49000204 (Lot # 031815100, 032415100 and 043015215). These parts were manufactured from 2/20/15 to 4/21/15 and distributed from 2/25/15 to 5/8/15.

**OmniPod Insulin Management System by Insulet: Recall – Possibility of Higher Rate of Failure** 8/27/15
Insulet Corporation has recalled 40,846 boxes (containing 10 Pods per box) of the OmniPod Insulin Management System following reports of device failure resulting in patients not receiving the expected insulin dose. The affected lots were distributed from December 2013 to March 2015. A list of affected lots can be found at: http://www.fda.gov/Safety/Recalls/ucm460169.htm

## ***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.

| ***Product*** | ***Promoted Use*** | ***Hidden/Undeclared Drug Ingredient(s)*** |
|---|---|---|
| Achieving Zero | Weight loss | Sibutramine |
| Kaboom Action Strips by Blue Market Square* | Sexual function | Sulfoaildenafil |
| LiDa DaiDaiHua by Blue Market Square* | Weight loss | Sibutramine and phenolphthalein |
| Thin and Slim, Fataway Ultimate Stack capsules by Novacare* | Weight loss | Salicylic acid |
| ThermoFX capsules by Novacare* | Weight loss | Salicylic acid |
| Thin and Slim, MaxOut Body capsules by Novacare* | Weight loss | Salicylic acid |
| Metabolic Accelerator capsules by Novacare* | Weight loss | Salicylic acid |
| Thin and Slim, Burn Fat Now capsules by Novacare* | Weight loss | Salicylic acid |
| Thin and Slim, Thermogenic Fat Burner capsules by Novacare* | Weight loss | Salicylic acid |
| TruTrim bulk by Novacare* | Weight loss | Salicylic acid |
| Thin and Slim Naturally AM capsules by Novacare* | Weight loss | Salicylic acid |
| Thin and Slim, Extreme Stack capsules by Novacare* | Weight loss | Salicylic acid |
| Xcellerator bulk by Novacare* | Weight loss | Salicylic acid |
| Asia Black capsules by Novacare* | Weight loss | Salicylic acid |
| Black Widow 25 capsules by Novacare* | Weight loss | Salicylic acid |
| Methyldrene Original 25 capsules by Novacare* | Weight loss | Salicylic acid |
| Miracle Diet 30 by The One Minute Miracle Inc* | Weight loss | Phenolphthalein |
| Miracle Rock 48 by The One Minute Miracle Inc* | Sexual function | Thiosildenafil |
| Ultimate Antioxidant Tablets by Dr. Venessa's* | Antioxidant supplement | Undeclared allergens: crustacean shellfish, milk |

*Recalled

| ***New Product Shortages Reported by the FDA:*** | ***Date Initially Posted*** |
|---|---|
| Meropenem for injection USP | 8/25/2015 |

| ***Product Discontinuations/Withdrawals*** | ***Date Posted*** |
|---|---|
| Memantine hydrochloride (Namenda, Forest) tablets 5 & 10 mg<br>The extended-release capsules and oral solution remain available. | 8/15/15 |

| ***New Drug Approvals:*** | ***Description*** | ***Date Approved*** |
|---|---|---|
| Flibanserin / Addyi / Sprout Pharmaceuticals | See attached drug summary | 8/18/15 |
| Evolocumab / Repatha / Amgen | See attached drug summary | 8/27/15 |

| ***New Indications:*** | ***Description*** | ***Date Approved*** |
|---|---|---|
| Dichlorphenamide / Keveyis / Taro | Treatment of primary hyperkalemic and hypokalemic periodic paralysis | 8/10/15 |
| Oxycodone HCl / Oxycontin / Purdue Pharma | Indication expanded to include use in opioid-tolerant pediatric patients 11 years of age and older | 8/13/15 |
| Cysteamine / Procysbi / Raptor | Indication expanded to include use in pediatric patients 2 years and older with nephropathic cystinosis | 8/14/15 |
| Brentuximab / Adcetris / Seattle Genetics | Treatment of patients with classical Hodgkin lymphoma at high risk of relapse or progression as post-autologous hematopoietic stem cell transplantation | 8/17/15 |
| Eltrombopag / Promacta / Novartis | Treatment of chronic immune thrombocytopenic purpura in pediatric patients one year and older | 8/24/15 |
| Rilpivirine / Edurant / Janssen | Indication expanded to include pediatric patients from 12 to less than 18 years with HIV RNA $\leq$ 100,000 copies/mL | 8/26/15 |
| Eslicarbazepine acetate / Aptiom / Sunovion Pharms | Monotherapy treatment of partial-onset seizures in adults | 8/27/15 |

| ***New Dosage Forms or Formulation:*** | ***Description*** | ***Date Approved*** |
|---|---|---|
| Empagliflozin & metformin / Synjardy / Boehringer Ingelheim | Tablets combining empagliflozin 5 mg and 12.5 mg with metformin HCl 500 mg and 1000 mg for twice daily administration in the management of type 2 diabetes mellitus | 8/26/15 |

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| Flibanserin / Addyi / Sprout Pharmaceuticals | |
|---|---|
| Generic Name / Brand Name / Company | Flibanserin / Addyi / Sprout Pharmaceuticals |
| Date of approval | 8/18/2015 |
| Drug Class (Mechanism of Action if novel agent) | Multifunctional serotonin agonist and antagonist (MSAA) |
| Indication | Treatment of premenopausal women with acquired, generalized hypoactive sexual desire disorder (HSDD) |
| Comparative agent – Therapeutic interchange? | Not applicable |
| Dosage forms/strengths. Common Dose/sig | Tablets: 100 mg<br>100 mg once daily at bedtime; discontinue after 8 weeks if patient does not report improvement |
| DEA Schedule | Not applicable |
| Date of market availability | October 17, 2015 |
| Similar Medications (Look-Alike Sound-Alike) | Alli |
| **CLINICAL USE EVALUATION** | |
| Common Adverse Effects | Dizziness (11%), somnolence (11%), nausea (10%), fatigue (9%), insomnia (5%), dry mouth (2%) |
| Severe Adverse Effects | Hypotension, syncope, somnolence, sedation |
| Severe Drug-Drug Interactions | Alcohol – contraindicated – increased risk of severe hypotension and syncope<br>Moderate or strong CYP3A4 inhibitors – contraindicated – increased flibanserin concentrations – increased risk of hypotension and syncope<br>Weak CYP3A4 inhibitors, including oral contraceptives, and strong CYP2C19 inhibitors – increase flibanserin concentrations and risk of adverse effects<br>CYP3A4 inducers – not recommended<br>Digoxin – increased digoxin concentrations – monitor closely |
| Severe Drug-Food Interactions | Grapefruit – contraindicated – moderate CYP3A4 inhibitor |
| Important Labs Values to assess prior to order entry or at point of clinical follow up. (Need Pop Up?) | None |
| Used in Pediatric Areas | Not indicated for use in pediatric patients |
| Renal or Hepatic Dosing | Contraindicated in patients with any degree of hepatic impairment.<br>No dosage adjustment in patients with renal impairment. |
| Critical Issues (i.e., contraindications, warnings, etc) that should be emphasized | • Contraindicated with use of alcohol, with concomitant moderate or strong CYP3A4 inhibitors, and in patients with hepatic impairment due to increased risk of hypotension and syncope.<br>• Assess likelihood of abstaining from alcohol use before prescribing; counsel about importance of abstaining from alcohol.<br>• Avoid use in nursing mothers<br>• CYP2C19 poor metabolizers have increased flibanserin exposure and increased risk for adverse effects<br>• REMS restrictions including certification of prescribers and pharmacies |
| Special administration technique or considerations | • Flibanserin should be administered at bedtime. Patients should avoid activities requiring full alertness for at least 6 hours after each dose. |
| Prepared by | Terri Levien, Pharm.D. |

| Evolocumab / Repatha / Amgen | |
|---|---|
| Generic Name / Brand Name / Company | Evolocumab / Repatha / Amgen |
| Date of approval | 8/27/15 |
| Drug Class (Mechanism of Action if novel agent) | Proprotein convertase subtilisin kexin type 9 (PCSK9) inhibitor |
| Indication | • Adjunct to diet and maximally tolerated statin therapy for treatment of adults with heterozygous familial hypercholesterolemia (HeFH) or clinical atherosclerotic cardiovascular disease (CVD), who require additional LDL-C lowering<br>• Adjunct to diet and other LDL-lowering therapies (statins, ezetimibe, LDL apheresis) in patients with homozygous familial hypercholesterolemia (HoFH) who require additional LDL-C lowering |
| Comparative agent – Therapeutic interchange? | Alirocumab |
| Dosage forms/strengths. Common Dose/sig | Injection: 140 mg/mL in single-use prefilled syringe or autoinjector<br>Primary hyperlipidemia with CVD or HeFH: 140 mg every 2 weeks or 420 mg monthly subcutaneously<br>HoFH: 420 mg once monthly subcutaneously |
| DEA Schedule | Not applicable |
| Date of market availability | Available |
| Similar Medications (Look-Alike Sound-Alike) | None identified |
| **CLINICAL USE EVALUATION** | |
| Common Adverse Effects | Greater than 5% in 52 week trial: nasopharyngitis, upper respiratory tract infection, influenza, back pain, injection site reactions |
| Severe Adverse Effects | Allergic reactions |
| Severe Drug-Drug Interactions | None known |
| 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?) | None required; LDL-C may be monitored to assess response to therapy |
| Used in Pediatric Areas | Safety and effectiveness in adolescent patients with HoFH was comparable to that observed in adults; safety and effectiveness have not been established in pediatric patients younger than 13 years with HoFH or in pediatric patients of any age with primary hyperlipidemia or HeFH. |
| Renal or Hepatic Dosing | No dosage adjustment is necessary in patients with mild or moderate renal or hepatic impairment; no data are available in patients with severe renal or hepatic impairment. |
| Critical Issues (i.e., contraindications, warnings, etc) that should be emphasized | • Contraindicated in patients with serious hypersensitivity reaction to evolocumab<br>• Discontinue if serious allergic reaction occurs<br>• Syringe and autoinjector contain natural rubber |
| Special administration technique or considerations | • Administered subcutaneously into the abdomen, thigh or upper arm<br>• Rotate injection sites<br>• It may take up to 15 seconds to inject evolocumab<br>• To administer 420 mg, give 3 injections consecutively within 30 minutes<br>• Store in the refrigerator; allow to warm to room temperature for at least 30 minutes prior to administration. Patient may store at room temperature for up to 30 days. |
| Prepared by | Terri L. Levien, Pharm.D. |