



Authored By: Richard J. Kraft, Pharm.D.
eMail Me

PHARMACY MONTHLY NEWSLETTER

FEBRUARY 5, 2009

TOPICS IN EVERY ISSUE:

In The News | Safety Updates | New Generic... | Emerging Therapies... | PharmD Monthly Q&A... | Disease State/Lit. Update | Formulary Updates

In The News:

- FDA supports **Vytorin®**: The results from ENHANCE do not change FDA's position that an elevated LDL cholesterol is a risk factor for cardiovascular disease and that lowering LDL cholesterol reduces the risk for cardiovascular disease. Recall that:
 - * LDL cholesterol decreased by 56% in the Vytorin group and decreased by 39% in the simvastatin group (stat significant diff).
 - * FDA plans to monitor ongoing IMPROVE-IT trial, results not expected until 2012.
- In response to a petition by Public Citizen, an FDA advisory committee voted 14—12 to pull **propoxyphene (Darvon®)** and **propoxyphene/APAP (Darvocet)** from the US market citing lack of efficacy, risks outweighing any potential benefits and abuse potential.
 - * Both Public Citizen and drug industry representatives have weighed in, FDA's official action is yet to be determined.
- FDA approves new Gel formulation of oxybutynin, **Gelnique® 10%**, for overactive bladder. The drug company feels topical administration in this manner (vs. oral formulation) will provide comparable efficacy with fewer adverse events (i.e., dry mouth, constipation). No head-to-head trials of the gel formulation vs. any oral formulation have been published to date.
 - * Oxytrol® is a transdermal patch formulation approved since 2003. Trends and small studies do indicate some advantage for topical vs. oral **immediate release** oxybutynin administration in regards to anticholinergic ADRs (i.e., dry mouth, constipation).
 - * This possible advantage appears to narrow significantly when comparing topical vs. **ER** oral formulations.
- Sudden **Metoprolol ER succinate shortage**. Previously, there were 2 companies manufacturing this generic for Toprol XL. One of the companies suddenly ceased production (see Ethex below) and the other (Par) can not keep up with demand at this point. Local and national pharmacies will have significant trouble obtaining metoprolol ER succinate tabs in the 50, 100, and 200 mg strengths for some time. Pharmacies will also have some trouble obtaining brand Toprol XL as well. Two options at the present time:
 - * Temporarily switch patient to metoprolol IR tartrate at ½ the ER dose but BID [[evidence based vs. non, BB info on January p.2](#)]
 - * If pharmacy can obtain brand XL but not generic ER, may switch and IHA will allow temporary copay override to tier 2.

Pharmacy—Clinical Sound Bytes:

- ACIP announces 2009 Adult immunization schedule updates. [[Link](#)] Changes highlighted here [[Link](#)]
- ACIP/AAP/AAFP announces 2009 Children and Adolescent immunization schedule updates. [[Link](#)]
- FDA approves fixed dose combination acne medication, **Epiduo® gel** (adeleprene 0.1%/benzoyl peroxide 2.5%) [[Link](#)]
- FDA approves another once-daily extended release formulation of tramadol, **Ryzolt®**. [[Link](#)]
- Meta-analysis of 117 randomized controlled trials suggests **sertraline** and **escitalopram (Lexapro®)** best overall of 12 newer antidepressants [[Link](#)]

FDA Vytorin
Gelnique
Oxytrol vs. oral
Public Citizen on propox
Industry on propoxyphene

Safety Updates:

[Submit ADR^s to MedWatch Online!](#)

- The FDA has launched an ongoing Early Communication regarding **clopidogrel (Plavix®)** and reports that the drug is LESS effective in some patients than others. Possible issues include genetic differences in drug metabolism and potential drug interactions with certain medications (such as certain proton pump inhibitors (PPIs)). FDA provides 3 clinical recommendations at their site.
 - * **Note:** H2RA's do NOT appear to interfere with clopidogrel's antiplatelet activity.
 - * Unclear at this point whether investigational prasugrel would be expected to elicit similar issues, different elimination pathways are involved.—**UPDATE:** FDA advisory committee voted unanimously that FDA should approve prasugrel
- **Ethex has recalled most of its generic products** (including metoprolol ER succinate as above) because they may have been manufactured under conditions that did not comply w/ current Good Manufacturing Practices.
 - * Previously some lots of products were recalled due to oversized tablets delivering higher than labeled doses.
- The FDA has launched an ongoing Early Communication regarding **Innohep (tizaparin)**. The Innohep in Renal Insufficiency Study (IRIS) that was stopped in February, 2008 because of an interim finding of an **increase in all-cause mortality** in patients who received Innohep.
 - * Per FDA, healthcare professionals should consider the use of alternative treatments to Innohep when treating elderly patients over 70 years of age with renal insufficiency and DVT, PE, or both. Final FDA analysis report expected shortly.

Plavix
Ethex recalls
Tizaparin
Prasugrel

Ask RPh to submit
ADR to Medwatch



New Generic Approvals*:

Letrozole 2.5 mg tablets, generic for Femara, approved by FDA.
Stavudine 15, 20, 30, and 40 mg caps and 1 mg/ml sol, generic for Zerit, approved by FDA.
Divalproex sodium 125 mg sprinkle caps, generic for Depakote Sprinkle Caps, approved by FDA.



- **HFA inhaler transition time is here!** Generic inhalers (with CFCs) are NO LONGER AVAILABLE.
 - * Help for patients to afford HFA inhalers is available.

Transition Now Help
Proventil HFA
ProAir HFA
InhalerTransition.org



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Emerging Therapies & the Drug Pipeline:

Skin and soft tissue infection (SSTI)—MRSA— At least two investigational drugs, **telavancin** and **oritavancin**, have been recently submitted to the FDA to gain approval for skin and structure infections including those caused by MRSA. Both entities are novel lipoglycopeptide antibiotic (similar to vancomycin) candidates with potent bactericidal (killing) activity against a broad spectrum of gram-positive bacteria. In 12/08 the FDA asked for additional studies before it could approve **oritavancin**. **Telavancin** has been studied for Hospital Acquired Pneumonia as well as SSTIs w/MRSA. **Telavancin** is a once-daily, (vs. typical BID vanco dosing) with a multifunctional mechanism of action. It inhibits the formation of the bacterial cell wall and disrupts bacterial cell membrane function. It may prove that the additive mechanisms of action seen with telavancin speed bacterial killing while also reducing the risks of inducing resistance to telavancin or cross-resistance with other antibiotics.

[Oritavancin](#)
[Telavancin](#)

Gardasil for boys?—The vaccine for HPV is already approved in 40 other countries for men. Merck will apply to FDA for approval in males aged 9—26 yrs. HPV can cause penile cancer and other cancers in men; however, there is no proof yet that the vaccine prevents cancer in men. Because HPV is spread through sexual contact, vaccinating men has the potential to reduce transmission of the virus to women.

Pharm.D. Monthly Q&A Review:

Incoming e-mail Question:

“What’s the difference between omega-3’s and omega 6’s?”

[O6FAs in Circulation](#)
[Heartwire O6FA update](#)

Excerpt of Outgoing e-mail Answer:

- Omega-3 fatty acids (O3FAs) are primarily derived from fish, especially when considering Rx’s and supplements. Conversely, omega-6 fatty acids (O6FAs) are primarily derived from plant sources (vegetable oils, etc).
- Unlike O6FAs, O3FAs are metabolized to products that inhibit platelet aggregation or products with little detrimental activity. O6FA is also known as arachidonic acid (AA), a substrate for the building blocks of many pro-inflammatory molecules.
- A recent review (2/2009) published in AHA’s journal, *Circulation*, concluded that consumption of at least 5-10% of energy from O6FA reduces the risk of CHD relative to lower intakes with no clinical evidence for adverse events. One author stated, “We’re basically not telling people to start doing something different; we’re telling people NOT to stop eating their omega-6.”
- NO recommendations can be made or supported by evidence to increase or supplement O6FAs at this point, vs. O3FAs.

Disease State Or Literature Update:

ACCF/ACG/AHA 2008 Expert Consensus—

[Expert Consensus Circ.](#) ↓
[GBS Score 2009/Lancet](#) ↓

Reducing the Gastrointestinal Risks of Antiplatelet Therapy and NSAID Use:

Recommendations:

1. As the use of any NSAID, including COX-2-selective agents and OTC doses of traditional NSAIDs, in conjunction with cardiac-dose ASA, substantially increases the risk of ulcer complications, a gastroprotective therapy should be prescribed for at-risk patients.
2. The use of low-dose ASA for cardioprophylaxis is associated with a 2– to 4–fold increase in UGIE^{§§} risk. Enteric coated or buffered preparations do NOT reduce risk of bleeding. For patients at risk of adverse events, GI protection should be prescribed. The risk of UGIE increases with ASA dose escalation; thus, for the chronic phase of therapy, doses greater than 81 mg should NOT be routinely prescribed.
3. The combination of ASA and anticoagulant therapy (including UFH, LMWH, and warfarin) is associated with a clinically meaningful and significantly increased risk of major extracranial bleeding events, a proportion from the upper GI tract. This combination should be used with established vascular, arrhythmic, or valvular indication; patients should receive concomitant PPIs as well. When warfarin is added to ASA plus clopidogrel, an INR of 2.0—2.5 is recommended.
4. Substitution of clopidogrel for ASA is NOT a recommended strategy to reduce the risk of recurrent ulcer bleeding in high-risk patients and is inferior to the combination of ASA plus PPI.
5. The combination of clopidogrel and warfarin therapy is associated with an increased incidence of major bleeding when compared with monotherapy alone. Use of combination antiplatelet and anticoagulant therapy should be considered only in cases in which the benefits are likely to outweigh the risks. When warfarin is added to ASA plus clopidogrel, an INR of 2.0—2.5 is recommended.
6. PPIs are the preferred agents for the therapy and prophylaxis of NSAID– and ASA-associated GI injury. [NOTE: FDA Medwatch on p.1!!]
7. Testing for and eradicating H pylori in patients with a history of ulcer disease is recommended before starting chronic antiplatelet therapy.
8. Decision for discontinuation of ASA in the setting of acute ulcer bleeding must be made on an individual basis, based upon cardiac risk and GI risk assessments to discern potential thrombotic and hemorrhagic complications.
9. Endoscopic therapy may be performed in high-risk CV patients on dual antiplatelet therapy, and collaboration between the cardiologist and endoscopist should balance the risks of bleeding with thrombosis with regard to the timing of cessation of antiplatelet therapy.

Formulary Updates:

Additions: Updates anticipated by 2/8/09 — *an e-mail brief update will follow...*

Crestor® (rosuvastatin) will be added to Tier 2 and tablet split allowed— **Beginning 1/1/2009**

Relistor® (methylnaltrexone bromide) added to Tier 2

Tier changes:

Vytorin® (simvastatin/ezetimibe) has been moved to Tier 3, non-formulary.

[Link to IHA Formulary](#) ↓
[Tablet Splitting Program](#) ↓



*All meds tier 1 unless otherwise specified; §ADR = Adverse Drug Reaction; PAR = Prior Auth Req’d; §§UGIE = Upper gastrointestinal events