Indiana Medicaid Therapeutics Committee
Therapeutic Class Review Summary

Therapeutic class:
Non-sedating antihistamines

Overview:
Allergic rhinitis is a common condition found in all age groups. In patients with other respiratory conditions such as asthma, allergic rhinitis can lead to serious complications. Pharmacological options for allergic rhinitis include traditional oral antihistamines, non-sedating antihistamines, nasal corticosteroids, nasal antihistamines, and leukotriene inhibitors.

The non-sedating antihistamines selectively block the peripheral H_1 receptors; selective blockade results in decreased drowsiness and dizziness as compared to the traditional antihistamines. The FDA approved indications for non-sedating antihistamines are relief of the symptoms associated with allergic rhinitis (both seasonal and perennial) and chronic idiopathic urticaria.

There are currently four non-sedating antihistamines in the US market. The older agents, such as terfenadine and astemizole were discontinued due to severe drug interactions with erythromycin, ketoconazole and other agents that are metabolized via the cytochrome P450 enzyme system. The newer agents have less significant drug interaction profiles. All of these agents (cetirizine, desloratidine, fexofenadine, and loratadine) are also available in combination with the decongestant, pseudoephedrine. Cetirizine is a prodrug of hydroxyzine. Because the incidence of somnolence is twice that observed in placebo, but less than traditional antihistamines, cetirizine is considered a second-generation antihistamine. Cetirizine has an indication for allergic rhinitis in children under the age of two and for urticaria in children 6 months of age or older. Additionally, Zyrtec® and Zyrtec-D® will soon be available for over-the-counter (OTC) use. Levocetirizine is the levo-isomer of Zyrtec®, and is available as the brand Xyzal®. Side effects, and onset /duration of action are not significantly different, but unlike Zyrtec®, Xyzal® is contraindicated in end stage renal disease, and dosing must be adjusted based on creatinine clearance. Desloratadine is an isomer of loratadine, which binds with stronger affinity to the H_1 receptors. However, in clinical trials, its efficacy is not substantially superior to other non-sedating antihistamines. Fexofenadine is the active metabolite of terfenadine; however, fexofenadine does not cause QT prolongation when given in doses up to 800 mg/day or when administered concomitantly with ketoconazole or erythromycin. Loratadine was the first OTC non-sedating antihistamine approved. Both tablet and liquid dosage forms became available over the counter in December 2002. The price of loratadine has dropped dramatically since the regulatory status change. Loratadine and fexofenadine are available in a generic formulation.

Generic Name	Brand Name	Manufacturer	OTC
Cetirizine	Zyrtec®, Zyrtec-D®	Pfizer	No
Desloratadine	Clarinex®, Clarinex- D® 12 Hour, Clarinex-D® 24 Hour, Clarinex® RediTabs®	Schering	No
Fexofenadine	Allegra®, Allegra-D® 12 Hour, Allegra-D® 24	Aventis	No
Levocetirizine	Xyzal®	UCB Inc	No
Loratadine	Claritin®, Claritin-D® 12 Hour, Claritin-D® 12 Hour, Alavert®, Claritin® RediTabs®	Schering, Wyeth	Yes

Summary:
The efficacy and safety profiles for all non-sedating antihistamines are similar. Coverage of over-the-counter products could eliminate the cost of doctor office visits, dispensing fees and incentives for providers to prescribe more expensive legend products.