



Should Singulair[®] be First Line Therapy for Allergic Rhinitis?

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Allergic rhinitis is a common disease that affects roughly 20-30% of the American adult population and roughly 40% of children. There are two types of allergic rhinitis: seasonal allergic rhinitis and perennial allergic rhinitis. Seasonal allergic rhinitis occurs in response to allergens at certain time periods throughout the year; whereas, perennial allergic rhinitis is a chronic disease lasting the entire year.

In order for an allergic reaction to occur, sensitization must first take place. Allergens, such as pollen, dust mites, or animal dander, interact with IgE antibodies bound to nasal mast cells and basophils, forming an antigen-specific antibody. Upon subsequent exposure to the same allergen, an allergic reaction occurs leading to rapid release of immune cell mediators from the mast cell. These mediators include histamine, leukotrienes, prostaglandins, tryptase, and kinines. Histamine release leads to the rhinorrhea, itching, and sneezing, and is the primary target of therapy for allergic rhinitis. Antihistamines have long been used to treat allergic rhinitis as histamine is a major inflammatory mediator.

Recently, questions have been raised regarding the effectiveness of Singulair[®] for the treatment of allergic rhinitis. Singulair[®] (montelukast sodium) is a leukotriene receptor antagonist which inhibits the cysteinyl leukotriene receptor. Leukotriene, like histamine, is a mediator released from the mast cell during an allergic response and is thought to cause symptoms such as sneezing, itching, rhinitis, and late stage congestion.

One study by Nayak¹ examined the efficacy of loratadine, loratadine/ montelukast, montelukast, or placebo for daytime nasal symptoms (congestion, rhinorrhea, pruritus, and sneezing). Secondary endpoints examined the nighttime symptoms score, the daily composite, and the eye symptoms score. When loratadine, loratadine/ montelukast, and montelukast were compared to placebo, they showed statistically significant improvements in daytime nasal symptom scores and the secondary endpoints. The montelukast/loratadine combination, however, did not show statistically significant improvements when compared to loratadine or montelukast alone.

Another study by Chen² published in *Pediatric Allergy and Immunology*, compared the efficacy of montelukast, cetirizine, and placebo by looking at the Pediatric Rhinoconjunctivitis Quality of Life Questionnaire (PRQLQ), Total Symptom Score (TSS), serum IgE, serum eosinophil cationic protein (ECP), blood eosinophil counts, nasal airway resistance (NAR), and eosinophil percentage in nasal smears. Compared to placebo, montelukast and cetirizine were statistically significant in improving NAR, eosinophil percentage in nasal smears, PRQLQ, and TSS. The study found that cetirizine was significantly better than montelukast for TSS at week 12 and for nasal itching.

In conclusion, montelukast sodium is not superior to antihistamines, but is shown to be equally effective for the treatment of allergic rhinitis. Data is lacking which compares Singulair[®] directly to antihistamine therapy. In addition, for the treatment of allergic rhinitis, the net cost of Singulair[®] is approximately \$800 to \$1,000 greater annually than the cost of loratadine or cetirizine oral tablets or

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Low/Non-Sedating Antihistamines Require Prior Authorization

Since September of 2002, low/non-sedating antihistamines (LSAs) have required Prior Authorization (PA) for Nebraska Medicaid patients. Listed in the table below are antihistamines which do not require PA, *if* the patient receives a *generic* product of a swallow tablet or the liquid formulation. Chewable tablets and orally disintegrating tablets of the listed medications require PA.

Antihistamines Which Do Not Require Prior Authorization (generic must be dispensed)	
Example Brand Name*	Generic Name
Tavist®	clemastine
Chlor-Trimeton®	chlorpheniramine
Benadryl®	diphenhydramine
Claritin®	loratadine
Zyrtec®	cetirizine

Before other LSAs will be approved for a Nebraska Medicaid patient over 24 months of age, a minimum 30-day trial of each loratadine and cetirizine is required, or the prescriber must provide documentation that addresses why loratadine and cetirizine cannot be used by the patient.

Nebraska Medicaid also requires that patients meet Criteria 1 **AND** either Criteria 2 or Criteria 3 defined as follows: **Criteria 1:** Diagnosis for which the LSA is requested matches the FDA-approved diagnoses for the medication class. **Criteria 2:** Patient has a condition or takes a medication which contraindicates the use of a first generation antihistamine. **Criteria 3:** Patient has documented hypersensitivity to loratadine and cetirizine products or their ingredients.

Combination products of LSAs and pseudoephedrine are covered as two separate prescriptions of the single ingredient. For example, Claritin D-12 Hour® would be coverable as a loratadine 10mg tablet prescription and a pseudoephedrine 12 hour tablet prescription separately.

More information about the Low/Non-Sedating PA criteria and PA fax form can be found on First Health Services Corporation website at <https://nebraska.fhsc.com/>

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syrops. Direct comparative studies are needed to justify the use of Singulair® as first line therapy in allergic rhinitis, especially when comparing the price of Singulair® to older, equally efficacious antihistamines.

References:

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2. Chen S-T, Lu K-H, Sun H-L, Chang W-T, Lue K-H, Chou M-C. Randomized placebo-controlled trial comparing montelukast and cetirizine for treating perennial allergic rhinitis in children aged 2-6 yr. *Pediatric Allergy and Immunology*. 2006;17:49-54. © 2006 Blackwell Munksgaard.
3. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2009. URL: <http://www.clinicalpharmacology.com>. Updated November 2007.
4. May JR, Smith PH. Allergic Rhinitis. In: DiPiro JT, Talbert RL, Yee GC, Matzke GR, Wells, BG, Posey, LM. *Pharmacotherapy: A Pathophysiologic Approach*. McGraw-Hill Companies, Inc; 2005: 1729-1740.