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Drugs & Therapy

B • U • L • L • E • T • I • N

FORMULARY UPDATE

The Pharmacy and Therapeutics Committee met March 15, 2011. 5 products were added in the *Formulary*, and 2 were deleted. 2 products were designated nonformulary and not available; 5 criteria for use were approved, including 3 restrictions and 1 dose-rounding protocol. 2 drugs were designated high-priority nonformulary drugs to facilitate acquisition, if needed.

◆ ADDED

Benzylpenicilloyl Polylysine Skin Test (Pre-Pen® by Alk-Abello)*

Ferrous Sulfate Drops (Generic by Silarx)†

†15 mg elemental iron per mL

Histamine Skin Test (Histatrol® AQ by Alk-Abello)*

Histamine in Glycerin Skin Test (Histatrol® by Alk-Abello)*

**Restricted to Infectious Diseases Approval*

Ribavirin Tablet (Generic)

◆ DELETED

Ferrous Sulfate Drops (eg, Enfamil® Fer-In-Sol® Drops)‡

‡15 mg elemental iron per 0.6 mL; nonformulary and not available.

Piperacillin (Generic)§

§Nonformulary and not available

◆ HIGH-PRIORITY NONFORMULARY DRUGS

Factor XIII (13) (Corifact®)

Hydroxyprogesterone Caproate (Makena®)

◆ CRITERIA-FOR-USE CHANGES

Darbepoetin (Aranesp®)*

**Restricted to ESA Order Form.*

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NEWS

What's so special about specialty pharmacies?

Over the past 30 years, specialty pharmacies have emerged from a novel concept to become a fledgling industry. With the biotechnology field growing each day, they have the potential to play a large role in providing patients with access to unconventional medications. Specialty pharmacies filled a niche in the market by enabling patients to obtain medications that historically had barriers to access.

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Specialty pharmacies have the potential to play a large role in providing patients with access to unconventional medications. They filled a niche in the market by enabling patients to obtain medications that historically had barriers to access.

Specialty pharmaceuticals are usually expensive injectable medications that may have special preparation or storage requirements and are traditionally used by a small patient population to treat chronic or life-threatening diseases. Examples include tumor necrosis factor-alpha inhibitors, recombinant blood factor products, and growth hormones. Specialty pharmaceuticals typically have intricate distribution and reimbursement systems. The combination of low patient volume, difficult storage, handling, administration, and/or preparation, and complicated reimbursement schemes make specialty agents difficult for conventional community pharmacies to manage.

Specialty pharmacies have the advantage of stocking a low volume of medications, and many are able to work directly with the drug manufacturers for reimbursement. In addition, specialty pharmaceuticals may require unique monitoring, and by focusing on a small number of patients, these pharmacies are able to follow their patients more closely to encourage correct usage and compliance. As specialty pharmacies develop further, they are increasingly focused on value-added services, including disease and utilization management. Data from a large specialty pharmacy has shown an increase in compliance rate in treating Hepatitis C from 76% to 98%.[1] Having the purported extra degree of attention can benefit all of those involved, including the manufacturer, physician, and most of all, the patient.

In the past decade, specialty pharmaceuticals have expanded to treat a broader range of conditions and patients. Recent data from Medco, one of the nation's largest pharmacy benefit managers (PBM), lists multiple sclerosis, autoimmune disorders including rheumatoid arthritis, cancer, pulmonary hypertension, and anticoagulation agents as the top five disease states or treatments accounting for specialty pharmaceutical use.[2] During this same time period, large PBMs, including CVS Caremark, Express Scripts, and Medco, have developed their own branches of specialty pharmacies, recognizing the lucrative growth potential that specialty pharmacies possess. While the rate of overall medication spending has slowed recently, due mainly to patent expiration of many popular high-ticket agents, spending for specialty agents has drastically increased. From 2008 to 2009, overall prescription

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Formulary update, *from page 1*

◆ CRITERIA-FOR-USE CHANGES (cont.)

Dexmedetomidine (Precedex®)

Epoetin (Procrit®)*

**Restricted to ESA Order Form.*

Ferrous Sulfate Drops (Generic)¶

¶New rounding guidelines approved

Ribavirin Inhaled (Virazole®)*

**Restricted to Infectious Diseases Approval*

Pre-Pen® is a **benzylpenicilloyl-polylysine (PPL)** skin test antigen that reacts with benzylpenicilloyl immunoglobulin E antibodies. This antigen is the major determinant used in the diagnosis of penicillin allergy. When the skin test is applied and a wheal and flare reaction occurs at the skin test site, the patient has immunoglobulins to penicillin. The patient may not manifest a systemic reaction to penicillin, but the likelihood of a reaction is much higher. If the skin test is negative, the history of penicillin allergy may be inaccurate or no longer relevant.

Penicillin allergy skin testing should be performed by trained practitioners. If the condition warrants the immediate start of antibiotic therapy, the patient can receive a non-penicillin derivative antibiotic while skin testing is performed. Since penicillin skin tests are infrequently prescribed, there is an increased risk of an adverse event when patients are followed by clinicians unfamiliar with the testing process. The use of penicillin skin testing provides only a second level of allergy review. An accurate penicillin allergy history determines whether the penicillin-allergy label is accurate or questionable. Whether patients should receive a penicillin or cephalosporin without concern, be skin tested, receive desensitization, or be treated with a different antibiotic requires a thorough evaluation of all options. The penicillin allergy skin test was restricted to Infectious Diseases to enable this review and to ensure the need for skin testing versus other options.

Histamine skin tests are used as controls to document that patients can mount reactions to skin tests, like penicillin. A negative histamine test makes a negative penicillin skin test questionable. Intradermal testing generally precedes intracutaneous (intradermal) tests.

Elemental **iron drops** have been listed in the *Formulary* at a concentration of 15 mg/0.6 mL elemental iron (ie, 75 mg/0.6 mL ferrous sulfate). This concentration of iron drops has been discontinued by all manufacturers. The only replacement available is a 15-mg/mL (75 mg ferrous sulfate/mL) drop, which is a less concentrated formulation. This allows for the measurement of lower doses, and changes how doses will be rounded to measurable amounts.

The standard doses for oral iron liquid based on a new concentration of 15 mg/mL are listed in the *Automatic Route and Dosage Changes Policy*, which can be found on the Portal.

Oral and **inhaled ribavirin** were reviewed because of increased use of inhaled ribavirin. Ribavirin is an antiviral. Increased use has been associated with better diagnostic tests that identify when patients are infected with respiratory syncytial virus (RSV).

Inhaled ribavirin has a labeled indication for the treatment of infants and young children with severe lower respiratory tract infections due to RSV. Ribavirin tablets have a labeled indication for the treatment of chronic hepatitis C virus infections [in combination with peginterferon alfa-2a] in patients who have compensated liver disease and have not been previously treated with interferon alfa. Inhaled and oral ribavirin are used off-label to treat RSV infections in adult patients, particularly immunocompromised patients.

Due to its expense (ie, nearly $4000 per day and $20,000 for a 5-day course of therapy) and lack of controlled clinical trials supporting its efficacy, a subgroup of the Anti-Infective Subcommittee met to develop a protocol on how best to use inhaled ribavirin therapy at Shands at UF. Following that review, a protocol for inhaled/oral ribavirin in managing both upper and lower respiratory tract infections associated with RSV was developed to generate consistency in application of this agent. The protocol categorizes patients by degree of immunosuppression and severity of RSV infection and has received the support of UF experts in RSV infections. Inhaled ribavirin is now restricted to approval by Infectious Diseases. Oral ribavirin was added in the *Formulary* for patients with mild disease and as step-down therapy for patients who have responded to inhaled therapy and is not restricted.

Piperacillin is a parenteral, extended-spectrum penicillin used to treat gram-negative infections. A combination of piperacillin-tazobactam (Zosyn®), which is listed in the *Formulary*, is often preferred because piperacillin [alone] is susceptible to inactivation by beta-lactamases. Tazobactam is a beta-lactamase inhibitor that enhances the antibacterial action of piperacillin.

Piperacillin has not been prescribed at Shands at UF for greater than 2 years. Following a review of available data (cost, utility, susceptibility patterns), piperacillin was removed from the *Formulary* and made nonformulary and not available.

Corifact® is the first **Factor XIII (13)** product approved by the FDA. It has a labeled indication for the prevention of bleeding in people with congenital Factor XIII deficiency. Factor XIII deficiency affects 1 out of every 3 million people in the United States. The deficiency may lead to soft tissue bruising, mucosal bleeding, and fatal intracranial bleeding. Newborns with Factor XIII deficiency have umbilical cord bleeding.

Corifact® was approved by the FDA's accelerated approval process, which requires an ongoing study to demonstrate that patients receive benefit from its use. The FDA approved Corifact® based on data from only 14 people. The most common adverse effects observed were hypersensitivity reactions, chills, fever, arthralgias, headache, elevated thrombin-antithrombin levels, and an increase in hepatic enzymes.

Corifact® was designated a high-priority nonformulary drug and will not be stocked. Computer entries have been created that describe how to obtain product, if it is ever needed. The Pharmacy Department's administrator on call should be contacted if this drug is needed.

Hydroxyprogesterone caproate in an intramuscular progesterone that has been shown to decrease the incidence of preterm birth in a large randomized placebo-controlled trial. Until recently, there was no commercial form of hydroxyprogesterone caproate, and it was available only from compounding pharmacies. Since it was a sterile product compounded from nonsterile ingredients, it required an informed consent for inpatient use at Shands at UF.

Thus, progesterone suppositories have been used for most inpatients experiencing preterm labor at Shands at UF. Since an informed consent was never created, compounded hydroxyprogesterone caproate was not used.

Recently, the FDA approved a commercial form of hydroxyprogesterone caproate, Makena®. It is administered at a dose of 250 mg IM once weekly. Treatment is begun between 16 weeks, 0 days and 20 weeks, 6 days of gestation and continued until week 37 of pregnancy.

Makena® is too expensive for most patients in the outpatient setting;

(continued on next page)

Formulary update, *from page 2*
therefore, progesterone suppositories will be used for most patients treated at Shands at UF. Compounding pharmacies charged $10 to $20 per injection for hydroxyprogesterone caproate. The cost of Makena® is reported to be as much as $1500 per dose, which would be as much as $30,000 over the course of a pregnancy.

Makena® was designated a high-priority nonformulary drug that will be used at Shands at UF only when a patient could not use progesterone suppositories and when the patient is able to continue therapy as an outpatient.

All erythrocyte-stimulating agents, also known as ESAs (Epogen®, **Procrit**®, and **Aranesp**®), require Risk Evaluation and Mitigation Strategies (REMS) for use in patients with cancer. The APPRISE (**A**ssisting **P**roviders and Cancer **P**atients with **R**isk **I**nformation for the **S**afe use of **E**SAs) Oncology program requires hospitals, healthcare professionals, and patients to undergo this process. The goal of this program is to support informed decisions between patients and healthcare professionals who are considering treatment with an ESA by educating them on the risks of ESAs. ESA have been associated with tumor growth in cancer patients and decreased survival. The APPRISE Oncology program is intended to help mitigate the risks of decreased survival and/or poorer tumor outcomes in patients with cancer. ESAs should only be used in cancer patients in whom their chemotherapy is not curative.

Healthcare professionals who prescribe ESAs in cancer have to complete a training module that covers the use of ESAs. Completion of the training module is required for enrollment in APPRISE. Healthcare providers and patients have to sign an acknowledgement that they understand the risks of ESAs for this indication. If not enrolled in APPRISE, healthcare providers should not prescribe ESAs in cancer.

Hospitals must be enrolled in the APPRISE program in order to dispense ESAs to patients with cancer. Hospitals must have a system in place that ensures that all healthcare providers who prescribe ESAs in the hospital are enrolled and comply with the APPRISE Oncology program. This implies that these agents will have to be restricted in a way that would do this verification.

Manufacturers supposedly will stop providing ESAs for ALL indications if this program is not followed. Full compliance with this program is now necessary. Therefore, the use of ESAs is now restricted to use by an *ESA Order Form*, which forces compliance with the REMS for all oncology uses.

Dexmedetomidine is a relatively selective alpha$_2$-adrenoceptor agonist with centrally mediated sympatholytic, sedative, and analgesic effects. It has a labeled indication for sedation of initially intubated and mechanically ventilated patients during treatment in an intensive care setting. The labeling states that dexmedetomidine should be administered by continuous infusion not to exceed 24 hours. Dexmedetomidine has been on the US market since 1999.

When the Shands criteria for use for dexmedetomidine were expanded in September 2008 to include use in patients who are difficult to wean from the ventilator, an order form was created to restrict use to the P&T-approved protocol. This form excluded cardiothoracic attendings. The *Dexmedetomidine Order Form* was modified to include CT Surgery attendings as prescribers using the previously approved criteria for use.

News, *from page 1*
drug spend increased by 6.4%.[3] In contrast, during this same period, specialty drug spend increased by 19.5%, and this rate is not expected to slow down any time soon. Moreover, between 30% and 40% of agents currently in the development pipeline are specialty agents. It is estimated that by 2013, generic drugs will account for 80% of the prescription market, but specialty agents will account for 50% of overall drug spend. It is projected that seven of the top ten drugs will be specialty agents by 2014.[4]

With the continued growth of the specialty market, healthcare providers in all types of settings must be prepared to handle the demand of these drugs and help their patients navigate the path for obtaining specialty pharmaceuticals.

Patients under Shands' employee insurance program are required to obtain specialty pharmaceuticals from any of the Shands-affiliated outpatient pharmacies. The Shands Medical Plaza Pharmacy is charged with handling the most unique agents, and has compounding, clinical services, and the infusion center onsite to aid patients in obtaining and administering many of these specialty agents. These outpatient pharmacies also utilize a mail-order system to provide patients with additional routes of obtaining these medications. Of note, the Shands outpatient pharmacies also offer the same services to patients utilizing other insurance providers, as well as indigent patients.

For patients who wish to have their prescriptions filled elsewhere, most insurance companies contract with one of the large PBMs, many of which have their own branches of specialty pharmacies that patients can use. In some cases, insurance companies may also have contracts with smaller, local specialty pharmacies to allow their patients to use this option instead of mail order from the PBM.

Continuation of care in the hospital setting also presents a problem for these unique, high-cost items. At Shands at UF, some specialty agents are in the *Formulary,* which makes for the smoothest transition and continuity in care. However, other agents are deemed nonformulary. If this is the case, the pharmacy department may be able to order the item for use in the hospital. Still other agents may be nonformulary and not available, in which case the patient may be able to use their own supply as long as it meets the requirements for patient's own use.[5] As a whole, patients are not permitted to use their own injectable medications, with a few exceptions including epoprostenol, treprostinil, and insulin when administered via the patient's own infusion device. Due to the varying degrees of formulary status possible, it is important that providers work together to ensure that patients are able to continue receiving medications that may be critical for optimal outcomes.

From a provider's viewpoint, it is essential that we educate our patients regarding specialty pharmaceuticals and why they may not be able to have their prescription filled at their neighborhood pharmacy. Additionally, it is important that patients understand why these agents may be different than their typical medications, especially if special monitoring or administration is required. By addressing these issues up front, it is possible to avoid frustrations that could arise from both the patient's and provider's perspectives.

by Kathryn Hernando, PharmD

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MEDICATION SAFETY

SALAS: Arista® versus Arixtra®

Sound-alike-look-alike drugs (SALADs) have been a major medication safety initiative…but what about sound-alike-look-alike "stuff" (SALAS)? Like most places, Shands at UF has a policy on SALAD drugs. Safety measures are taken to use special lettering on labels, separate products on storage shelves, and other safety measures. The ISMP has a published list of *Confused Drug Names.*[1] The U.S. Department of Veterans Affairs also has done a lot in the area of look-alike/sound-alike drugs.[2-3]

Little emphasis has been given to when non-drug products have similar names to drug names. Recently, there was confusion between Arista® and Arixtra®. Although no harm occurred, this confusion is being discussed to increase awareness.

Arista™ AH is a synthetic hemostatic device [not a drug] that includes an absorbable hemostatic powder.[4] It is intended to help stop bleeding. Arixtra® is the brand name for the anticoagulant fondaparinux.[5] Its therapeutic effect can cause bleeding. It may be difficult to confuse these products, since they are used differently; however, it is possible that these products could both be used in an Operating Room (OR) environment. Awareness of these brand names, which could be confused, could potentially prevent errors.

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Drug information questions?

Contact the Drug Information Service **Call 265-0408**

Or submit your question online at www.shands.org/professionals/druginfo/default.asp

- This service is for referring physicians and other healthcare professionals taking care of Shands patients
- Phones are staffed from 9 am to 4:30 pm, Monday – Friday
- All answers are thoroughly researched and referenced

For emergent questions that do not need thorough research, go to the pharmacy servicing your area.