

Drugs & Therapy

B • U • L • L • E • T • I • N

FORMULARY UPDATE

The Pharmacy and Therapeutics Committee met May 21, 2013. 4 drugs were added in the *Formulary*, 1 drug was deleted, and 5 drugs were designated nonformulary and not available. 1 drug was designated a high-priority nonformulary drug. Criteria for use were established or changed for 6 drugs.

◆ ADDED

Acarbose (Generic)

Apixaban (Eliquis®)*

*Restricted based on use, renal function, age, and interactions

Aripiprazole Depot

(Abilify® Maintena)*

*Restricted to Shands Vista with specific criteria

C1-Esterase Inhibitor (Berinert®)*

*Restricted to a treatment algorithm

◆ DELETED

Sulfacetamide 10% Ophthalmic Drops (Generic)†

†Nonformulary and not available

◆ NONFORMULARY AND NOT AVAILABLE

Ado-Trastuzumab Emastine

(Kadcyla®)*

*Available for use in the Infusion Center only

Canagliflozin (Invokana®)‡

‡MAY NOT USE in the hospital

Levonorgestrel-Ethinyl Estradiol

(Quartette®)§

§Patients may use their own

Tobramycin Inhalational Powder

(Tobi® Podhaler)§

§Patients may use their own

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PHARMACOTRIVIA

How do I pronounce generic drug names?

There are new drugs being approved each month. The first time you see the generic name, if you are like most practitioners, you struggle to say the generic name. Often, you just follow someone else's lead, and often they are wrong. Manufacturer's representatives frequently do not know the correct pronunciation for the generic name.

Generic names do not appear to make sense. Even worse, generic drug names often do not follow typical rules for pronunciation. So, how can you possibly pronounce generic names correctly?

Generic names are established by the United States Adopted Name (USAN) Council. This council is a sponsored collaboration of the United States Pharmacopeial (USP) Convention, the American Medical Association (AMA), and the American Pharmacists Association (APhA). USAN works with the World Health Organization's (WHO) International Nonproprietary Name (INN) Expert Committee to harmonize new generic names. This avoids having different generic names in various countries, like acetaminophen and paracetamol, which are the same drug.

USAN attempts to select simple, informative, and unique generic names. Drugs in the same category will have parts of the name (ie, "stems") that are similar, like lisinopril and ramipril, which are both angiotensin converting enzyme inhibitors and both contain "pril."

Monoclonal antibodies have a convention that tells that it is a monoclonal antibody (last syllable "mab"), the animal source (next to last syllable, eg, "ix" for chimeric), and the target (eg, "li" for lymphocytes).¹ The first syllable is unique, and may or may not have some meaning. Inf-li-xi-mab is a chimeric monoclonal antibody that targets lymphocytes to decrease inflammation. The spelling of a generic name is constructed "logically," but the correct pronunciation is based on different rules.

USAN also determines the correct pronunciation for generic names. The correct pronunciation can be found in the *USP Dictionary of USAN and International Drug Names*, which is available online via the Health Center Library.

How do you pronounce "dabigatran?" Many people will be surprised to find out there is no BIG in dabigatran. According to USAN, the correct pronunciation is da" bi gat' ran. The accent mark (ie, ') is the syllable that should be emphasized, and the double accent mark (ie, ") is the syllable with secondary emphasis. Another way to represent this pronunciation would be Dah-bih-GAT-ran. There may be no BIG in dabigatran, but there is a "GAT."

That may sound awkward to you, but Dah-bih-GAT-ran is correct, and may require some practice to get it right. Perhaps USAN will change it someday; there is precedent for that.

Ibuprofen was originally pronounced eye bue' proe fen (eye-BWUE-pro-fen). It is now correctly pronounced eye" bue proe' fen (Eye-bwue-PRO-fen).

A few drugs have more than one correct pronunciation listed in the *USP Dictionary*. Metoprolol was originally [and correctly] pronounced met" oh proe' lol (Met-oh-PRO-loll). Now me toe' proe lol (meh-TOE-pro-loll) is an acceptable alternate pronunciation. The common mispronunciation, meh-TOP-proe-lol is incorrect.

USAN rules only apply to generic names. Generic names and their correct pronunciation are set by standard making organizations. Brand names are selected by a manufacturer, and only that company sets the correct pronunciation for a brand name.

REFERENCES

1. Hatton RC. Making sense out of "mabs." *Drugs & Therapy Bulletin* 2002;16(1):3-4.

◆ **HIGH-PRIORITY
NONFORMULARY DRUGS**

**Varicella Zoster Immune
Globulin (Varizig®)***

*Restricted to approval by an ID physician

◆ **CRITERIA FOR USE CHANGES**

Capsaicin Topical (Generic)*

* "DO NOT apply heat to area of application"

**Cytomegalovirus Immune
Globulin (Cytogam®)***

*Restricted: Approval by ID or AMP required

Dabigatran (Pradaxa®)*

*Restricted based on use, renal function, age, and interactions

Parenteral Nutrition*

*Restricted to ASPEN/SCCM/Medicare-Medicaid criteria

Parenteral Phosphate*

*Restrictions modified

Rivaroxaban (Xarelto®)*

*Restricted based on use, renal function, age, and interactions

Acarbose is an alpha-glucosidase inhibitor that works to slow the intestinal absorption of carbohydrates. This class of hypoglycemics acts at the brush border of the proximal small intestinal epithelium to inhibit the breakdown of complex carbohydrates. Given its mechanism of action, its glucose lowering effects are most evident postprandially. It is administered 3 times daily with meals. The maximum recommended dose for patients less than or equal to 60 kg is 50 mg 3 times daily.

Acarbose was deemed nonformulary and not available in 2003 for its labeled indication, as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus. Its formulary status was reconsidered for use in the treatment of dumping syndrome.

Dumping syndrome is a postoperative complication of Nissen fundoplication. There is better diagnosis of this condition in children, and its off-label use was requested by Pediatric Endocrinology. Dumping syndrome is characterized by early postprandial hyperglycemia (within 60 minutes of feeding) followed by late hypoglycemia (within 1 to 4 hours of feeding). These states of hyper- and hypoglycemia are associated with what are characterized as early dumping symptoms (EDS) and late dumping symptoms (LDS). The severity and extent of EDS and LDS are associated with the rate of change in blood

sugar, not necessarily their ultimate values. The proposed pathophysiologic mechanism for this syndrome is that there is "dumping" of hyperosmolar carbohydrate-containing solutions into the small bowel with subsequent rapid glucose absorption.

The usual therapies for this condition include cornstarch, pectin, octreotide, and dietary manipulations. There are patients that continue with symptoms despite these therapies. There are case reports and case series that report the use of acarbose in children with dumping syndrome. Typical starting doses were 12.5-25 mg before each feeding. Doses are titrated until postprandial glucose levels were stable up to a dose as high as 50 mg. Though limited, data suggest that acarbose attenuates the postprandial rate of glucose decline and elevation, which leads to an improvement of symptoms. Common adverse effects are flatulence, abdominal bloating, and loose stools.

Apixaban is an oral factor Xa inhibitor anticoagulant with a labeled indication to reduce the risk of stroke and systemic embolism in patients with nonvalvular atrial fibrillation.

The efficacy of apixaban in treating patients with atrial fibrillation not caused by cardiac valve disease was studied in a clinical trial of more than 18,000 patients that compared apixaban with warfarin. In the trial, patients taking apixaban had fewer strokes than those who took warfarin.

Patients with prosthetic heart valves should not take apixaban, nor should patients with atrial fibrillation that is caused by a heart valve problem. These patients were not studied in clinical trials. Bleeding, including life-threatening and fatal bleeding, is the most serious risk with apixaban. There is no agent that reverses apixaban's anticoagulant effect.

Best Practice Alerts (BPAs) will be developed to limit the use of apixaban. It is anticipated that most of the use of apixaban will be for patients admitted taking the drug, based on data for other oral anticoagulants. If the dose or drug needs to be changed, appropriate medication reconciliation upon discharge will be made.

The safety mechanisms for apixaban will draw attention to its labeling that recommends that the dosage be halved (ie, from 5 mg twice a day to 2.5 mg twice a day) for any patient with 2 of the following 3 characteristics: age greater than or equal to 80, weight less than or equal to 60 kg, or a serum creatinine greater than or equal to 1.5 mg/dL. Since apixaban is metabolized by CYP3A4, the dosage should be halved for patients on strong inhibitors of CYP3A4 (or P-glycoprotein) and NOT used if the dose has already been halved. Apixaban should also not be used with strong CYP-inducers (eg, phenytoin, rifampin,

and phenobarbital). Unlike warfarin, there is no way to monitor the effects of these interactions and to modify the dosage. Finally, using apixaban in patients with a mechanical heart valve is not recommended.

Similar restrictions were approved for **dabigatran** (Pradaxa®) and **rivaroxaban** (Xarelto®), which were previously added in the *Formulary*.

For dabigatran, BPAs will alert physicians and pharmacists if a patient's estimated creatine clearance (CrCl) is less than 30 mL/min, so that the dosage can be reduced to 75 mg twice a day. If the estimated creatinine clearance is less than 15 mL/min, dabigatran will not be used. Pharmacists will be alerted when the patient's renal function changes after the initial order.

Alerts will fire to warn not to use dabigatran with CYP3A4 or P-glycoprotein inducers, which could decrease its effectiveness. If patients have a CrCl less than 30 mL/min and are on inhibitors of CYP3A4 or P-glycoprotein, dabigatran should not be used. With CrCls of 30-50 mL/min in patients on dronedarone or ketoconazole, the dabigatran dosage should be reduced. Dabigatran use will not be allowed in patients with a mechanical heart valve.

For rivaroxaban, a BPA will fire for patients with a CrCl less than 50 mL/min allowing no more than a 20-mg-per-day dosage. If the CrCl declines to less than 20 mL/min, pharmacists will receive an alert. BPAs will also fire warnings against using rivaroxaban with P-glycoprotein and strong CYP3A4 inhibitors (eg, ketoconazole, itraconazole, ritonavir and conivaptan) or inducers (eg, carbamazepine, phenytoin, rifampin, and St. John's Wort). It should not be used in patients with a mechanical heart valve.

Abilify Maintena® is an extended-release intramuscular form of the atypical antipsychotic aripiprazole. It has a labeled indication for the treatment of schizophrenia and is given monthly to patients unable to take oral aripiprazole reliably.

Like all depot antipsychotic injections, patients should have established tolerability to oral drug before using the extended-release injection. Patients must also take 14 days of concurrent oral aripiprazole to allow time for the injection to release therapeutic quantities of aripiprazole.

Abilify Maintena® was added in the *Formulary* and restricted to use at Shands Vista under the following conditions. Abilify Maintena® will only be obtained when patients can continue therapy as an outpatient (ie, discharge plan in place that continues therapy). Patients must have a documented history of noncompliance, documented positive response to oral aripiprazole, and plan to be hospitalized for 2 weeks

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following the first injection or there will be a plan in place that ensures continuation of oral aripiprazole for 2 weeks following the first dose.

Beriner[®] is a **C1-esterase inhibitor** that has a labeled indication for the treatment of acute attacks of hereditary angioedema (HAE) caused by C1-esterase deficiency and dysregulation of the complement and coagulation systems. In March 2012, the P&T Committee reviewed medications designed to treat acute attacks of hereditary angioedema (HAE) and designated Beriner[®] nonformulary and not available. This decision was based on the rarity of the disease, the self-limiting nature of most acute attacks, and the high acquisition costs of these medications.

Beriner[®] was shown to be effective in reducing the time to onset of symptom relief for abdominal and facial attacks. It has not been shown to be effective for laryngeal attacks in clinical trials.

Most of the adverse events for Beriner[®] are mild and temporary. The most common adverse events seen in clinical trials include injection site reactions, nausea, dizziness, and headache. Subsequent HAE attacks and diarrhea have been reported with Beriner[®]. There is also a risk of prion or virus transmission with C1-esterase inhibitor because it comes from pooled plasma.

Beriner[®] costs approximately \$5,000 for a dose for a 70-kg patient. The P&T Committee voted to add it in the *Formulary* and restrict it to appropriate patients. Pharmacists will use an algorithm to screen orders before they are dispensed. Beriner[®] will be limited to patients with a diagnosis of type I or type II HAE.

The first dose can be ordered without restriction, if no diagnosis has been made. Subsequent doses will be restricted.

Sulfacetamide is a topical sulfonamide **ophthalmic** antibiotic that has been on the market since 1946. It has a labeled indication for the treatment of conjunctivitis and other superficial ocular infections due to susceptible microorganisms, and as an adjunct in systemic sulfonamide therapy of trachoma.

This product has not been used for years at Shands UF. After consulting with the Department of Ophthalmology, sulfacetamide ophthalmic drops were deleted from the *Formulary* and designated nonformulary and not available.

Ado-trastuzumab emastine is a HER2-targeted antibody (trastuzumab) and microtubule inhibitor conjugate (emastine) with a labeled indication for the treatment of patients

with HER2-positive metastatic breast cancer as a single agent after patients have received trastuzumab and a taxane, separately or in combination. Patients should have either received prior therapy for metastatic disease or developed disease recurrence during or within 6 months of completing adjuvant therapy.

HER2 is a protein involved in normal cell growth, but is found in increased amounts in some types of cancer (HER2-positive), including some breast cancers. Almost 20% of breast cancers have increased amounts of the HER2 protein. In these cancerous cells, HER2 contributes to cancer cell growth and survival.

Ado-trastuzumab emastine was reviewed under the FDA's priority review program. A priority review provides for an expedited 6-month review of drugs that may provide safe and effective therapy when no satisfactory alternative therapy exists or it offers significant improvement compared to marketed products. Other FDA-approved drugs used to treat HER2-positive breast cancer include trastuzumab, lapatinib, and pertuzumab. Trastuzumab was listed in the *Formulary* in 2005; lapatinib and pertuzumab are listed in the Chemotherapy Policy, but are not listed in the *Formulary*.

The effectiveness of ado-trastuzumab emastine was evaluated in a clinical study of 991 patients randomly assigned to receive ado-trastuzumab emastine or lapatinib plus capecitabine. Patients received treatment until either the cancer progressed or the adverse effects became intolerable. The study was designed to measure progression-free survival (ie, the length of time patients lived without the cancer progressing) and overall survival (ie, the length of time patients lived before death).

Results showed that patients treated with ado-trastuzumab emastine had a median progression-free survival of 9.6 months compared to 6.4 months in patients treated with lapatinib plus capecitabine. The median overall survival was 30.9 months in the ado-trastuzumab emastine group and 25.1 months in the lapatinib plus capecitabine group.

Ado-trastuzumab emastine has a boxed warning alerting that it can cause liver toxicity, heart toxicity, and death. It can also cause severe life-threatening birth defects, and pregnancy status should be verified before starting ado-trastuzumab emastine treatment.

The most common adverse effects reported in patients treated with ado-trastuzumab emastine were nausea, fatigue, pain in the muscles or joints, thrombocytopenia, increased levels of liver enzymes, headache, and constipation.

Ado-trastuzumab emastine was designated nonformulary and not available for inpatient use, but it will be available for use in the Infusion Center

with appropriate safety measures (eg, supplies separated from trastuzumab and tall-man lettering using the complete generic and brand names).

Canagliflozin is a sodium-glucose co-transport 2 (SGLT2) inhibitor with a labeled indication as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus. Canagliflozin is the first diabetes drug with this mechanism of action.

Canagliflozin works by blocking the reabsorption of glucose by the kidney, increasing glucose excretion, and lowering blood glucose levels in diabetic patients. Its efficacy was evaluated in 9 clinical trials that included over 10,000 patients with type 2 diabetes. These trials showed lower hemoglobin-A1C levels and fasting plasma glucose levels compared to placebo.

Canagliflozin has been studied as stand-alone therapy and in combination with other type 2 diabetes drugs including metformin, sulfonylureas, pioglitazone, and insulin. It is not recommended for patients with type-1 diabetes or in patients with severe renal impairment, end stage renal disease, or patients on dialysis.

The FDA is requiring postmarketing studies examining the effect of canagliflozin on cardiovascular outcomes, and studies to monitor for malignancies, pancreatitis, hypersensitivity, photosensitivity, liver abnormalities, and pregnancy outcomes. A bone safety study and pediatric studies are also being done.

The most common adverse effects are vulvovaginal candidiasis and urinary tract infections. Canagliflozin causes a diuretic effect, which can cause orthostatic or postural hypotension and result in dizziness or fainting, especially in the first 3 months of therapy.

Canagliflozin was designated nonformulary and do not use in the hospital. Patients will not be allowed to use their own supply from home.

Tobi[®] Podhaler is an **inhalational powder** form of the aminoglycoside antibiotic **tobramycin** that was approved with a labeled indication for the management of cystic fibrosis patients with *Pseudomonas aeruginosa* lung infections. The Podhaler is a handheld device that contains tobramycin as a dry powder. The powder is inhaled twice daily for 28 days. The treatment is then stopped for 28 days before resuming therapy.

Tobi[®] Podhaler's efficacy was established in a placebo-controlled study of 95 children and adults with cystic fibrosis with *Pseudomonas aeruginosa* lung infections. Improvement in lung function (FEV₁) was shown. Additional safety data are available for another 487 patients.

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Common adverse effects include cough, hemoptysis, shortness of breath, fever, mouth and throat pain, dysphonia, and headache.

Tobi® Podhaler is an alternative to Cayston®, which is an inhaled version of aztreonam, and Tobi®, which is a nebulized tobramycin solution. Tobi® is listed in the *Formulary*, while Cayston® is a high-priority nonformulary drug only available via a restricted distribution system.

Tobi® Podhaler was designated nonformulary and not available, but patients will be allowed to use their own supply from home or they must be switched to nebulized Tobi®.

Quartette® is a combination oral contraceptive used to prevent pregnancy. It contains **ethinyl estradiol** (estrogen) and **levonorgestrel** (progestin). It is an extended-regimen (91-day duration) oral contraceptive. The dose of ethinyl estradiol increases at 3 points during the first 84 days, while the amount of progestin remains constant. The last 7 days of the cycle is just ethinyl estradiol.

The goal is for patients to experience 4 “light” periods per year. Like all extended-regimen oral contraceptives, breakthrough bleeding is a possibility, but increasing the dose of ethinyl estradiol is an attempt to minimize the risk of this adverse effect.

The listed risks and adverse events are as expected with other oral contraceptives and include the risk of thromboembolism, cancer, and liver disease. It should not be used in women with uncontrolled hypertension or dyslipidemias. If headaches increase, Quartette® may need to be stopped, as headache is a common adverse effect. Nausea and vomiting, acne, dysmenorrhea, weight gain, mood changes, and breast pain may occur.

Like other oral contraceptives, patients should use their own supply in the hospital; Quartette® was designated nonformulary and not available.

Varicella zoster immune globulin (VZIG) is a purified human immune globulin preparation approved by the FDA in December 2012 with a labeled indication for passive immunization of high-risk susceptible patients up to 4 days after exposure to the varicella-zoster virus to reduce the severity of varicella infection. A previous FDA-licensed VZIG was removed from the U.S. market by the manufacturer in 2006, and Varizig® has only been available under an investigational expanded access protocol (EAP) during the licensing process.

VZIG has a reasonable safety profile and may have a role in minimizing varicella disease in at risk populations. VZIG was rarely used under the expanded access protocol prior to FDA approval. With few requests, a limited population of patients in which this agent may be useful, and ease of shipping with recent FDA approval, VZIG was designated a high-priority nonformulary drug. Computer entries will guide prescribers to how it can be obtained when it is reasonable.

VZIG is indicated as prophylaxis in high-risk patients. It should be given within 4 to 10 days of an exposure to varicella. It should only be approved by an Infectious Diseases physician for the following populations (as

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outlined by the CDC): immunocompromised children and adults; newborns of mothers with varicella before or after delivery; premature infants; infants less than 1 year of age; adults without evidence of immunity; and, pregnant women.

Capsaicin is used over-the-counter for multiple conditions, including diabetic neuropathy, mild to moderate pain, rheumatoid and osteoarthritis, and post-herpetic neuralgia. Although capsaicin has shown limited efficacy in the treatment of chronic musculoskeletal or neuropathic pain, it may be useful as an adjunct or as sole therapy for a small number of patients who are unresponsive to, or intolerant of, other treatments. Capsaicin 0.075% topical cream is listed in the *Formulary*.

Topical capsaicin therapy has several advantages and disadvantages. There are currently no known drug interactions, so patients unable to take other analgesic products would be possible candidates for this therapy. The topical route may also be preferred in patients intolerant of oral analgesics. However, the frequency of administration (3-4 times per day), time to pain relief (2-6 weeks), and relatively common incidence of local adverse effects (burning, stinging, and tingling) may detract from the pain reduction found in clinical trials.

To reduce the risk of adverse effects, nurses should wear gloves when applying capsaicin cream. Patients and nurses should avoid touching the area of application then touching mucous membranes (eg, eyes).

The FDA reports that there have been rare reports of serious chemical burns associated with topical capsaicin products used for muscle and joint pain. Some of these second- and third-degree burns have been serious enough to require hospitalization. Most reports have been with topical products for muscle and joint pain containing greater than 3% of menthol or 10% methyl salicylate. However, a few cases have been reported with capsaicin containing products.

At Shands UF, there is no topical menthol or methyl salicylate-containing product in the *Formulary*. There has been no warning in Epic regarding the possible risks associated with topical capsaicin.

The Medication Safety Subcommittee recommended the addition of administration instructions to the Medication Administration Record (MAR) for capsaicin in Epic, since heat and barriers are commonly used in the hospital and practitioners may be unaware of this risk.

A “negative” warning was recommended, although this is not typically recommended by human factor experts. The warning states, “DO NOT apply heat to the area of application.”

Cytomegalovirus immune globulin (CMV IVIG) is an intravenous immune globulin (IgG) with a standardized amount of antibody to cytomegalovirus. It has a labeled indication for the prophylaxis of CMV disease associated with solid-organ transplantations. Treatment of CMV disease is an off-label use.

In September 2011, the P&T Committee approved the use of CMV IVIG for treatment

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of primary CMV infections during pregnancy. The Anti-infective Subcommittee recently reviewed available published data and guidelines to assess clinical need for CMV IVIG for treatment of CMV disease outside of pregnancy.

There are few data to support CMV IVIG use in many situations. The only area where there may be benefit is in patients with CMV pneumonitis. In addition, the review highlighted challenges to data evaluation. With improvements in CMV detection, prevention strategies, and earlier treatment of CMV syndrome, the value of CMV IVIG has been diminished. Based on this assessment, the following criteria are recommended.

CMV IVIG is recommended for resistant CMV infections refractory to other therapies and must meet ALL of the following criteria. First, patients should be bone marrow or solid organ transplant recipients, or other similarly immunosuppressed patients. Second, they must have CMV pneumonitis (with cytological or histological evidence) or CMV syndrome with viremia. Third, they must have a poor clinical response, defined by a viral load greater than 1000 copies/mL that has not responded to appropriately dosed

ganciclovir and foscarnet for greater than or equal to 1 week. In addition, a sample must be sent for CMV genotyping to determine presence of antiviral resistance. Samples may be obtained from blood, CSF, BAL, tissue, or culture. Fourth, CMV IVIG must be given in combination with 1 or more systemic antiviral agents (never as monotherapy) for the treatment of CMV disease.

CMV IVIG may be prescribed for primary CMV infection during pregnancy identified during the first or second trimester of pregnancy.

Parenteral nutrition (PN) is the intravenous administration of nutrients. It is a mixture of protein, carbohydrates, electrolytes, minerals, and sometimes fat that is used to meet a patient's nutritional needs when they cannot take sufficient nutrients orally or enterally.

Although very important for patient care, over-use of the parenteral route of nutritional support is detrimental to patients (eg, increasing their risk of infection). The P&T Committee restricted the use of PN to Medicare-Medicaid, ASPEN, and SCCM guidelines. Further, when 2/3 of a patient's nutritional needs can be met with oral or enteral nutrition, PN will be automatically stopped. These restrictions are limited to patients equal to or greater than 18 years of age or if they are in an adult unit.

Parenteral Phosphate has been in short supply. Emergency restrictions have been necessary. Whenever possible, the use of oral phosphate has been encouraged. When supplies were critically low, patients were automatically changed to oral phosphate replacements per a P&T Authorized Change except for the following situations: sodium phosphate therapy during CRRT, phosphate replacement in any patient with a serum phosphorous below 1, and phosphate replacement in any patient with a serum phosphorous 1 to 1.5 where no other oral or enteral medications are currently prescribed.

After passing these restrictions, a supply of compounded parenteral phosphate from JCB Laboratories was received. Additional supplies of parenteral phosphate have also been obtained.

Thus, the restrictions for parenteral phosphate were changed to the following: sodium phosphate therapy during CRRT, phosphate replacement in any patient with a serum phosphorous below 1.5, and phosphate replacement in any patient with a serum phosphorous 1.5 to 2.0 where no other oral or enteral medications are currently prescribed.