FDA MedWatch Alerts:

Olmesartan Medoxomil: Drug Safety Communication – Label Changes to Include Intestinal Problems (Sprue-Like Enteropathy) [Posted 7/3/13]
Labeling of all olmesartan containing products (Benicar, Benicar HCT, Azor, Tribenzor, and generics) updated to include information on sprue-like enteropathy with the use of olmesartan. Enteropathy may develop months to years after starting olmesartan, and sometimes require hospitalization. The FDA recommends health care professionals counsel patients to contact them if they develop severe, chronic diarrhea with substantial weight loss while taking an olmesartan-containing product, even if it takes months to years for symptoms to develop. Patients should contact their health care professional right away if they take an olmesartan-containing product and experience severe diarrhea, diarrhea that does not go away, or significant weight loss.

Drug Information Update – FDA alerts companies to stop illegal sale of treatments for diabetes [Posted 7/23/13]
The FDA issued a warning to 15 companies whose products, some of which are labeled as supplementary products, violate federal law. They are being sold illegally online and in retail stores with the claim that these products can mitigate, treat, cure, or prevent diabetes and related complications. Consumers are advised not to use these or similar products because they may contain ingredients that are harmful. A list of the companies and their products can be found below:
- Anastasia Marie Laboratories, Inc. – Anastasia Diapedic Foot & Leg Treatment
- Glytain Internal Remedies, Inc. – Glytain
- Health Care Products, Hi-Tech Pharmacal Co. – Zostrix Diabetic Foot Pain Relief Cream, Zostrix Diabetic Joint & Arthritis Pain Relief Cream, and Diabeti-Derm Antifungal Cream
- Health King Enterprises & Balanceuticals Group, Inc. – Sugar Balancer
- The Magni Group, Inc. dba MagniLife – Diabetic Neuropathy Foot Cream, Diabetic Foot Cream, and Diabetic Hand & Body Cream
- Naturecast Products – Eradicator
- Nature’s Health Supply, Inc. – Diabetes Daily Care
- Neuliven Health – Glucocil
- Nutrient Synergy – Nepretin
- PharmTerra – ProBeta
- Amrutam Life Care Pvt. Ltd. – Diexi
- Enhance Nutraceutical – Diaberex
- INS Bioscience Berhad, HLS International Sdn. Bhd., Easy Pha-max – Insupro Forte
- Origin BioMed Incsc. – Neuragen PN and Neuragen Cream

FDA recommends the use of oral Nizoral only for the treatment of certain life-threatening mycoses. The patient’s liver status should be assessed prior to initiation of the drug and also ALT should be monitored throughout therapy. Adrenal function should also be monitored in those with adrenal insufficiency or with borderline adrenal function and in patients under prolonged periods of stress. In addition, concomitant medications should be reviewed for potential drug interactions. Label changes have been approved and a new Medication Guide addressing these safety issues have been added.
Mefloquine Hydrochloride: Drug Safety Communication – Label Changes Due to Risk of Serious Psychiatric and Nerve Side Effects

A boxed warning regarding neurologic and psychiatric side effects associated with the antimalarial drug has been added to the drug label. If patients are experiencing neurologic side effects such as dizziness, loss of balance, or ringing in the ears or if they are experiencing psychiatric side effects including feeling anxious, mistrustful, depressed, or having hallucinations, they are encouraged to contact their prescribing health professional. Neurologic side effects may occur at any time during drug use and can last for months up to years after the drug is stopped or can be permanent. Information on these adverse effects are also provided in the patient Medication Guide.

Major Product Recalls Announced Through MedWatch:

Benztropine Mesylate Injection by Fresenius Kabi USA: Recall – Potential Presence of Glass Particles

Benztropine Mesylate Injection, USP, 2 mg/2 mL (1 mg/mL) single dose vials recalled due to the potential presence of glass particles in the vials. Recalled lot numbers are 030712, 071212, 090512 and 111412.

RECOMBIVAX HB (Hepatitis B Vaccine (Recombinant)) Adult Formulation by Merck Sharp and Dohme Corp.: Recall – Potential for Cracked Vials

The lot number: J001183 of RECOMBIVAX HB Adult Formulation distributed by Merck between March 12, 2013 and May 2, 2013 recalled due to the potential for cracked vials within the lot.

Estarylla (norgestimate and ethinyl estradiol) by Sandoz Company: Recall – Report of Placebo Tablet Present in Row of Active Tablets

Recalled lot number LF01213A, expiration date 02/2014, NDC 00781-4058-15, supplied in cartons containing 3 blister cards of 28 tablets each recalled due to a report of a placebo tablet in a row of active tablets.

Verathon, Inc., GlideScope Video Laryngoscope (GVL) 3, 4, 5 and GlideScope (AVL) 2, 3, 4 and 5 Reusable Blades: Class 1 Recall – Risk of Blade Tip Breakage and Premature Failure

The GlideScope Video Laryngoscope (GVL) and GlideScope Advanced Video Laryngoscope (AVL) are used by qualified medical professionals to obtain a clear, open view of the vocal cords for medical procedures. Breakage of the blade tip in a patient’s mouth could result in airway blockage.

Medtronic MiniMed Paradigm Insulin Infusion Sets: Class 1 Recall – Potential for Over or Under Delivery of Insulin

If insulin or other fluids come into contact with the inside of the tubing connector, the fluid can temporarily block the vents that allow the pump to prime, which can result in too much or too little insulin delivery.

Bryan Medical Tracoe Mini 3.0mm Tracheostomy Tubes: Class 1 Recall – Mislabeled Packaging

The lot number: 000-1000071752 manufactured from December 12, 2012 to January 14, 2013 and distributed from April 9, 2013 to April 12, 2013 labeled as containing 3 mm neonatal tube actually contains a 3 mm pediatric tube which is 4 mm longer than a neonatal tube.

MedStream Programmable Infusion Pump: Class 1 Recall – Malfunction in the Fill Level Sensor

The Fill Level Sensor, which is intended to measure the contents of the drug reservoir, may malfunction resulting in the pump’s low reservoir alarm sounding too early. Affected products were distributed starting July 2009 through June 2013 and include Models 91-4200US 20 mL pump, 91-4201US 40 mL pump, 91-4200 20 mL pump, and 91-4201 40 mL pump.
LeMaitre Vascular, Inc., Albograft Vascular Graft: Class I Recall – Blood Leak  
[Posted 7/24/13]

The Albograft Vascular Graft was recalled due to blood leakage from the surface of the graft after implantation. Affected models were distributed only in Pennsylvania between April 2011 through June 2013 and include AMC1408, AMC1506, AMC1608, AMC1810, AMC2010, AMC4007, AMC4008, AMC6006, AMC6007, AMC6008, ATC1526, ATC1530, ATC3016, ATC3018, ATC3024, ATC3026, and Batch 56890A.

GE Healthcare Nuclear Medicine Systems: Class I Recall – Serious Injuries or Deaths Could Occur  
[Posted 7/29/13]

Healthcare facilities are instructed to discontinue use of these systems until they can be inspected and repaired following an incident in which a patient died due to injuries sustained while being scanned on an Infinia Hawkeye 4 Nuclear Medicine System. These Nuclear Medicine Systems are used to perform general Nuclear Medicine imaging procedures for detection of radioisotope tracer uptake in the patient’s body. Affected products include: Infinia Nuclear Medicine Systems, VG and VG Hawkeye Nuclear Medicine Systems, Helix Nuclear Medicine Systems. Brivo NM615, Discovery NM630, Optima NM/CT640, Discovery NM/CT670.

[Posted 07/29/2013]

Nova Diabetes Care initiated a voluntary recall of 21 lots of the Nova Max Glucose Test Strips distributed both in the USA and outside the continental USA. Nova Max Plus glucose meter kits that include test strips from the recalled lots are also included in this voluntary recall. A list of affected lots can be found on the MedWatch page.

Public Notifications/Recalls due to Undeclared Drug Ingredients

In July, 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>Esbelin silouette te &amp; Esbelin silouette Herbal Blend with L-Carnitine (Herbal Care LLC)*</td>
<td>Weight loss</td>
<td>Sibutramine, N-desmethylsibutramine, and N-di-desmethylsibutramine</td>
</tr>
<tr>
<td>Healthy Life Chemistry B-50 Lot # F03Q and CO2R, Healthy Life Chemistry Multi-Mineral Lot # 12-829, &amp; Healthy Life Chemistry Vitamin C Lot # E03Q (Purity First Health Products)*</td>
<td>Dietary supplements</td>
<td>Methasterone (an anabolic steroid), dimethazine, and dimethyltestosterone</td>
</tr>
<tr>
<td>Silver Sword &amp; Clalis (Hardmenstore.com)*</td>
<td>Erectile dysfunction</td>
<td>Sildenafil</td>
</tr>
<tr>
<td>Volcano Male Enhancement Liquid &amp; Volcano Male Enhancement Capsules (Volcano Company)*</td>
<td>Erectile dysfunction</td>
<td>Desmethyl carbodenafil and dapoxetine</td>
</tr>
<tr>
<td>*Recalled</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

New Drug Shortages Reported by the FDA:

No new drug shortages reported by the FDA in July 2013

Product Discontinuations/Withdrawals

Isradipine extended-release tablets (DynaCirc CR 5 mg and 10 mg, GlaxoSmithKline)  
Isradipine 2.5 mg and 5 mg capsules remain available.

[07/05/2013]
**New Drug Approvals:**

<table>
<thead>
<tr>
<th>Drug Name / Brand Name / Company</th>
<th>Description</th>
<th>Date Approved</th>
</tr>
</thead>
<tbody>
<tr>
<td>Afatinib / Gilotrif™ / Boehringer Ingelheim Pharmaceuticals, Inc.</td>
<td>See accompanying drug summary</td>
<td>[07/12/2013]</td>
</tr>
<tr>
<td>Golimumab injection / Simponi Aria / Janssen</td>
<td>Intravenous formulation, administered as 2 mg/kg IV infusion over 30 minutes at weeks 0 and 4, and then every 8 weeks in conjunction with methotrexate in the treatment of adult patients with moderately to severely active rheumatoid arthritis</td>
<td>[07/18/2013]</td>
</tr>
<tr>
<td>Tacrolimus extended-release capsule / Astragraf XL / Astellas</td>
<td>New extended-release formulation for once daily administration in kidney transplant rejection prophylaxis</td>
<td>[07/19/2013]</td>
</tr>
<tr>
<td>Levomilnacipran / Fetzima / Forest</td>
<td>See accompanying drug summary</td>
<td>[07/25/2013]</td>
</tr>
<tr>
<td>Ferric carboxymaltose / Injectafer / Luitpold</td>
<td>See accompanying drug summary</td>
<td>[07/25/2013]</td>
</tr>
</tbody>
</table>

**Compiled by:**

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Jasen Cong, Pharm.D., PGY1 Drug Information Resident
Stacey Nguyen, Pharm D. Candidate 2014
Sharon Valdez, Pharm.D. Candidate 2014

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**Afatinib / Gilotrif™ / Boehringer Ingelheim Pharmaceuticals, Inc.**

<table>
<thead>
<tr>
<th>Generic Name / Brand Name / Company</th>
<th>Afatinib / Gilotrif™ / Boehringer Ingelheim Pharmaceuticals, Inc.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Date of approval</td>
<td>July 12, 2013</td>
</tr>
<tr>
<td>Drug Class (Mechanism of Action if novel agent)</td>
<td>Antineoplastic agent, tyrosine-kinase inhibitor, epidermal growth factor receptor (EGFR) inhibitor – covalently binds to the kinase domains of EGFR, HER2, and HER4 and irreversibly inhibits tyrosine kinase autophosphorylation resulting in downregulation of ErbB signaling and thus, tumor growth inhibition</td>
</tr>
<tr>
<td>Indication</td>
<td>First-line treatment for metastatic non-small cell lung cancer whose tumors have EGFR exon 19 deletions or exon 21 (L858R) substitution mutations</td>
</tr>
<tr>
<td>Comparative agent – Therapeutic interchange?</td>
<td>Erlotinib</td>
</tr>
<tr>
<td>Dosage forms/strengths. Common Dose/sig</td>
<td>20, 30, and 40 mg tablets 40 mg orally once daily until disease progression or no longer tolerated by patient</td>
</tr>
<tr>
<td>DEA Schedule</td>
<td>n/a</td>
</tr>
<tr>
<td>Date of market availability</td>
<td>Currently unknown</td>
</tr>
<tr>
<td>Similar Medications (Look-Alike Sound-Alike) that Increase Potential for Error. Tallman lettering?</td>
<td>Axitinib, dasatinib, lapatinib</td>
</tr>
</tbody>
</table>

**CLINICAL USE EVALUATION**

<table>
<thead>
<tr>
<th>Common Adverse Effects</th>
<th>Diarrhea, rash/dermatitis acniform, stomatitis, paronychia, dry skin, decreased appetite, pruritus</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severe Adverse Effects</td>
<td>Withhold if experiencing: persistent diarrhea, cutaneous reactions lasting more than 7 days, renal dysfunction – resume treatment when adverse reaction fully resolves, reinstitute dose at 10 mg less than dose at which</td>
</tr>
</tbody>
</table>
reaction was observed
Permanently discontinue for: life-threatening skin reactions, confirmed interstitial lung disease, severe drug-induced hepatic impairment, persistent ulcerative keratitis, symptomatic left ventricular dysfunction, severe or intolerable adverse reaction occurring at a dose of 20 mg per day

| Severe Drug-Drug Interactions | Co-administration of P-gp inhibitors can increase afatinib exposure – reduce dose by 10 mg per day if not tolerated
Co-administration of P-gp inducers can decrease afatinib exposure – increase dose by 10 mg per day as tolerated |
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Severe Drug-Food Interactions</td>
<td>n/a</td>
</tr>
</tbody>
</table>
| Important Labs Values to assess prior to order entry or at point of clinical follow up. (Need Pop Up?) | Assess for EGFR mutation
Liver function periodically |
| Used in Pediatric Areas | Safety and effectiveness in pediatric patients have not been established |
| Renal or Hepatic Dosing | Has not been studied in patients with severely impaired renal or hepatic impairment; adjustments to starting doses not considered necessary |
| Critical Issues (i.e., contraindications, warnings, etc) that should be emphasized | Limitation of use: safety and efficacy have been established only in patients whose tumors have EGFR exon 19 deletions or exon 21 L858R substitution mutations as detected by FDA-approved test
Limit time in the sun as afatinib may make skin sensitive
Provide loperamide for treatment of diarrhea. |
| Special administration technique or considerations | Take dose on an empty stomach - at least 1 hour before or 2 hours after meal
Do not take a missed dose within 12 hours of next dose |
| Prepared by | Sharon Valdez, PharmD Candidate 2014; Stacey Nguyen, PharmD Candidate 2014 |

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### Levomilnacipran / Fetzima / Forest Labs Inc.

<table>
<thead>
<tr>
<th>Generic Name / Brand Name / Company</th>
<th>Levomilnacipran / Fetzima / Forest Labs Inc.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Date of approval</td>
<td>July 25, 2013</td>
</tr>
<tr>
<td>Drug Class (Mechanism of Action if novel agent)</td>
<td>Serotonin and norepinephrine reuptake inhibitor (SNRI)</td>
</tr>
<tr>
<td>Indication</td>
<td>Major depressive disorder</td>
</tr>
<tr>
<td>Comparative agent – Therapeutic interchange?</td>
<td>Other SNRIs indicated for major depression (desvenlafaxine, duloxetine, venlafaxine)</td>
</tr>
</tbody>
</table>
| Dosage forms/strengths. Common Dose/sig | Extended release oral capsules :20 mg, 40 mg, 80 mg, and 120 mg
Titration up to 40 mg to 120 mg orally once daily. |
| DEA Schedule | N/A |
| Date of market availability | Fourth quarter 2013 |
| Similar Medications (Look-Alike Sound-Alike) that Increase Potential for Error. Tallman lettering? | milnacipran |

#### CLINICAL USE EVALUATION

**Common Adverse Effects**

ADRs ≥ 2% in levomilnacipran patients and twice the placebo rate: nausea, constipation, vomiting, tachycardia, palpitations, erectile dysfunction, testicular pain, ejaculation disorders, increased heart rate and blood pressure, urinary hesitation, hyperhidrosis, rash, hot flush, hypotension, hypertension, and decreased appetite.
### Severe Adverse Effects

(Also see “Critical Issues”)

<2% in levomilnacipran patients: angina, supraventricular/ventricular extrasystoles, conjunctival hemorrhage, syncope, extrapyramidal disorder, hematuria, and proteinuria.

### Severe Drug-Drug Interactions

- **MAOIs:** Allow at least 14 days between discontinuation of an MAOI and initiation of levomilnacipran. If stopping levomilnacipran, allow at least 7 days before starting an MAOI.
- **Linezolid or Methylene Blue:** Do not start levomilnacipran concurrently with linezolid or intravenous methylene blue due to increased risk of serotonin syndrome.
- **Other serotonergic drugs:** Caution of potential increased risk for serotonin syndrome and monitor for emergence.
- **Strong CYP3A4 inhibitors:** Max of 80 mg of levomilnacipran once daily.
- **Drugs interfering with hemostasis:** Caution of potential increased risk of bleeding including GI bleeding, ecchymosis, hematoma, epistaxis, and petechiae to life-threatening hemorrhages.

### Severe Drug-Food Interactions

None known

### Important Labs Values to assess prior to order entry or at point of clinical follow up.

- Blood pressure and heart rate should be measured prior to initiating and periodically throughout treatment. Pre-existing hypertension, tachyarrhythmias, or other cardiac disease should be treated before initiating levomilnacipran.
- Monitor for signs and symptoms of hyponatremia especially those that are elderly, volume depleted, or on diuretics.

### Used in Pediatric Areas

Not approved for use in pediatric patients.

### Renal or Hepatic Dosing

<table>
<thead>
<tr>
<th>Estimation</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>CrCl 30–59 mL/min</td>
<td>max maintenance dose of 80 mg once daily</td>
</tr>
<tr>
<td>CrCl 15-29 mL/min</td>
<td>max maintenance dose of 40 mg once daily</td>
</tr>
</tbody>
</table>

Not recommended in end stage renal disease.

No dose adjustment recommended in mild, moderate, or severe hepatic impairment.

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

- **Boxed warning:** Increased risk of suicidal thoughts and behavior in children, adolescents, and young adults. Monitor closely for worsening or emergence of suicidal thoughts and behaviors.
- **Contraindications:** Hypersensitivity to levomilnacipran, milnacipran HCl, or any excipient in the formulation, uncontrolled narrow-angle glaucoma, MAOIs, linezolid, or methylene blue.
- **Warnings and Precautions:** 1) Increased risk of serotonin syndrome particularly with other serotonergic agents, treatment initiation, or dose increases. 2) Possible increases in blood pressure and heart rate. 3) May increase risk of bleeding events. 4) Use caution with controlled narrow-angle glaucoma due to reports of mydriasis. 5) Use caution in patients prone to obstructive urinary disorders due to risk of urethral resistance. 6) Use cautiously in patients with a history or family history of bipolar disorder, mania, or hypomania. 7) Although not evaluated in patients with seizure disorder, one case of seizure has been reported. 8) Monitor and reduce dose gradually due to reports of adverse events occurring upon discontinuation of serotonergic antidepressants. 9) Use with caution in the elderly, volume depleted, or those taking diuretics, due to potential hyponatremia.
**Special administration technique or considerations**

- Titration: Initiate at 20 mg once daily for 2 days then increase to 40 mg once daily. May increase by 40 mg every 2 days or more to a max dose of 120 mg once daily based on efficacy and tolerability.
- Gradual dose reduction is recommended, instead of abrupt discontinuation.
- Take approximately at the same time each day, swallow whole, and do not open, chew, or crush the capsule.

**Prepared by**
Jasen Cong, PharmD
Drug Information Pharmacy Resident

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**Ferric carboxymaltose / Injectafer / American Regent**

<table>
<thead>
<tr>
<th>Generic Name / Brand Name / Company</th>
<th>Ferric carboxymaltose / Injectafer / American Regent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Date of approval</td>
<td>July 25, 2013</td>
</tr>
<tr>
<td>Drug Class (Mechanism of Action if novel agent)</td>
<td>Iron parenteral</td>
</tr>
<tr>
<td>Indication</td>
<td>Iron deficiency anemia in adult patients with intolerance or unsatisfactory response to oral iron or with non-dialysis dependent chronic kidney disease</td>
</tr>
<tr>
<td>Comparative agent – Therapeutic interchange?</td>
<td>Ferumoxytol, iron dextran, iron sucrose, sodium ferric gluconate complex</td>
</tr>
</tbody>
</table>
| Dosage forms/strengths. Common Dose/sig | Injection: 750 mg iron/15 mL single use vial  
For patients weighing 50 kg or more: 2 doses of 750 mg IV separated by at least 7 days  
For patients weighing less than 50 kg: 2 doses of 15 mg/kg IV separated by at least 7 days |
| DEA Schedule                       | n/a                                               |
| Date of market availability        | Available                                        |
| Similar Medications (Look-Alike Sound-Alike) | None |

**CLINICAL USE EVALUATION**

- **Common Adverse Effects**: Nausea, hypertension, flushing, hypophosphatemia, dizziness
- **Severe Adverse Effects**: Hypersensitivity reactions, hypertension
- **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?)**: Hemoglobin levels, iron status
- **Used in Pediatric Areas**: Safety and effectiveness not established
- **Renal or Hepatic Dosing**: No dosage adjustment required
- **Critical Issues (i.e., contraindications, warnings, etc) that should be emphasized**: Contraindicated in patients with known hypersensitivity to the product or any of its ingredients. Hypersensitivity reactions, including life-threatening anaphylactic-type reactions have occurred in patients treated with ferric carboxymaltose. Hypertension has been observed immediately after dosing and generally resolved within 30 minutes. Patients should be monitored for hypertension following each administration.

**Special administration technique or considerations**

Administered IV as undiluted slow IV push (at a rate of approximately 100 mg per minute) or by IV infusion diluted in no more than 250 mL of 0.9% sodium chloride injection, USP and administered over at least 15 minutes.

Patients should be monitored for at least 30 minutes and until clinically stable following completion of administration. Personnel and therapies available to treat hypersensitivity reactions must be immediately available.

**Prepared by**
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