

# PHARMACY MONTHLY NEWSLETTER

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## In The News:

**Vytorin and Cancer?** Still in the news. NEJM published 3 major articles on the subject. My previous month's points:

- \* NOTE: numerous other combinations of cholesterol medications w/statins have shown to be safe and effective (Niaspan, Welchol, etc)
- \* These results should serve to re-enforce need to maximize statin dose and encourage lifestyle modifications.
- \* Perhaps also illustrating need to capture entire lipid profile, not just pushing LDL as low as we can go.

- FDA approved a new formulation (oral) of palonosetron, **Aloxi**®, indicated for moderately emetogenic cancer chemotherapy -- prevention of acute nausea and vomiting associated with initial & repeat courses. This 5HT<sub>3</sub> inhibitor has 100-fold greater binding affinity than any other 5HT<sub>3</sub> inhibitor & a much longer t<sub>1/2</sub> (40.0h, vs. 7.5h dalesetron, 4.0h ondansetron, 8.9h granisetron). These differences appear to support greater efficacy in delayed chemotherapy induced nausea and vomiting. However, demonstrated differences were small & whether pharmacoeconomic benefits over other 5HT<sub>3</sub>'s exists is still uncertain.
- FDA approved a new formulation (delayed release) of valproic acid, **Stavzor**®, indicated for 1) acute treatment of manic episode of bipolar, 2) mono- and adjunctive therapy of complex partial seizures and simple and complex absence seizures; adjunctive therapy in patients with multiple seizure types that include absence seizures, 3) prophylaxis in migraine headaches. No clear clinical advantage over now generic Depakote®.
- The American Academy of Otolaryngology-Head and Neck Surgery Foundation has published **clinical practice guidelines regarding adult sinusitis**. These guidelines propose methodology to distinguish between viral and bacterial and acute versus chronic sinusitis and recommendations on initial and follow up treatment. If acute bacterial rhinosinusitis, amoxicillin is their first line agent.

[NEJM Article 1](#)  
[NEJM Article 2](#)  
[NEJM Editorial](#)  
[SEAS Debate](#)

[Aloxi®'s PI](#)   
[Stavzor®'s PI](#)   
[Sinusitis Guidelines](#)


## Safety Updates:

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



- Following recent news, FDA now reports that it is investigating a report from the SEAS trial of a possible link between **Vytorin**® and a potentially increased incidence of cancer. FDA indicated final report from SEAS investigators in 3 months, then 6 months for FDA complete review.
- FDA warned of risk of rhabdomyolysis (which can lead to renal failure or death) when **simvastatin** used w/ **amiodarone**. Risk is dose-related, increases when simvastatin >20mg/day is used w/amiodarone.
- Since issuing an advisory in October 2007, FDA has received reports of 6 cases of hemorrhagic or necrotizing **pancreatitis** in patients taking **Byetta**®. This is still a VERY rare event, current recommendations are only to avoid Byetta® in patients with a history of pancreatitis and d/c immediately if pancreatitis suspected.

[FDA on SEAS](#)  
[Simva+Amiodarone](#)  
[FDA on Byetta](#)

[Ask RPh to submit  
ADR to Medwatch](#) 

## New Generic Approvals\*:

- **Eplerenone** (tier 1 PAR), generic for **Inspira**® (tier 3 PAR), an aldosterone antagonist indicated for: 1) improving survival of stable patients w/ LV systolic dysfunction (LVEF ≤40%) and CHF after an AMI; 2) HTN, alone or in combination w/ other anti-HTNs. A major advantage of eplerenone over the nonselective spironolactone is lack of binding to progesterone and androgen receptors, which is associated with drug-induced gynecomastia, breast pain, and impotence. For a recent review comparing spironolactone to eplerenone please [e-mail me](#).
- **HFA inhaler transition** information is again available for your assistance.

[Eplerenone Drug Info](#)  
[Transition Now Help](#)  
[Proventil HFA](#)  
[ProAir HFA](#)  
[RxAssist.org](#)  
[InhalerTransition.org](#)

## Emerging Therapies & the Drug Pipeline:

**Atrial Fibrillation—Multaq**®, dronedarone, is a multi-channel blocker that affects Ca<sup>++</sup>, K<sup>+</sup> and Na<sup>+</sup> channels and has anti-adrenergic properties. Unlike amiodarone, dronedarone does NOT contain iodine radical and did NOT show evidence of thyroid or pulmonary toxicity in clinical trials. ATHENA trial showed significantly decreased risk of CV hospitalizations or death from any cause in patients w/ aFib.

[Multaq](#)®  
[ATHENA](#)

## Disease State Or Literature Update:

[NEJM Full Text](#) 

A Genomewide study shows at least one common variant in the SLC01B1 gene substantially alters the risk of **simvastatin-induced myopathy**.

- The incidence of myopathy (muscle pain or weakness in association with elevated creatinine kinase) has been reported as about 1 case per 10,000 patients per year with standard doses of statins. Please note that one statin has NOT been shown to be more likely than another to cause myopathy. However, this number does go up when higher statin doses are used (dose-related, NOT potency-related, ADR regardless of statin choice) and when combined with certain other interacting medications (amiodarone, etc). This is reflected in the recent FDA MedWatch warning above.
- As we push LDL numbers lower and the population being treated with statins gets both older and younger (i.e. recent AAP guidelines) we will be using higher doses of statins in greater numbers of patients. In addition achieving LDL goals in high risk patients will often exceed the ability of current generic statins or at least require the highest dosage.

In short, identifying a method to prevent myopathy (and subsequently rhabdomyolysis) due to statin use will become even more essential. Pharmacogenomic science is clearly in its infant stages, but promises to provide essential guidance in areas such as these.

- Study used approximately 300,000 markers (and additional find-mapping) in 85 subjects w/definite or incipient myopathy and 90 controls, all of whom were taking simvastatin 80mg daily as part of a trial involving 12, 000 subjects. Also, replication was tested in a trial of simvastatin 40mg daily involving 20,000 subjects.
- SLC01B1 encodes the organic anion-transporting polypeptide OATP1B1, which mediates the uptake of various drugs, including most statins and statin acids.
- More than 60% of the myopathy cases in this study could be attributed to the "C variant" genotype of this gene.

## Formulary Updates:

Changes based on availability of generic products: **Inspira**®, moved to Tier 3 PAR, generic placed on Tier 1 PAR

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