New Classification for Rasagiline Results in Multiple Label Changes
As the result of a recent study, Teva’s drug product, Azilect® (rasagiline), has been classified as a selective monoamine oxidase (MAO)-B inhibitor at the approved dose of 1 mg. Non-selective MAO inhibitors may have some contraindications with certain foods (tyramine containing) and drugs. These limitations are not associated with selective MAO inhibitors; therefore, they can be more broadly prescribed. Label modifications based on these study results are being developed by Teva in conjunction with the U.S. Food and Drug Administration (FDA).

Selectivity for MAO was tested by evaluating the interaction between tyramine and rasagiline in healthy subjects. This double blind placebo-controlled study was conducted in order to comply with the FDA’s requirement for full characterization of the selectivity of rasagiline. In the study, rasagiline was compared to phenelzine, a known non-selective MAO inhibitor. Rasagiline is indicated for the treatment of the signs and symptoms of idiopathic Parkinson’s disease as initial monotherapy and as adjunct therapy to levodopa.

New Safety Information: Simponi™ and Remicade®
According to a FDA update, effective November 18, 2009, Simponi™ (golimumab) and Remicade® (infliximab), TNF-alpha inhibitors, will have changes in their labeling. The label changes add new safety information regarding the risk of malignancies in pediatric patients, leukemia in adults and psoriasis-like lesions associated with TNF blockers.

Sources:
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Pulmonary Arterial Hypertension (PAH) Treatment Algorithm: 4th World Symposium on Pulmonary Hypertension (PH)
The 4th World Symposium on Pulmonary Hypertension (PH) took place in Dana Point, CA, in 2008. 1 A resulting updated pulmonary arterial hypertension (PAH) evidence-based treatment algorithm was published in 2009 in the Journal of the American College of Cardiology. The joint PH Expert Consensus Document (ECD) from the American College of Cardiology Foundation (ACCF) Task Force on ECDs and the American Heart Association (AHA) are generally in line with the 4th World Symposium recommendations. 2

Classification: 3
Previously, PH referred to idiopathic pulmonary arterial hypertension (IPAH), also formerly known as primary pulmonary hypertension (PPH), or secondary PH. In an effort to organize PH, the World Health Organization (WHO) updated the PH nomenclature. WHO classifies PH patients into five groups based on etiology. Now, only Group I refers to pulmonary arterial hypertension (PAH). The other four groups describe PH. Collectively, all five groups are now referred to as PH.

Measuring baseline severity in PH is important prior to initiation of therapy since response to therapy is measured as change from baseline. Functional and hemodynamic impairment are central in PH. The patient’s ability to function is measured by determining exercise capacity. This in turn determines the WHO functional class (FC). The WHO FC classifications are defined as: class I: no limitation of physical activity; class II: mild limitation of physical activity; class III: marked limitation of physical activity; class IV: inability to perform any physical activity.

Summary of the evidence-based PAH treatment algorithm developed at the 4th World Symposium on PH:

- Generally, the expert opinion recommends oral anticoagulation, diuretics, oxygen, and digoxin; however, data on long-term effects are lacking.
- A trial of high dose oral calcium channel blockers (CCBs) dihydropyridine type or diltiazem, is recommended in only a minority of patients with IPAH demonstrating a positive acute vasoreactive test. These patients should be followed closely to assure both safety and efficacy of this therapy. Patients with PAH due to conditions other than IPAH have a very low rate of long-term responsiveness to oral CCBs.
- Patients with a negative response to the acute vasoreactivity test, or positive responders who remain in WHO FC III-IV, are candidates for treatment with prostacyclins, endothelin receptor antagonists (ERAs), or a phosphodiesterase-5 inhibitor (PDE-5 inhibitor). Treatments for the other functional classes are:
  - WHO FC II: ambrisentan (Letairis®), bosentan (Tracleer®), and sildenafil (Revatio®) (Grade A for all); Tadalafil (Adcirca®) (Grade B). Note: At the time of the 4th World Symposium on PH, Adcirca® was investigational.
  - WHO FC III: ambrisentan, bosentan, IV epoprostenol, inhaled iloprost (Ventavis®), sildenafil (Grade A for all); tadalafil, SC treprostinil (Remodulin®) (Grade B)
  - WHO FC IV: The treatment of choice for these most critically ill patients is continuous intravenous epoprostenol (Flolan®) (Grade A). This improves exercise capacity, hemodynamics, and survival in FC IV. Epoprostenol is also the only therapy for PAH that has been shown to prolong survival. Inhaled iloprost (Grade B); SC treprostinil (Grade C)

In patients who are not responding adequately to PAH monotherapy, combination therapy with two agents having different mechanisms of action is recommended. The optimal combination on the basis of overall risk-benefit remains unknown.

- Atrial septostomy and lung transplantation are indicated for refractory patients, or where medical treatment is unavailable.

PAH is a complex disorder and drug selection is complicated. Therefore, in conclusion, the following comments should be considered:

- Nonresponders to acute vasoreactivity testing or responders who remain in WHO FC III PAH are candidates for treatment with a PDE-5 inhibitor or an ERA. The guidelines do not recommend one drug class over another. Among prostanoids, iloprost (Ventavis®) and...
treprostinil (Tyvaso®) can be administered by oral inhalation. Note: At the time of the 4th World Symposium on PH, Tyvaso® was investigational.

- Due to its demonstrated survival benefit, continuous IV epoprostenol, a synthetic prostacyclin, remains first-line for PAH FC IV. Ultimately drug selection depends on a variety of factors including functional severity, route of administration, adverse events, patient preference, physician experience, and clinical judgment.

Reference: