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Drugs & Therapy

B • U • L • L • E • T • I • N

FORMULARY UPDATE

The Pharmacy and Therapeutics Committee met November 16, 2010. 2 drugs were added in the *Formulary*, and none were deleted. 8 products were designated nonformulary and not available. 2 interchanges, 1 restriction, and 1 product extension were approved.

◆ ADDED

Dihydroergotamine Injection (generic by Paddock Laboratories)

Telavancin (Vibativ® by Astellas Pharma)*

**Restricted to ID or Antimicrobial Management Team approval*

◆ DELETED

None

◆ NONFORMULARY AND NOT AVAILABLE

Aliskiren (Tekturna®)

Calcipotriene Foam (Sorilux®)

Capsaicin 8% Patch (Qutenza®)

Drospirenone-Ethinyl estradiol-Levomefolate (Beyaz®)

Norethindrone acetate-Ethinyl estradiol-Ferrous fumarate (Lo-Loestrin Fe®)

Pegloticase (Krystexxa®)

Risedronate ER Tablet (Atelvia®)†

Sibutramine (Meridia®)†

†Patients may NOT use their own supply

◆ INTERCHANGES

Levothyroxine (generic interchange)

Mycophenolate mofetil (generic) for **CellCept®**

(continued on next page)

MEDICATION SAFETY

DTaP and Tdap: Understanding the letters

There has been much confusion among many health care practitioners regarding the combination vaccines for diphtheria, pertussis and tetanus. Hundreds of mix-ups, including one involving 80 clinic patients, have been reported to the ISMP Medication Errors Reporting Program and many more may go unreported or even unnoticed.[1] The similar initials and letters lend themselves to mix-ups in ordering, dispensing, and administration of these products.

Many combinations exist using the diphtheria toxoid, tetanus toxoid, and acellular pertussis vaccine.[2] For most patients, trivalent combination products are the preferred agents due to their convenience and coverage. Immunization is recommended to begin as a 5-injection series using a combination vaccine starting at 2 months and finishing at 4–6 years. Booster vaccinations with the combination should be given at age 11–12 years and once as an adult.[3]

The products used for these vaccinations at Shands at UF are the DTaP and Tdap. Some key differences exist between these products that make them suitable for different age groups.

The DTaP vaccine is used for inducing active immunity against diphtheria, tetanus, and pertussis in infants and children up to the age of 7 years. The capital "D" and "P" in the name indicate higher antigen quantities of diphtheria toxin and pertussis vaccine than the Tdap vaccine. The DTaP product is contraindicated in children under the age of 6 weeks due to the fact that it may not be immunogenic in that age group. It is also contraindicated after 7 years of age due to a decreased risk of pertussis in this population and an increased risk of adverse effects, such as a sore arm. An increased amount of antigen is needed for initial immunization to provoke a proper immunogenic response.

The Tdap product contains reduced amounts of diphtheria toxin and pertussis vaccine, as indicated by the lower case "d" and "p." This product is for booster shots for adults and children over the age of 7 years and does not create enough immunogenic response to be given as the initial immunization. Tetanus is the main ingredient in Tdap.

The concentrations of each component in the vaccines vary largely between their uses and even slightly between manufacturers within the same use. In the DTaP vaccine, the diphtheria toxoid amount ranges from 6.7–25 Lf units, the tetanus toxoid ranges from 5–10 Lf units, and the pertussis toxin ranges from 10–46.8 mcg. In the Tdap vaccine the diphtheria toxoid amount ranges from 2–2.5 Lf, the tetanus toxoid is 5 Lf, and the pertussis toxin ranges from 2.5–8 mcg.

Children under the age of 7 who are given Tdap in the initial immunization series may not respond adequately and may need to be revaccinated. Adults who receive the DTaP vaccine with higher antigen quantities do not need revaccination but may have more adverse effects from the vaccine and have an increased chance of a sore arm at the vaccination site.

Using brand names along with the generic initials may help alleviate the confusion between these products. The brand names of the DTaP product with higher antigen levels are Daptacel®, Infanrix®, and Tripedia®. Only Tripedia® is stocked for inpatient use. The brand names of the Tdap product with lower antigen levels are Boostrix® and Adacel®. Only Adacel® is stocked for inpatient use. When ordering, dispensing, or administering the vaccine, remember the age differences between the vaccines and that big letters are for little kids.

By Robyn Keen, PharmD

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INSIDE THIS ISSUE

Formulary update, *from page 1*

◆ CRITERIA-FOR-USE CHANGES

Aztreonam (Azactam®)*

**Restricted to ID or Antimicrobial Management Team approval after 1st dose*

Antivenin Micrurus fulvius, Equine (North American Coral Snake Antivenin)‡

‡Expiration date extended to October 31, 2011

Dihydroergotamine (DHE) is a serotonin (5-HT) agonist that has affinity for 5-$HT_{1D\alpha}$ and 5-$HT_{1D\beta}$ receptors located on intracranial blood vessels and on sensory nerve endings of the trigeminal system. There are 2 theories behind its mechanism for treatment of acute migraines: 5-HT_{1D}-mediated vasoconstriction of intracranial blood vessels and 5-HT_{1D}-mediated inhibition of pro-inflammatory neuropeptide release from the trigeminal system.

DHE was approved by the FDA in 1946 for use in migraine and cluster headaches. DHE was listed in the *Formulary* until 1993 when it was removed after the FDA approval of sumatriptan, which is more specific for central serotonin receptors and has been associated with less nausea and vomiting.

DHE is still indicated for the acute treatment of migraine and cluster headaches. Its labeled dosage is 1 mg (ie, 1 mL) intravenously (IV), intramuscularly (IM), or subcutaneously (SQ), but it is usually given IV. The dose can be repeated at 1-hour intervals but should not exceed 3 mg (3 mL) for IM or SQ injections or 2 mg (2 mL) for IV injections. DHE is not indicated for chronic use due to possible fibrotic complications.

Most of the trials for DHE are small and have poor generalizability. The authors of a 2005 meta-analysis concluded that DHE, alone, was not as effective as sumatriptan or phenothiazines; however, DHE in combination with an antiemetic was as effective as opiates, ketorolac, or valproate. The results of 2 studies comparing DHE with sumatriptan suggested that sumatriptan and DHE are both effective in treating migraine headaches, however, sumatriptan works faster. One head-to-head study reported more migraine recurrence within 24 hours with sumatriptan compared with DHE.

Use of DHE is contraindicated in patients taking strong CYP 3A4 inhibitors, patients with ischemic heart disease, patients with uncontrolled hypertension, patients who have taken 5-HT_1 agonists or other ergotamine products in the last 24 hours, patients with hemiplegic or basilar migraine, patients with impaired hepatic or renal function, or women who are pregnant. Nausea and vomiting are the most frequently reported adverse events associated with DHE. DHE should only be used in patients who have first received an antiemetic.

Telavancin is a lipoglycopeptide derivative of vancomycin that received FDA approval in September 2009 for the treatment of adult patients with complicated skin and skin structure infections (cSSSI) caused by susceptible gram-positive bacteria. It is currently undergoing FDA review for the treatment of hospital-acquired pneumonia (HAP). Telavancin's spectrum of activity is similar to vancomycin, with activity against a wide range of aerobic and anaerobic gram-positive bacteria, including some multidrug-resistant strains. Telavancin has a dual mechanism of action: inhibition of peptidoglycan synthesis and disruption of membrane potential. This dual mechanism accounts for its enhanced activity as well as rapid bactericidal properties.

Telavancin has been compared to vancomycin for the treatment of cSSSI and HAP in several non-inferiority studies. For the treatment of cSSSI, telavancin was compared to vancomycin in 2 parallel, randomized, double-blind, controlled, phase III trials (known as the ATLAS trials). Patients received either telavancin or vancomycin for 7–14 days. Telavancin was shown to be non-inferior to vancomycin based on clinical cure rates. In a subanalysis of the ATLAS trials, clinical cure rates in the telavancin treatment group were lower in patients with impaired renal function, defined as a creatinine clearance (CrCl) less than 50 mL/min, compared to patients with normal renal function. The ATTAIN studies were randomized, double-blind, phase III trials in patients with HAP secondary to suspected or documented gram-positive pathogens. Once again, telavancin was non-inferior to vancomycin. Telavancin has also been used off-label for the treatment of bacteremia and endocarditis.

Telavancin has predictable linear pharmacokinetics that support once-daily dosing. The labeled dosage of telavancin for cSSSI is 10 mg/kg IV every 24 hours for 7–14 days. The actual duration of therapy should be determined by the patient's infection, clinical status, and progress. Renal function should be monitored closely and dosage adjustments are required in patients with impaired renal function. Rapid infusions can lead to Red-man Syndrome; thus, telavancin should be administered over 60 minutes to reduce this risk. The most common adverse events reported are taste disturbance, nausea, vomiting, and foamy urine. The drug is classified as pregnancy category C and carries a black box warning about potential fetal risks. Precaution should also be taken when prescribing telavancin to patients with a prolonged baseline QTc interval or taking drugs known to prolong the QT-interval.

The acquisition cost for telavancin is approximately $150 per day (for a 70-kg patient), which is less than the alternatives currently in the *Formulary*, excluding vancomycin and tigecycline. Telavancin was added in the *Formulary* and restricted to Infectious Diseases or the Antimicrobial Management Program for the management of gram-positive infections in patients who fail or who are intolerant to other therapies (ie, vancomycin).

Aliskiren is a direct renin inhibitor with a labeled indication for the treatment of hypertension. Aliskiren blocks the renin-angiotensin-aldosterone system at the first step.

Adverse events are similar to angiotensin-converting enzyme (ACE) inhibitors and angiotensin receptor blockers (ARBs), including cough, hyperkalemia, and the possibility of angioedema. Dose-related diarrhea has been reported.

Although there are currently no contraindications for aliskiren, it should not be used in pregnancy or concomitantly with cyclosporine or itraconazole. Because CYP 3A4 metabolizes aliskiren, drug interactions may be a concern. No renal adjustment is necessary, but caution is advised in those with renal impairment.

Studies evaluating the blood pressure-reducing ability of aliskiren have demonstrated clinically equal reduction in blood pressure in comparison to ACE inhibitors, ARBs, and hydrochlorothiazide. No studies have evaluated the cardiovascular benefits of aliskiren.

The cost of the aliskiren is substantially greater than the cost of the ACE inhibitors that are currently listed in the *Formulary*, but similar to the cost of the ARBs.

Aliskiren offers no advantage over ACE inhibitors or ARBs. It costs more without demonstrating superiority in blood pressure reduction or improved outcomes. Additionally, its safety profile is still not fully known, since it is the first drug in a new category of drugs.

Aliskiren was designated nonformulary and not available; however, patients may use their own supply of aliskiren from home if it is ordered.

Sorilux® is a **foam** form of **calcipotriene** with a labeled indication for the topical treatment of plaque psoriasis. Calcipotriene is a vitamin D_3 analog. Calcipotriene cream is rarely used nonformulary (ie, 3 patients in the last year) but may offer an alternative.

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Formulary update, *from page 2*

Qutenza® patch is a high-concentration (8%) transdermal form of **capsaicin** with a labeled indication for the management of pain associated with postherpetic neuralgia (PHN). Qutenza® is 80 to 320 times more potent than over-the-counter capsaicin cream, which is available as 0.025% and 0.1%. The high concentration of capsaicin in Qutenza® causes a brief period of acute pain, followed by a prolonged period of decreased nerve sensitivity. It takes time for nerves to re-innervate, thus, the long period between applications. Qutenza® is applied for only 60 minutes every 3 months.

In addition to being expensive, this product is difficult to use (eg, topical anesthetic and systemic pain medications must be used prior to administration; it must be handled only with nitrile [not latex] gloves; must be administered by a healthcare professional). Qutenza® will not be acquired for inpatient use and its application should be deferred to the outpatient setting.

Beyaz® is a low-dose, monophasic oral contraceptive with labeled indications for the prevention of pregnancy and for the following indications in women who choose to use an oral contraceptive for contraception: the treatment of premenstrual dysphoric disorder (PMDD), treatment of moderate acne, and to raise folate levels.

Drospirenone, which is an analogue of spironolactone, is the progesterone component of Beyaz®. It has antimineralocorticoid and antiestrogenic properties and is intended to improve premenstrual symptoms, including negative mood, water retention, and increased appetite. Drospirenone may increase potassium levels in some patients.

Ethinyl estradiol is the most common estrogen component of combination oral contraceptives. Beyaz® contains a relatively low dose of ethinyl estradiol (20 mcg). **Levomefolate** is also known as L-methylfolate, and is the biologically active form of folic acid.

Beyaz® was designated nonformulary and not available. Patients should use their own supply from home. The only combination oral contraceptive listed in the *Formulary* is a generic version of Lo Ovral®, which contains the progestin norgestrel and ethinyl estradiol.

Lo Loestrin Fe® is a combination oral contraceptive with the lowest dosage of estrogen (ethinyl estradiol 10 mcg) of any product currently marketed in the United States. It contains half the estrogen in Loestrin 24 Fe®. It also contains the progestin norethindrone acetate and ferrous fumarate as an oral iron supplement.

Like Beyaz®, the Lo Loestrin Fe® was designated nonformulary and not available and patients should use their own supply from home.

Pegloticase is an injectable, recombinant, pegylated form of urate oxidase enzyme. It decreases uric acid concentrations by converting uric acid to allantoin, which is benign and can be excreted in the urine. It is similar to rasburicase (Elitek®), which is also a recombinant form of urate oxidase. Rasburicase, which is listed in the *Formulary,* is not pegylated and has a labeled indication for the initial management of hyperuricemia associated with tumor lysis syndrome. Rasburicase is restricted to use by oncology prescribers for tumor lysis syndrome. Pegloticase's labeled indication is for the treatment of gout that is refractory to conventional therapy. The IV dose is given every 2 weeks. It is not clear how much longer pegloticase inhibits urate oxidase compared with rasburicase.

While pegloticase is effective in decreasing uric acid levels within 6 hours of administration, it has been associated with acute gouty flares during initiation. Elevated uric acid levels (>6 mg/dL) are associated with increased risk of hypersensitivity reactions as well as infusion reactions.

Initiation of pegloticase caused a gouty flare in 2/3 of patients in clinical trials. Therefore, it is recommended that there be 1 week of prophylaxis with colchicine and/or NSAIDs to prevent these gouty flares. Thus, acute use in the inpatient setting could be harmful. Pegloticase was designated nonformulary and not available for inpatient use.

Atelvia® is a once-weekly delayed-release tablet formulation of the bisphosphonate **risedronate** with a labeled indication for the treatment of postmenopausal osteoporosis. It has the same restrictive administration requirements as all oral bisphosphonates (ie, take in the morning with at least 120 mL of plain water and do not lie down for 30 minutes). Irritation of the upper GI tract, even esophageal ulceration, is possible if risedronate is not administered properly.

Therefore, Atelvia® was designated nonformulary and not available. Like all bisphosphonates, patients will not be allowed to use their own supply of Atelvia® for safety reasons. The only oral bisphosphonate listed in the *Formulary* is alendronate, which is restricted to use in patients who have been in the hospital for at least 7 days. The alendronate order must specify administration instructions consistent with the labeling and patients must be able to comply with this method of administration.

Sibutramine is primarily a norepinephrine and serotonin reuptake inhibitor, which was thought to enhance satiety. This prescription weight-loss drug was recently withdrawn from the market when postmarketing surveillance data showed a higher rate of cardiovascular events (eg, non-fatal MIs, non-fatal strokes, and death).

Sibutramine has never been listed in the *Formulary*. Sibutramine was designated nonformulary and not available and patients cannot use their own supply.

Levothyroxine is a synthetic version of the endogenous thyroid hormone tetraiodothyronine (T4). It is used as replacement therapy for patients with hypothyroidism.

In August 1997, the FDA announced that oral drug products containing levothyroxine were new drugs, requiring drug companies to submit a New Drug Application (NDA). Currently, there are 7 brand name and 2 generic levothyroxine products available on the market.

In Florida, levothyroxine has been on and off the *Negative Formulary* for several years. Generic manufacturers have argued that there is no difference between generic and brand name levothyroxine products, while manufacturers of brand name levothyroxine products, as well as certain thyroid and endocrine societies, maintain that there is a therapeutic difference. The *Negative Formulary* is not applicable to the inpatient setting. The P&T Committee determines which products can be interchanged.

The FDA's *Approved Drug Products With Therapeutic Equivalence Evaluations,* better known as the "*Orange Book*," contains a list of currently approved drug products, as well as therapeutic equivalence evaluations, for products with multiple sources, like levothyroxine. Therapeutically equivalent levothyroxine products share a 3-character code (ie, AB1, AB2, AB3, etc.). The number in the 3-character code refers to the reference-listed drug (RLD) that other products are compared with. According to the *Orange Book*, not all levothyroxine products have been shown to be equivalent to each other; however, Mylan's levothyroxine sodium is equivalent to all reference listed drug products of levothyroxine (ie, brand name levothyroxine products).

There have been several studies looking at the bioequivalence and therapeutic equivalence of the different levothyroxine products. Newer studies that follow current FDA guidelines for bioequivalency studies have found that levothyroxine products fall within the FDA's definition of bioequivalent.

The cost difference between different levothyroxine products is negligible. However, when considering cost implications from the view of a hospital's *Formulary*, storage and packaging of the medication, become factors in the decision. Availability in unit-dose packaging has resulted in the use of brand name Synthroid®,

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Formulary update, *from page 3*
but it is not always available. We have been routinely converting patients from other brands and generics to Synthroid® for years without any patient- noticeable impact.

Therefore, the P&T Committee determined that levothyroxine products can be interchanged to any marketed levothyroxine product. Preference will be given to products that are available in a unit-dose format (eg, Synthroid®), but any unit-dose product could be substituted while a patient is hospitalized. Prescribers may choose to prescribe a specific brand or generic upon discharge and should consider this as part of the medication reconciliation process.

Mycophenolate mofetil is an immunosuppressive drug that was originally approved under the brand name CellCept®. There are now A-rated generic equivalents for CellCept® listed in the *Orange Book*. Until recently, Roche/Genentech matched the generic pricing. They recently terminated this agreement and the brand name costs increased 10-fold. There are no generic equivalents for the injection or oral suspension. If we do not use a generic mycophenolate capsule, pharmaceutical costs will increase approximately $150,000. Expenses will increase an additional $150,000 for mycophenolate injection and suspension. Thus, without the switch to the generic capsule, pharmaceutical expenditures would increase $300,000.

By policy, generic mycophenolate mofetil capsules will be used in the inpatient setting. Patients are admitted to the hospital already receiving the generic product. In the past, we would have switched them from the generic to the brand. This has been done without any clinical consequences.

Aztreonam is a monobactam antibiotic with activity against gram-negative bacteria. Compared with other options, like beta-lactam antibiotics, it is far less potent. Aztreonam is generally reserved for use for the treatment of gram-negative infections (including Pseudomonas) when patients cannot tolerate a beta-lactam because of Type-1 hypersensitivity reactions. Unfortunately, beta-lactam allergies are often poorly documented and/or inaccurate, which may lead to providing suboptimal antimicrobial therapy. Aztreonam is overused, which contributes to the development of resistance (ie, poor sensitivities) to this niche antibiotic. This could result in poor results when aztreonam is used empirically to treat suspected infections like Pseudomonas.

Therefore, aztreonam has been restricted to approval by Infectious Diseases or the Antimicrobial Management Team after the first dose has been administered. This balances the need for rapid use in the setting of a suspected gram-negative infection, while preventing more than one dose.

Coral snake antivenin has been used as the antidote to the neurotoxin in coral snake bites. Coral snakes are common to this part of Florida.

Wyeth originally announced that there would be no more coral snake antivenin after the end of October 2008, when the last remaining product was scheduled to go out-of-date. Product has not been manufactured for several years. The last 2 years, the FDA granted the remaining product extended dating. Recently, the FDA again extended the dating for the remaining lots of coral snake antivenin until October 31, 2011. Once this product is gone, there will no longer be a commercially available antidote and patients will have to be managed with symptomatic support.

EDITORIAL

Twenty-five years of *Bulletin*

The *Drugs & Therapy Bulletin* is entering its 25th year of publication. I have been the editor and primary author of the *Bulletin* for those 25 years. I have received favorable feedback and some criticism for its content; regardless, I appreciate those who take the time to read the *Bulletin*.

The *Bulletin* is the primary written method of communicating decisions made by the Pharmacy and Therapeutics Committee. The P&T Committee is the medical staff committee that is the formal line of communications between the hospital and the medical staff regarding drug-related matters. If medical staff members do not receive the *Bulletin* or read it, we cannot do an effective job of communicating. If you are aware of medical staff members who should be added to the mailing list, please let me know.

Throughout the last 25 years, I have tried to explain why the P&T Committee makes its decisions. Why was a drug added or not added in the *Formulary?* Why was a drug's use restricted? Why was a drug use policy adopted? You may not agree with the P&T Committee's decisions, but you should understand the rationale for those decisions.

The newsletter also contains articles that are intended to be informative but brief. I welcome feedback on any of these articles. Please send any comments to my email address (hatton@ufl.edu). If you have ideas for topics that should be covered in the *Bulletin*, I would appreciate the suggestions. The best topics would have broad appeal to all practice areas and would focus on promoting safe and cost-effective use of medications.

Any suggestions that would make the *Bulletin* more informative or useful are welcomed.

By Randy C. Hatton, PharmD, FCCP, BCPS

CONTROVERSIES

Is erythromycin preferred to azithromycin as a prokinetic?

In last month's issue of the *Bulletin*, the article, *Oral Erythromycin for Gastroparesis: The More Stable Choice?,* stimulated some controversy.[1]

A recently published, retrospective, nonrandomized, quasi-experimental study done at UF suggests that azithromycin and erythromycin given intravenously were equally effective at stimulating gastric emptying as measured by technetium-egg gastric emptying scintigraphy (GES).[2] The study was done on 60 patients with symptoms of gastroparesis undergoing GES showing similarly accelerated gastric emptying with IV injections of each medication after a delayed emptying was diagnosed by GES. Drs. Moshiree and Toskes suggest azithromycin is preferred because of the longer duration of effect with azithromycin (with a longer duration of antral contractions seen during antroduodenal manometry), a longer half-life requiring fewer doses needed per day improving patient compliance, better adverse-effect profile (eg, less risk of QT prolongation and gastrointestinal adverse effects),

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Controversies, from page 5

and lack of CYP3A interactions with azithromycin as compared with erythromycin. Erythromycin has been associated with an increased risk of sudden cardiac death if given concomitantly with other medications metabolized through the P450 pathway.[3] Additional research like that being done here at UF will help determine the relative long-term efficacy and safety of these agents.

In a case-series of 30 patients comparing erythromycin (250 mg IV) to azithromycin (250 mg IV [n=15] or 500 mg IV [n=15]), antroduodenal manometry showed statistically greater mean amplitude of antral contractions, longer duration of antral contractions, and a greater motility index (a calculated measurement of motility) with azithromycin compared with erythromycin.[4] This study, however, was nonrandomized, open-labeled, and did not measure any symptomatic improvement. Currently, Moshiree and Toskes have an ongoing randomized control trial comparing the efficacy of erythromycin versus azithromycin for the symptomatic treatment of gastroparesis (showing equivalence) funded through a Pilot Grant from the CTSI.

Despite these ongoing trials, a known disadvantage for chronic use of these motilin agonists (erythromycin and azithromycin) is the risk of overuse, which could contribute to resistance for antibiotics that are still widely used (especially in the case of azithromycin). For example, azithromycin is commonly used for the treatment of community-acquired pneumonia and is still listed in the most recent treatment guidelines.[5] Azithromycin's long half-life and low intracellular levels may contribute more to resistance than other macrolide antibiotics. Motilin agonists without the antibiotic properties are currently being investigated for use in patients with gastroparesis, 2 of which are in Phase II trials.

The main point of last month's newsletter article was the 10-day stability for azithromycin suspension compared with 35-day stability for erythromycin suspension.[1] Studies examining longer stability for azithromycin suspension are needed. Studies have not been done since chronic use of azithromycin is not a labeled indication. Now, patients must return to their outpatient pharmacy every 10 days to obtain a freshly made supply of azithromycin suspension. This can be a disadvantage for a chronic medication, when an alternate medication could be picked up once a month. Also, it is not clear whether tachyphylaxis, which often occurs with erythromycin, occurs with azithromycin. This lack of response to the medication over time is a known problem with chronic use of erythromycin. Also, despite the known fact that erythromycin is currently the most potent prokinetic for use in gastroparesis, it is still not FDA-labeled for that indication. The only drug that is FDA-approved is metoclopramide, which now has a black-box warning due to risk of tardive dyskinesia.

Finally, erythromycin can interact with medications such as statins, SSRIs, calcium channel blockers, antifungal medications, warfarin, and drugs that prolong the Q-T interval. For those patients who may experience serious interactions, azithromycin is the more rational choice since it is the least arrhythmogenic option for treatment of this chronic and debilitating condition.

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