



A Partnership for Medical Excellence



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PHARMACY MONTHLY NEWSLETTER

JANUARY 4, 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:

- '08—'09 season's flu virus found to be largely resistant to **Tamiflu (oseltamivir)** in early tests.
 - * 99% of Influenza Type A (H1N1) strains tested and reported to CDC were resistant to oseltamivir
 - * As a result, CDC has updated its recommendations; "*When influenza A (H1N1) virus infection or exposure is suspected, zanamivir or a combination of oseltamivir and rimantadine are more appropriate options than oseltamivir alone.*"
 - * They also indicate that flu vaccines should cover currently circulating strains, including the H1N1 oseltamivir-resistant strain
- Another study questioning the value of intensive glucose control (A1C <7) emerges—**Veteran Affairs Diabetes Trial (VADT)**
 - * Please NOTE: This study utilized Avandia® (rosiglitazone) within its interventions, i.e. cardiovascular impact?
 - * 1791 military vets, avg 60.4 yrs, avg 11.5 yrs of DM diagnosis, 40% had prior CV event, 1°—CV event composite
 - * NO significant difference between intensive group (A1C-6.9%) vs standard group (8.4%) in any component of 1° outcome
 - * Authors' Conclusion—Intensive glucose control in patients with poorly controlled T2DM had NO significant effect on the rates of major CV events, death, or microvascular complications. Additional perspectives see also ACCORD, ADVANCE
- FDA approved **Trilipix (fenofibric acid)** delayed release capsules for mixed dyslipidemia and hypertriglyceridemia alone and in combination with optimal statin therapy.
 - * In clinical trials using Trilipix 135mg, HDL up by 9.8—22.9%, TGs down by 23.5—54.5%, LDL-C down by 2.2—12%
 - * In addition LDL particles shifted away from small, dense to larger, buoyant particles better recognized by LDL receptors
 - * Fenofibric acid is one of the active metabolites for fenofibrate, slightly fewer ADRs were apparent in clinical trials
 - * Pending future efficacy/safety trials; continue to utilize generic fenofibrate when looking to a fibrate derivative

Pharmacy—Clinical Sound Bytes:

- ACCOMPLISH trial finds that benazepril/amlodipine superior to benazepril/hctz in reducing CV events in those w/ HTN at risk for them. [Link]
- NEW evidence for benefit of statins in reducing risk of Alzheimer's Disease—Info from Rotterdam Study. [Link]
- In survey of 3,005 community-dwelling persons 57—85yrs, 42% used at least 1 OTC medication and 49% used a dietary supplement. Authors of JAMA article concluded that nearly 1 in 25 were potentially at risk for a MAJOR drug-drug interaction. [Link]. New NIH survey finds that 38% of American adults use some form of CAM^{§§}. [Link]
- FDA approves Zolpimist® (zolpidem) nasal spray for short term treatment of insomnia. [Link]
- EHR that provides drug cost information could save millions each year per Archives of Internal Med article. [Link]

Flu resistance at CDC	}
FluView CDC	
VADT Trial	
Trilipix	

Safety Updates:

Submit ADR[§] to MedWatch Online!

- **Oral sodium phosphate (OSP)** products for bowel cleansing (i.e., Fleet Phospho-soda, Visicol, OsmoPrep, etc.) update warning regarding acute phosphate nephropathy (APN). Identifiable risk factors include: >55yrs, hypovolemic or decreased intravascular volume, baseline kidney disease, bowel obstruction, active colitis, and meds that affect renal perfusion or function.
 - * Be sure to instruct patients to drink sufficient quantities of clear fluids before, during and after bowel cleansing. Some evidence indicates use of electrolyte or carbohydrate-electrolyte solution may better decrease risk of APN.
- FDA Public Advisory Committee met to debate **Long acting beta-agonist (LABAs)** specifically for ASHTMA.
 - * Briefing report (460 pages!) details all aspects of meta-analysis. LABAs, as a group, showed an increased risk in the asthma composite (asthma composite = asthma-related hospitalization, intubation, and death).
 - * Increased risk was NOT apparent when LABA used with an inhaled corticosteroid (ICS).
- FDA requires ALL **anti-epileptic (AEDs)** drugs to add a black box warning and a medication guide re: increased risk of suicidality.
 - * In FDA analysis, increased risk of suicidality observed as early as 1 week after starting AED, continued through 24 weeks.
 - * Risk higher among those utilizing AEDs for epilepsy vs. off-label conditions (absolute risk low, 0.43% AEDs vs. 0.22% placebo)
 - ◆ (which may indicate a dose-related effect since epilepsy doses are typically higher).

OSP at FDA
LABAs (FDA
Full Docket)
AEDs at FDA

Ask RPh to submit
ADR to Medwatch



New Generic Approvals*:

- **Calcitonin-salmon** nasal spray, generic for Miacalcin nasal spray, approved by FDA, and should be available at pharmacies now. No packaging or efficacy differences to date.
- **Methylergonovine maleate injection**, generic for Methergine, approved by FDA (tablets still branded only).
- **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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MONTHLY

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Emerging Therapies & the Drug Pipeline:

Obesity/Weight Loss—The investigational drug **lorcaserin** targets the 5HT_{2C} serotonin receptor in hypothalamus of brain only. Previous drugs investigated for obesity/weight loss, such as endocannabinoid receptor antagonist rimonabant or Fen-phen appear to benefit weight but carry significant risks such as increased risk of suicidality or CV risk. Thus far in its development, lorcaserin appears devoid of these risks. Lorcaserin has demonstrated early evidence suggesting a potential benefit in lipid profiles as well.

{ [lorcaserin](#)
[pegloticase](#) }

Gout—The investigational drug, **pegloticase** (Puricase®), recently submitted BLA** and FDA accepted it for priority review for treatment-failure gout. Treatment-failure gout occurs in patients who have failed to normalize serum uric acid and whose signs and symptoms are inadequately controlled with allopurinol at the maximum medically appropriate dose or for whom allopurinol is contraindicated.

Pharm.D. Monthly O&A Review:

Incoming e-mail Question:

“How and why would I use metolazone together with furosemide for my heart failure patient?”

{ [ACC/AHA 2005](#)
[Rosenberg, et al](#) }

Outgoing e-mail Answer:

- Sequential nephron blockade to combat ceiling diuresis of loop diuretic.
- This combination is NOT necessary until the ceiling diuresis of the loop diuretic has been reached (usually around 80mg furosemide), i.e., generally in cases of refractory HF.
- Metolazone is “thiazide-like”, but inhibits Na⁺ reabsorption from the cortical diluting site AND to lesser proportions in the proximal convoluted tubule (vs. distal like hctz) and thus works synergistically with a loop diuretic such as furosemide in the setting of heart failure.
- Presumably as a consequence of the drug action in the proximal tubule, metolazone, in contrast to other thiazides, is able to produce a diuresis despite of a low glomerular filtration rate (typically present in the heart failure patient due to low cardiac output).
- If this sort of combination is utilized, must start low (metolazone 2.5mg 1/2 hour before loop) and go slow to obtain diuresis without over-diuresing, weight must also be carefully monitored (this approach is addressed w/in the ACC/AHA HF guidelines (2005) - see link above)

Disease State Or Literature Update:

2 articles, recently in Archives of Internal Medicine, compare the efficacy of various beta-blockers (BBs) in patients w/ heart failure:

Prior to comparisons such as these, BBs have traditionally been placed into 2 general categories with respect to HF:

- **Evidence-based Beta-blockers (EBBBs)**—Metoprolol succinate (ER), carvedilol, bisoprolol fumarate
- **Non-Evidence-based Beta-blockers (non-EBBBs)** - Metoprolol tartrate (IR), atenolol

{ [Go et al, BBs in CHF 1](#)
[Kramer et al, BBs in CHF 2](#) }

Go A, et al: Comparative Effectiveness of Different B-Adrenergic Antagonists on Mortality Among Adults With Heart Failure in Clinical Practice.

This was a retrospective cohort study performed using data from a series of managed care organizations. They compared mortality associated with different BBs following hospitalization for HF between 2001 and 2003. Longitudinal exposure to BB was captured.

- **Results**—7976 of 11,326 (70.4%) patients surviving hospitalization for HF rec'd BBs. Rate of death/100 person-years during the 12 months after discharge varied by exposure AND type of BB (atenolol, 20.1; metoprolol IR, 22.8; carvedilol, 17.7; and no BBs, 37.0).
- **Conclusion**—Compared w/ atenolol, adjusted risks of death were slightly higher w/ metoprolol IR but did NOT significantly differ w/ carvedilol.
* Also, NO significant difference amongst BBs for those using digoxin as well (as marker for poor systolic function).
- **Limitations**—Specific indications for BB use were not available (carvedilol typically used for HF vs. atenolol typically used for HTN) thus level of severity of disease at baseline between groups is more difficult. Retrospective bias. Dosage comparisons not available (carvedilol doses tend to NOT be titrated to optimal doses).

Kramer J, et al: Comparative Effectiveness of B-blockers in Elderly Patients With Heart Failure.

This was also a retrospective cohort analysis, but used elderly patients (≥65yrs) with Medicare and/or Medicaid. They compared differences between EBBBs, non-EBBBs and no-BBs in regards to primarily survival from 30 days to 1 year after HF hospitalization and secondarily for number and days of rehospitalization for HF & number of outpatient visits. **Results**—No significant difference between EBBB and non-EBBB.

Recall that COMET trial was randomized & prospective and demonstrated superiority for carvedilol vs. metoprolol IR (doses debatable).

Formulary Updates:

Additions: Updates anticipated by 2/8/09

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

Relistor® (methylalntrexone bromide) added to Tier 2

Changes based on availability of generic products: Tier 3 w/their respective generics now Tier 1

Yasmin®, Risperdal®, Dovonex®, Activella®, Efudex®, Precose®, Wellbutrin® XL 150mg, Lamictal®, Marinol®, Depakote® ER, Sonata®, Loprox®, Sular®, Cellcept®, Inspra®, Prilosec DR caps

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

