



Authored By: Richard J. Kraft, Pharm.D.  
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# PHARMACY MONTHLY NEWSLETTER

DECEMBER 4, 2008

## 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:

- **EHR records suggest reduced malpractice claims.** An recent article in Archives of Internal Medicine utilized a survey of 1884 physicians (71.4% responded) to perform a logistic regression to assess the relationship between the adoption and use of EHRs and paid malpractice claims.
  - \* 6.1% of physicians with EHR had a history of a paid malpractice claim vs. 10.8% without EHR.
- FDA approved **tapentadol** (trade name TBD) immediate-release tabs for relief of moderate to severe acute pain in adults  $\geq 18$  yrs . Tapentadol acts in 2 ways, combining mu-opioid receptor agonism and norepinephrine (NE) reuptake inhibition.
  - \* Benefit of tapentadol vs. separate narcotic plus drug affecting NE is unclear at this point.
- **Crestor®** (rosuvastatin) approved by FDA for 2 NEW indications, primary dysbetalipoproteinemia (Fredrickson Type III Hyperlipoproteinemia) and to slow the progression of atherosclerosis (adjunct to diet).
  - \* These (FDA approved) indications are NOT unique compared to other statins. See CIPA Statin Drug Class Review for comparisons. [[Link](#)]
- **Apriso®** (mesalamine) approved by FDA as 0.375 mg extended-release caps for maintenance of remission of ulcerative colitis in adults. Dose is 4 caps (1.5 grams) ONCE daily with or without food, do NOT co-administer with antacids.
  - \* Unlike tablets, Apriso® caps outer capsule dissolves dispersing delayed-release microgranules into GI tract where inner polymer matrix core controls the release of mesalamine at the site of action.
- A systematic review and meta-analysis published this month in JAMA provides insight into utilization of **brand vs. generic** medications and outcomes in cardiovascular disease. **The authors found NO evidence of superiority of brand to generic medications.**
  - \* Clinical equivalence was noted in **100%** of all RCTs of beta-blockers, diuretics, statins, antiplatelets, ACE, alpha-blockers; 5 of 7 (71%) of RCTs of CCBs; and among narrow therapeutic index drugs, equivalence was noted in **100%** of class 1 antiarrhythmic and warfarin trials.
  - \* *Despite these results*, 53% of the editorials of these RCTs expressed a negative view of generic substitution

### Pharmacy—Clinical Sound Bytes:

- More on TZDs and CHF, rosiglitazone vs. pioglitazone saga continues. [[Link](#)]
- Change in HR over time predicts mortality. [[Link](#)]
- Review of SELECT trial finds NO benefit for use of selenium and Vit E supplements. [[Link](#)]
- Written instructions cut bleeding risk for blood thinner use. [[Link](#)]
- Avapro® (irbesartan) did NOT improve outcomes of patients with heart failure and a preserved LVEF. [[Link](#)]

[EHR's & Malpractice](#)  
[Tapentadol](#)  
[Crestor® info](#)   
[Crestor® FDA](#)   
[Apriso® info](#)  
[Brand vs. Generics](#)

### Safety Updates:

Submit ADR<sup>s</sup> to MedWatch Online!

FDA updated an early warning communication regarding **bisphosphonates** and possible association with **afib**. Their conclusion was that across ALL studies investigated, NO clear association between bisphosphonate exposure and the rate of serious or non-serious afib was observed. Also, dose or duration did NOT contribute.

**Benzoyl peroxide 10% acne gels**, ALL Lots of particular brands—specifically 'Equate: Medicated Acne Gel sold' at Wal-mart, recalled due to presence of bacteria (*Burkholderia cepacia*).

**Starcaps™** dietary supplement for weight loss, Lot 12/2011—84810, recalled due to presence of undeclared drug ingredient. The potent loop diuretic, bumetanide (0.8 mg/cap), was found in the capsules. This amount is significant as usual dosage range is typically 0.5—2.0 mg/day.

*Note:* Interestingly, Starcaps™ is apparently the product that at least 1 NFL player utilized to maintain his weight and is now under investigation by NFL for abuse of drug policy (steroid masking).

**Zhen De Shou™** fat loss capsules, ALL Lots, recalled due to presence of undeclared drug ingredient. The ingredient was identified as sibutramine (FDA approved as appetite suppressant for weight loss, as Meridia®). Sibutramine is known to substantially increase blood pressure and/or pulse.

[Bisphosphonates](#)  
[Acne gels...](#)  
[Starcaps™](#)  
[Zhen De Shou™](#)

Ask RPh to submit  
ADR to Medwatch

### New Generic Approvals\*:

- **Sumatriptan**, generic for Imitrex®, approved as first generic triptan to come to market. Anticipate formulary changes to triptan class follow in the near future.
- **Dorzolamide HCL & timolol maleate**, generic for Cosopt®; **Dorzolamide HCL**, generic for Trusopt®
- **Levetiracetam**, generic for Keppra®, approved by FDA.
  - Note that **Keppra XR**, allowing once daily dosing vs. twice daily dosing was recently FDA approved. Debate is ongoing regarding generic conversion of patients maintained on brand name anticonvulsants. Compliance is likely a more significant issue than between brand drug differences, continue to individualize generic conversion approach for sensitive patients.
- **Budesonide respules** for inhalation, generic for Pulmicort® respules, despite ongoing litigation...stay tuned.
- Again, HFA inhaler transition time fast approaching (by 2009). Help for patients to afford HFA inhalers is available.

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**MONTHLY**

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**Emerging Therapies & the Drug Pipeline:**

{ [Telcagepant](#) }

**Migraine Headache**—The investigational drug **telcagepant** functions to improve migraine HA via a unique mechanism of action (MOA) and initial studies indicate that the drug has comparable efficacy to triptans but is better tolerated.

- Telcagepant is a calcitonin gene-related peptide (CGRP) antagonist
- CGRP antagonists don't seem to have blood vessel narrowing properties and, therefore, may not carry the same CV-related risks as triptans
- However, telcagepant studies to date have excluded patients with CV disease, thus additional studies are needed
- In addition, the safety profile of telcagepant needs to be studied beyond more than one migraine attack

**Pharm.D. Monthly Q&A Review:**

**Incoming e-mail Question:**

{ [NEJM Review](#)  
[Flexible dosing](#) }

“**Chantix (varenicline)** is approved for smoking cessation as a maintenance dose of 1mg bid, any evidence to support use of higher doses? What about combination with other cessation drugs?”

**Outgoing e-mail Answer:**

- **Dose > 1mg Bid?** - No. I was unable to identify even dose ranging studies during drug's development to indicate that doses over 1 mg bid were either safe or effective. However, an extended release version of varenicline is currently under investigation w/ doses up to 2.4mg bid being tested. Complicating interpretation is the way the current tablet formulation releases the drug. For example, the 0.5 mg dose is actually provided as 0.85 mg of varenicline tartrate within the tablet. Thus, hard to say what the 'effective dose' from new formulation is.
  - \* Note that evidence exists suggesting that doses of LESS than 2 mg/day ARE still effective as maintenance, and that 'flexible dosing' retains efficacy as well. 'Flexible dosing' of varenicline article link to the right as well.
- **Combination therapy?** - **Bupropion** represents completely different, potentially complementary MOA vs. varenicline. No trials to support this approach yet, but there are a few ongoing trials. **Nicotine replacement** does NOT appear advisable in combination with varenicline. Logically, if part of varenicline's mechanism of action is reducing the reward of smoking, replacing nicotine doesn't give the patient a chance to smoke and NOT feel the reward. However, may be beneficial, very short term, at varenicline initiation to reduce cravings.

**Disease State Or Literature Update:**

The UK's National Institution for Health and Clinical Excellence (NICE) published **osteoporosis guidance** after more than six years of consultation. Geared toward use of drugs to prevent 1° and 2° osteoporitic fractures in postmenopausal women.

Drugs reviewed include: alendronate, etidronate, risedronate, raloxifene, and strontium ranelate.

{ [Quick guide](#)  
[Full guide](#)

- Strontium ranelate NOT currently available within U.S., etidronate is NOT approved for osteoporosis in U.S.
- High doses or during prolonged use, etidronate is associated w/ significant impairment of bone mineralization (osteomalacia)

**Pharm.D. Interpretation:**

At first read, the NICE guidance does NOT appear to add much to National Osteoporosis Foundation (NOF) guidance. In fact, it appears lacking of information useful in the U.S.. Thus, for the time being, pharmacy recommends continuing to follow NOF guidelines [[Link](#)].

- Consider utilizing the **FRAX™** assessment tool [[Link](#)] from World Health Organization (WHO) in your daily practice for a more comprehensive assessment of fracture risk in women AND men over 50, especially useful in those with a low **hip** BMD.
- Developed by WHO & integrates clinical risk factors w/ BMD of femoral neck to provide a 10-year risk for probability of fracture.
- Due to BMD scanner brand differences & NHANES datasets used in developing FRAX™, a FRAX™ Patch tool required [[Link](#)]

Per NOF, the following post-menopausal women and men over 50 with the following should receive treatment:

- A hip or vertebral (clinical or morphometric) fracture
- T-score ≤ -2.5 at femoral neck or spine after appropriate exclusion of secondary causes
- Low bone mass (T-score between -1.0 and -2.5 at the femoral neck or spine) and a 10-year probability of a hip fracture ≥ 3% or a 10-year probability of a major osteoporosis-related fracture ≥ 20% based on the US-adapted WHO algorithm

**Formulary Updates:**

**Additions:**

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

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

**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

