

# PHARMACY MONTHLY NEWSLETTER

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## In The News:

- **Spiriva, Atrovent for COPD and INcreased risk for death?** A meta-analysis in JAMA this month concluded that COPD patients who used inhaled anticholinergics (IACGs) for at least a month, compared to placebo or other inhaled agents, showed a significant 58% independent increase in risk of CV death, MI, or stroke. For CV death alone, risk increased 80%.
  - The number needed to treat (NNT) for harm was 40/year and CV mortality rate was 31.9 per 1000 person-years
  - To put in perspective, NNT for statin benefit in moderate risk ( $\geq 10\%$  risk) patients for 15 years of treatment is 42.
- INSPIRE study showed that **Advair** (50/500) was associated w/lower withdrawal rate, lower mortality, INcreased pneumonia, and similar lung function, health status, and rate of ADRs compared w/ **Spiriva** (tiotropium).
  - Found 52% all-cause mortality reduction in **Advair** vs. **Spiriva**, but power of study to support claim limited
- *Evidence to this point suggests at least avoiding IACGs for COPD patients with arrhythmias or history of stroke until prospective trials can clarify*
- **Keppra XR**, new once daily levetiracetam formulation approved by FDA. Regular Keppra is tier 2 PAR except neuro or physical medicine. Given that no generic Keppra yet, XR formulation is tier 3 IHA, but allows for once daily dosing convenience.
- Forest Labs receives FDA Warning Letter regarding unsubstantiated superiority and mechanism of actions claims, omits and minimizes risk associated with the use of **Bystolic**® (nebivolol), & makes unsubstantiated efficacy claims for the drug.
- **Nasacort AQ** new indication, now approved for children **2—5 yrs** as 1 spray in each nostril once daily (110mcg/day) in seasonal/perennial rhinitis
- **ProAir HFA** new indication, now approved for ages as low as **4 years and up** for treatment, prevention of RAD, and prevention of EIB<sup>§§</sup>
- FDA delays decision on **prasugrel** for second time, NO evidence of drug issue, appears FDA needs more time for complex NDA submission

[COPD meta-analysis](#)  
[COPD Medscape](#)  
[COPD INSPIRE](#)  
[COPD TORCH](#)  
[Keppra XR](#)   
[FDA on Bystolic](#)  
[ProAir HFA](#)   
[Nasacort AQ](#)  
[Prasugrel ??](#)


## Safety Updates:

[Submit ADR<sup>§</sup> to MedWatch Online!](#)



- **TNF-alpha blockers** (Cimzia, Enbrel, Humira, Remicade), FDA notifying physicians that invasive fungal infections are not consistently recognized in patients taking these medications. Delay in treatment may lead to death.
- **Tysabri**® (natalizumab), 2 more cases of PML have been documented in Europe. Both patients were treated for greater than 1 year. Significantly, this time (compared to most other reports) the patients were on MONOtherapy).
- FDA denies entry of generic drugs from Indian company, **Ranbaxy Ltd.**, from entering U.S.. FDA reports no evidence of harm to U.S. patients yet; pre-emptive action given recent charges in NOT maintaining quality mfg.

[TNF-alpha blockers](#)  
[Tysabri and PML](#)  
[FDA on Ranbaxy](#)

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

## New Generic Approvals\*:

- **Galantamine**, generic for Razadyne®, tabs taken twice daily approved for mild-to-moderate Alzheimer's dementia. Razadyne ER®, taken once daily, does NOT yet have a generic.
  - Start at 4mg bid, taken w/full meals am and pm, w/stepwise increments to 16, 24mg/day (max) after >4wks at each dose. MDD is 16mg/day. If treatment is interrupted for >1wk, lowest dose should be reinitiated & retitrated.
  - In general this drug is much less tolerable than Aricept®, and studies have NOT shown consistent superiority or inferiority between Aricept® (donepezil) or galantamine. **Tolerability, necessary titration and dosing interval remain galantamine's issues when compared with Aricept® (donepezil).**

[Galantamine](#)  
[AAN Guidelines](#)  
[Alz. Tx Algorithms](#)  
[Transition Now Help](#)  
[Proventil HFA](#)  
[ProAir HFA](#)  
[RxAssist.org](#)  
[InhalerTransition.org](#)

## Emerging Therapies & the Drug Pipeline:

**Diabetes:** **liraglutide**, a once daily GLP-1 analogue injection (like exenatide) demonstrated superiority to glimepiride 8mg/day in the LEAD-3 study. *Importantly*, this GLP-1 was tested for MONOtherapy AND as initial therapy (exenatide currently only as adjunct). A once weekly exenatide currently showing great promise (greater A1C reduction and ~half the GI ADRs). **Osteoporosis:** **denosumab** is a novel, fully human, highly specific, monoclonal antibody to receptor activator of nuclear factor-kappa-beta ligand (RANKL), a potential alternative to bisphosphonates, info available from FREEDOM trial

[Liraglutide in Lancet](#)  
[Medscape Liraglutide](#)  
[Qweek Exenatide](#)  
[FREEDOM trial](#)



## Disease State Or Literature Update:

First Phase Insulin Response (FPIR), Second Phase Insulin Response (SPIR), Type II DM and GLP-1 analogues

- FPIR = the incremental insulin response in the first 10 min after the IV glucose bolus (26% of response in 1hr)
- SPIR = the incremental insulin response 10—60 min after IV glucose

Type II DM patients lose FPIR, evident when FBG>115mg/dL (see link to right)

**Oral** glucose load stimulates greater insulin response than **IV** glucose load (i.e., the 'incretin effect')

[FPIR and SPIR](#)   
[FBG > 115](#)   
[IGT vs. Obesity](#)

- According to Muscelli et al in Diabetes 2008, Impaired Glucose tolerance (IGT) and obesity impair the incretin effect independently of one another
- According to Quddusi et al in Diabetes Care 2003, a 3-hr GLP-1 infusion restored FPIR in Type II DM patients (up to 22% of response in 1hr), where as administration of GLP-1 concurrent with glucose provided minimal increase in FPIR (up to 6% of response in 1 hr).

The idea that extended administration of GLP-1 may lead to restoration of FPIR (vs. acute GLP-1 bursts and other antidiabetic medications) seems to be supported by recent studies involving once weekly exenatide (see above). The preservation of beta-cell mass by these drugs, weight loss (vs. weight gain w/other antidiabetic drugs) and restoration of FPIR may prove to change our treatment algorithm for type II DM in the near future.

## Formulary Updates:

**Changes based on availability of generic products:** **Razadyne**® moved to Tier 3 PAR, generic placed on Tier 1 PAR  
**Aloxi**® billed under Medical benefit, NOT Pharmacy benefit  
**Stavzor**® placed on Tier 3

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

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