



LEUKOTRIENE MODIFIERS
Preauthorization Criteria for Approval

Medications and Dosage Forms Included in Criteria

Table with 3 columns: Generic Name, Brand Name, Dosage Form. Rows include Montelukast sodium (Singularir), Zafirlukast (Accolate), Zileuton (Zyflo), and Zileuton (Zyflo CR).

† Excluded from program: Singularir 4 mg chewable tablet, Singularir 5 mg chewable tablet, and Singularir 4 mg oral granules
‡ Excluded from program: Accolate 10mg oral tablet
§ Limited availability – Drug discontinued by manufacturer

FDA Approved Indications

Montelukast sodium (Singularir) is indicated for:

- Prophylaxis and chronic treatment of asthma in adults and pediatric patients 12 months of age and older
• Prevention of exercise-induced bronchoconstriction in patients 15 years of age and older
• Relief of symptoms of allergic rhinitis (seasonal allergic rhinitis in adults and pediatric patients 2 years of age and older, and perennial allergic rhinitis in adults and pediatric patients 6 months of age and older)

Zafirlukast (Accolate)

Zafirlukast is indicated for the prophylaxis and chronic treatment of asthma in adults and children 5 years of age and older.

Zileuton (Zyflo, Zyflo CR)

Zileuton and zileuton extended-release is indicated for the prophylaxis and chronic treatment of asthma in adults and children 12 years of age and older.

Description

The leukotriene modifier (LM) preauthorization program is intended to optimize the utilization of cost-effective medications by promoting the use of LM medications for asthma, exercise-induced bronchoconstriction (EIB), seasonal allergic rhinitis (SAR), and perennial allergic rhinitis when determined to be medically necessary.

## Criteria

### Montelukast sodium (Singulair®)

#### *Initial and Renewal Evaluation*

1. Is the patient 15 years of age or older?  
If yes, continue to 2.  
If no, medication does not need preauthorization.
  
2. Does the patient have a diagnosis of one or more of the following:
  - a. Asthma
  - b. Exercise-induced asthma/bronchoconstriction (EIB)
  - c. Seasonal allergic rhinitis (SAR), or seasonal allergies
  - d. Perennial allergic rhinitisIf a, continue to 3.  
If b, continue to 7.  
If c or d, continue to 11.  
If none, deny.

#### *Asthma*

3. Is the patient currently taking an inhaled corticosteroid or a combination inhaled corticosteroid product?  
If yes, confirm in claims history any inhaled corticosteroid claim in the past 3 months.  
If a claim is found in claims history, approve for 12 months.  
If no, continue to 4.
  
4. Does the patient have a documented allergy, intolerance, or contraindication to corticosteroid therapy?  
If yes, approve indefinitely.  
If no, continue to 5.
  
5. Has the patient failed therapy with an inhaled corticosteroid or a combination inhaled corticosteroid product?  
If yes, confirm in claims history any inhaled corticosteroid claim in the past 3 months.  
If a claim is found in claims history, approve for 12 months.  
If no, continue to 6.
  
6. Is the patient able to use an inhaler effectively?  
If yes, deny.  
If no, approve for 12 months.

#### *Exercise-induced asthma/bronchoconstriction (EIB)*

7. Is the patient currently using an inhaled short-acting beta-agonist (SABA) for EIB?  
If yes, confirm in claims history any SABA claim in the past 3 months.  
If a claim is found in claims history, approve for 12 months.  
If no, continue to 8.
  
8. Does the patient have a documented allergy, contraindication, or intolerance to SABA therapy for EIB?  
If yes, approve indefinitely.  
If no, continue to 9.
  
9. Has the patient failed therapy with an inhaled SABA for EIB?  
If yes, confirm in claims history any SABA claim in the past 3 months.  
If a claim is found in claims history, approve for 12 months.  
If no, continue to 10.

10. Is the patient able to use an inhaler effectively?  
If yes, deny.  
If no, approve for 12 months.

*Seasonal allergic rhinitis (SAR)/Perennial allergic rhinitis*

11. Is the patient currently taking a nasal corticosteroid?  
If yes, confirm in claims history any nasal corticosteroid claim in the past 3 months.  
If a claim is found in claims history, approve for 12 months.  
If no, continue to 12.
12. Does the patient have a documented allergy, contraindication, or intolerance to nasal corticosteroids?  
If yes, approve indefinitely.  
If no, continue to 13.
13. Has the patient failed therapy with a nasal corticosteroid?  
If yes, confirm in claims history any nasal corticosteroid claim in the past 3 months.  
If a claim is found in claims history, approve for 12 months.  
If no, continue to 14.
14. Is the patient able to use a nasal spray device effectively?  
If yes, deny.  
If no, approve for 12 months.

**Zafirlukast (Accolate<sup>®</sup>), Zileuton (Zyflo<sup>®</sup>, Zyflo CR<sup>™</sup>)**

***Initial and Renewal Evaluation***

1. Is the patient 12 years of age or older?  
If yes, continue to 2.  
If no, medication does not preauthorization.
2. Does the patient have a diagnosis of one or more of the following:  
a. Asthma  
b. Exercise-induced asthma/bronchoconstriction (EIB)  
If a, continue to 3.  
If b, continue to 6.  
If none, deny.

***Asthma***

3. Is the patient currently taking an inhaled corticosteroid or a combination inhaled corticosteroid product?  
If yes, confirm in claims history any inhaled corticosteroid claim in the past 3 months.  
If a claim is found in claims history, approve for 12 months.  
If no, continue to 4.
4. Does the patient have a documented allergy, intolerance, or contraindication to corticosteroid therapy?  
If yes, approve indefinitely.  
If no, continue to 5.
5. Has the patient failed therapy with an inhaled corticosteroid or a combination inhaled corticosteroid product?  
If yes, confirm in claims history any inhaled corticosteroid claim in the past 3 months.  
If a claim is found in claims history, approve for 12 months.  
If no, continue to 6.

*Asthma (cont'd)/Exercise-induced Bronchoconstriction (EIB)*

6. Is the patient able to use an inhaler effectively?

If yes, deny.

If no, approve for 12 months.

## Rationale

### *Asthma*

Leukotriene modifier (LM) medications are FDA approved for the prophylaxis and chronic treatment of asthma (Singulair<sup>®</sup>, Accolate<sup>®</sup>, Zylflo<sup>®</sup>, Zylflo CR<sup>TM</sup>).<sup>1-4</sup> The leukotriene modifier (LM) preauthorization program is intended to optimize the utilization of cost-effective medications for asthma, exercise-induced bronchoconstriction (EIB), seasonal allergic rhinitis (SAR), and perennial allergic rhinitis. Based on available medical literature, the evidence suggests that LM medications as monotherapy are less effective than inhaled corticosteroids (ICS) or nasal corticosteroids in the treatment of asthma and allergic rhinitis, respectively.<sup>5-12</sup> Short-acting beta-agonists (SABAs) are the treatment of choice for the prevention of EIB according to current clinical guidelines.<sup>5-7</sup> Therefore, the LM preauthorization program utilizes a protocol where patients must utilize ICS, short-acting beta-agonists (SABAs), and nasal corticosteroids prior to or along with LMs in patients with asthma, EIB, and seasonal or perennial allergic rhinitis, respectively.

The “gold standard” of asthma prevention, inhaled corticosteroids (ICS), are available only in the form of inhalers. This has created interest in the LM medication class as these are comprised of orally administered tablets. Since the introduction of the LM medications in the mid-1990’s newer trials have been conducted to compare the class to first-line therapy, inhaled corticosteroids. A Cochrane review analyzed 18 trials comparing LMs to ICS and their use for preventing asthma exacerbations.<sup>8</sup> The trials were reviewed for a primary outcome of the number of asthma exacerbations requiring systemic corticosteroids.<sup>8</sup> Secondary outcomes consisted of severity of asthma exacerbations, chronic asthma control, adverse effects, and withdrawal rates.<sup>8</sup> The primary outcome revealed a 65% increase in asthma exacerbations requiring systemic steroids in patients taking LMs [Relative risk (RR), 1.65; 95% Confidence Interval (CI): 1.36-2.00]; number of patients needed to treat with ICS instead of LMs to prevent one exacerbation = 26 (95% CI: 17-47)].<sup>8</sup> The authors concluded, “In symptomatic adult asthmatics with mild to moderate asthma, anti-leukotrienes [leukotriene modifiers] are less effective than inhaled corticosteroids in maintaining asthma control.”<sup>8</sup> The results presented in this review are consistent with results from a meta-analysis that examined the difference between LMs and ICS to reduce exacerbations in the adult population (RR, 1.72; 95% CI: 1.28-2.31).<sup>9</sup>

A second Cochrane review examined the use of adding LMs to current ICS therapy versus increasing the ICS dose in patients with symptomatic asthma.<sup>13</sup> The outcomes measured were the reduction in frequency and severity of asthma exacerbations and the magnitude of ICS dose reduction with the addition of LM medications.<sup>13</sup> According to the review, adding a LM medication at approved doses to current ICS therapy provides no benefit at reducing exacerbations requiring systemic corticosteroids than the same dose of ICS as monotherapy (RR, 0.64; 95% CI: 0.38-1.07).<sup>13</sup> Adding an LM medication at approved doses to current ICS dosing versus doubling the ICS dose as monotherapy provided no benefit over doubling the ICS dose in preventing exacerbations (RR, 0.92; 95% CI: 0.56-1.51).<sup>13</sup> The authors concluded that “the addition of licensed [approved] doses of montelukast to inhaled glucocorticoids may improve lung function, symptoms, and use of relief beta2-agonists by a modest amount” and “use of licensed [approved] doses of leukotriene receptor antagonists are associated with improvement similar to that of dose doubling of inhaled glucocorticoids but there is insufficient power to conclude to equivalency.”<sup>13</sup>

There is evidence for patients with uncontrolled or symptomatic asthma on low- to medium-dose ICS therapy for adding long-acting beta-2 agonists (LABA).<sup>5,6,12,15,16</sup> Head-to-head comparative trials comparing the efficacy of different therapies, ICS plus LM versus ICS plus LABA, have found the ICS/LABA combination to be more effective.<sup>17,18</sup> A Cochrane review evaluated these different therapy options from 11 clinical trials and concluded “asthmatic adults inadequately controlled on low doses of inhaled steroids, the addition of LABA is superior to LTRA [leukotriene modifiers] for preventing

exacerbations requiring systemic steroids, and for improving lung function, symptoms, and the use of rescue  $\beta_2$ -agonists.<sup>19</sup> These results are consistent with a recent trial<sup>20</sup> and current asthma guidelines recommend LABA as adjunct therapy to ICS versus LM/ICS therapy.<sup>5-7</sup>

The National Asthma Education and Prevention Program (NAEPP) *Expert Panel Report 3 (EPR-3): Guidelines for the Diagnosis and Management of Asthma-Full Report 2007* reaffirms from the previous guidelines (EPR-2)<sup>21</sup> that “inhaled corticosteroids are the most effective long-term control medication across all age groups.”<sup>5</sup> The panel also recommends “that when patients  $\geq 12$  years of age require more than low-dose ICS alone to control asthma (i.e., step 3 care or higher), a therapeutic option is to add LABA to ICS. Alternative, but not preferred adjunctive therapies include LTRA, theophylline, or, in adults, zileuton.”<sup>5</sup> The Global Initiative for Asthma (GINA) guidelines from the *Global Strategy for Asthma Management and Prevention-Updated 2007* echo the recommendations from the NAEPP’s EPR-3 on ICS use as first-line therapy, “inhaled glucocorticosteroids are currently the most effective anti-inflammatory medications for the treatment of persistent asthma.”<sup>6</sup> As monotherapy and as adjunct therapy, the GINA guidelines state, “when used alone as controller, the effect of leukotriene modifiers are generally less than that of low doses of inhaled glucocorticosteroids, and, in patients already on inhaled glucocorticosteroids, leukotriene modifiers cannot substitute for this treatment without risking the loss of asthma control”, and “...leukotriene modifiers are less effective than long-acting inhaled  $\beta_2$ -agonists as add-on therapy.”<sup>6</sup>

#### *Exercise-Induced Bronchoconstriction (EIB)*

Montelukast sodium (Singulair<sup>®</sup>) is FDA approved for prevention of exercised-induced bronchoconstriction (EIB) in patients 15 years of age and older.<sup>1</sup> EIB is classified as respiratory difficulty often triggered by aerobic exercise and occurs during or shortly after the aerobic activity. EIB symptoms encompass the majority of symptoms characteristic of asthma; shortness of breath, wheezing, cough, chest tightness. The prevalence of EIB is 12-15% of the US population and generally occurs more frequently in cool, dry climates and environments with poor air quality. In asthmatics that have symptoms due to EIB may be an indication of poorly controlled asthma and the appropriate use of long-term controller medications can help prevent EIB.<sup>5,6</sup>

The NAEPP guidelines recommend that “SABAs are the drug of choice...for preventing EIB” and this is consistent with the GINA guidelines.<sup>5,6</sup> SABA should be administered shortly (5-15 minutes) prior to physical activity. In cases where LABAs are prescribed for EIB prevention, they should be dosed 15-30 minutes prior to physical activity with duration of up to 12 hours. Patients using LABAs for EIB prevention are advised not to use frequently and chronically as LABA duration may shorten with such use.<sup>5,6</sup> Frequent and chronic use of LABAs for prevention of EIB is also discouraged as it may disguise poorly controlled persistent asthma.<sup>5</sup> Montelukast sodium, with a slower onset of action, can attenuate EIB for some patients, and can potentially be used in patients that are involved in prolonged physical activities or in patients where beta-agonists are not offering needed control.<sup>5,6</sup> Due to the prolonged onset of action of montelukast sodium, administration should be at least 2 hours prior to physical activity.<sup>1</sup>

#### *Seasonal and Perennial Allergic Rhinitis*

Montelukast sodium (Singulair<sup>®</sup>) is FDA approved for the relief of symptoms of seasonal and perennial allergic rhinitis (seasonal allergic rhinitis in adults and pediatric patients 2 years of age and older, and perennial allergic rhinitis in adults and pediatric patients 6 months of age and older (Singulair<sup>®</sup>)).<sup>1</sup> Trials that evaluated the effect of montelukast sodium versus placebo in allergic rhinitis have provided mixed results.<sup>22-24</sup> Evidence shows montelukast sodium is more effective than placebo<sup>22,23</sup>, however, this was not evident in a separate trial.<sup>24</sup> Also, evidence is lacking showing montelukast sodium is more effective than non-sedating antihistamines (NSA) when added to NSA therapy.<sup>22</sup> Other trials have revealed that montelukast sodium is no more effective than NSA<sup>22,23</sup>, and less effective than intranasal corticosteroids.<sup>10,25</sup> Nasal corticosteroids are considered first-line agents for the treatment allergic rhinitis and is considered the most cost-effective treatment available.<sup>12,26-28</sup> A systematic review of the role of LM therapy in seasonal allergic rhinitis concluded that LMs were more effective than placebo and similar to NSA, and combination LM/NSA was more effective than NSA alone, however, all studied therapies were inferior to intranasal corticosteroids.<sup>29</sup>

### *Other Conditions*

Guidelines outlining treatment of chronic obstructive pulmonary disease (COPD) provide no support for the use of LMs.<sup>30-32</sup> COPD treatment includes short- and long-acting bronchodilators (beta-agonists and anticholinergics), inhaled corticosteroids, and theophylline.<sup>30-32</sup>

### **Automatic Claims History Edit**

Children and certain dosage forms are excluded from the PA criteria because, even though corticosteroids are the preferred first-line therapy and benefits outweigh the risks,<sup>ERP, 8</sup> evidence evaluating safety of inhaled and intranasal corticosteroids in children remains unclear.<sup>5,19,20,22,26,33-42</sup>

Pediatric age edits that will automatically approve LM therapy included in the criteria are less than 12 years of age for Accolate<sup>®</sup>, Zflo<sup>®</sup>, and Zflo CR<sup>™</sup>, and less than 15 years of age for Singulair<sup>®</sup>. Also included in the pediatric edit are dosage forms approved for pediatric use. The products included are Singulair<sup>®</sup> 4 mg chewable tablet, Singulair<sup>®</sup> 5 mg chewable tablet, Singulair<sup>®</sup> oral granules, and Accolate<sup>®</sup> 10 mg tablet.

Patients that are 12 years of age and older requesting Accolate<sup>®</sup>, Zflo<sup>®</sup>, and Zflo CR<sup>™</sup>, and patients 15 years of age and older requesting Singulair<sup>®</sup> must meet the claims edit for the claim to adjudicate without a PA. These age limits are set based on dosage and administration guidelines provided by the manufacturer of each product and state the following for patients 12 years of age and older: Accolate 20 mg twice daily<sup>2</sup>, Zflo 600 mg four times daily<sup>3</sup>, Zflo CR 1200mg twice daily.<sup>4</sup> The recommended Singulair dosage for patients 15 years of age and older is 10 mg once daily.<sup>1</sup>

The automatic claims history edit also identifies patients that are using LM medications as adjunct therapy. The edit is applied to patients 15 years of age and older requesting Singulair 10 mg tablets and patients 12 years of age and older requesting Accolate 20 mg tablets, Zflo 600 mg tablets, or Zflo CR 1200 mg tablets. The edit will examine the prescription claims history for an inhaled or intranasal corticosteroid or combination inhaled corticosteroid/LABA claim in the previous 60 days to capture current therapy. The claims system is designed to look-back 60 days prior to the LM prescription claim for certain medications outlined above. The electronic edit will identify claims in these classes that have a day supply that overlaps with 60 day look-back period. Due to differences in package sizes and variability of individual dosing an inhaler may last longer than 30 days, therefore, a 60 day look-back period is utilized. Patients older than the respective medication age edits that do not meet the automatic edits just described will receive a rejection message stating that preauthorization is necessary. These patients will then have to meet the Criteria documented previously upon requests submitted by the patients practitioner for evaluation.

### **Explanation of PA Criteria**

The purpose of the PA criteria is to allow children and adult patients who are starting or currently on LM therapy are concomitantly utilizing inhaled or intranasal corticosteroids, SABA therapy for prevention of EIB, or have a documented and explicit contraindication for use of inhaled or intranasal corticosteroids, or SABA therapy for EIB.

SABA is the preferred treatment for EIB and Singulair is the only approved LM with an indication to help prevent EIB.<sup>5,6</sup> A single dose of Singulair should be administered at least 2 hours prior to exercise and patients should not take another dose for EIB if they are currently taking Singulair for another indication (including chronic asthma).<sup>1</sup> All patients should have a SABA available as rescue therapy.<sup>1</sup> Accolate, Zflo, and Zflo CR are not indicated for the prevention of EIB and these medications will not be approved as monotherapy for prevention of EIB unless the patient is unable to use an inhaler.

Montelukast sodium is indicated for the relief of symptoms associated with seasonal and perennial allergic rhinitis, however, nasal corticosteroids have been proven to be the most effective treatment.<sup>12,26-28</sup> LM therapy has also not been proven to be superior to non-sedating antihistamines for treatment of allergic rhinitis.<sup>10,22-28</sup>

In patients utilizing LM therapy for asthma, or seasonal or perennial allergic rhinitis, with a documented allergy, intolerance, or contraindication to inhaled or intranasal corticosteroids will be approved

indefinitely. Similarly, patients with a documented allergy, intolerance, or contraindication to SABA therapy for EIB will be approved indefinitely. The indefinite approval in these patients is applied due to conditions where chronic, long-term use is required without changes in the reasoning for approval. Indefinite preauthorizations are subject to review based on new information, changes in criteria, or identified safety concerns. All other diagnoses and conditions applied in the PA Criteria will be approved for 12 months to allow for annual evaluation of therapy.

## References

1. Singulair<sup>®</sup> (montelukast sodium) [package insert]. Whitehouse Station, NJ: Merck & Co., Inc., March 2008.
2. Accolate<sup>®</sup> (zafirlukast) [package insert]. Wilmington, DE: AstraZeneca LP, July 2004.
3. Zyflo<sup>®</sup> (zileuton) [package insert]. Lexington, MA: Critical Therapeutics, Inc., November 2005.
4. Zyflo CR<sup>™</sup> (zileuton) [package insert]. Lexington, MA: Critical Therapeutics, Inc., May 2007.
5. Expert panel report: guidelines for the diagnosis and management of asthma (EPR-3 2007). NIH Publication No. 08-4051. Bethesda, MD: U.S. Department of Health and Human Services; National Institutes of Health; National Heart, Lung, and Blood Institute; National Asthma Education and Prevention Program, 2007.
6. Global Initiatives for Asthma: Global Strategy for Asthma Management and Prevention 2007. Updated December 2007. Available at: <http://www.ginasthma.com>.
7. British Thoracic Society Scottish Intercollegiate Guidelines Network. British guideline on the management of asthma. *Thorax* 2008;63:1-121.
8. Ducharme FM, Di Salvo F. Anti-leukotriene agents compared to inhaled corticosteroids in the management of recurrent and/or chronic asthma in adults and children. *Cochrane Database of Systematic Reviews* 2004, Issue 1. Art. No.: CD002314. DOI:10.1002/14651858.CD002314.pub2.
9. Sin DD, Man J, Sharpe H, et al. Pharmacological management to reduce exacerbations in adults with asthma: a systematic review and meta-analysis. *JAMA* 2004;292(3):367-76.
10. Pullerits T et al. Comparison of a nasal glucocorticoid, antileukotriene, and a combination of antileukotriene and antihistamine in the treatment of seasonal allergic rhinitis. *J Allergy Clin Immunol* 2002;109(6):949-55.
11. Aronson N, Lefevre F, Piper M et al. *Management of Chronic Asthma*. Evidence Report/Technology Assessment Number 44. (Prepared by Blue Cross and Blue Shield Association Technology Evaluation Center under Contract No. 290-97-0015.) AHRQ Publication No. 01-E044. Rockville, MD: Agency for Healthcare Research and Quality. September 2001.
12. Weiner JM, Abramson JM, Puy RM. Intranasal corticosteroids versus oral H1 receptor antagonists in allergic rhinitis: systematic review of randomised controlled trials. *BMJ* 1998;317:1624-9.
13. Ducharme F, Schwartz Z, Kakuma R. Addition of anti-leukotriene agents to inhaled corticosteroids for chronic asthma. *Cochrane Database of Systematic Reviews* 2004, Issue 1. Art. No.: CD003133. DOI: 10.1002/14651858.CD003133.pub2.
14. O'Byrne PM, Barnes PJ, Rodriguez-Roisin R, et al. Low dose inhaled budesonide and formoterol in mild persistent asthma: The OPTIMA randomized trial. *Am J Respir Crit Care Med* 2001;164:1392-7.
15. Shrewsbury S, Pyke S, Britton M. Meta-analysis of increased dose of inhaled steroids or addition of salmeterol in symptomatic asthma. *BMJ* 2000;320:1368-73.
16. Pauwels RA, Lofdahl CG, Postma DS, et al. Effect of inhaled formoterol and budesonide on exacerbations of asthma. *New Engl J Med* 1997;337(20):1405-11.
17. Fish JE, Israel E, Murray JJ, et al. Salmeterol powder provides significantly better benefit than montelukast in asthmatic patients receiving concomitant inhaled corticosteroid therapy. *Chest* 2001;120(2):423-30.
18. Nelson HS, Busse WW, Kerwin E, et al. Fluticasone propionate/salmeterol combination provides more effective asthma control than low-dose inhaled corticosteroid plus montelukast. *J Allergy Clin Immunol* 2000;106(6):1088-95.

19. Ducharme FM, Lasserson TJ, Cates CJ. Long-acting beta2-agonists versus anti-leukotrienes as add-on therapy to inhaled corticosteroids for chronic asthma. *Cochrane Database of Systematic Reviews* 2006, Issue 4. Art. No.: CD003137. DOI: 10.1002/14651858.CD003137.pub3.
20. Sorkness CA, Lemanske RF, Mauger DT, et al. Long-term comparison of 3 controller regimens for mild-moderate persistent childhood asthma: The Pediatric Asthma Controller Trial. *J Allergy Clin Immunol* 2007;119(1):64-72.
21. National Asthma Education and Prevention Program. Expert Panel Report: Guidelines for the Diagnosis and Management of Asthma. Update on Selected Topics—2002. *J Allergy Clin Immunol* 2002;110(5 Suppl):S141-219.
22. Nayak AS, Philip G, Lu S, et al. Efficacy and tolerability of montelukast alone or in combination with loratadine in seasonal allergic rhinitis: a multicenter, randomized, double-blind, placebo-controlled trial performed in the fall. *Ann Allergy Asthma Immunol* 2002;88:592-600.
23. Philip G, Malmstrom K, Hampel, Jr FC, et al. Montelukast for treating seasonal allergic rhinitis: a randomized, double-blind, placebo-controlled trial performed in the spring. *Clin Exp Allergy* 2002;32:1020-8.
24. Meltzer EO, Malmstrom K, Lu S, et al. Concomitant montelukast and loratadine as treatment for seasonal allergic rhinitis: A randomized, placebo-controlled clinical trial. *J Allergy Clin Immunol* 2000 May;105(5):917-22.
25. Wilson AM, O'Bryan PM, Parameswaran K. Leukotriene receptor antagonists for allergic rhinitis: a systematic review and meta-analysis. *Am J Med* 2004;116(5):338-45.
26. Dykewicz MS, Fineman S, Skoner DP, et al. Diagnosis and management of rhinitis: complete guidelines of the Joint Task Force on Practice Parameters in Allergy, Asthma and Immunology. *Ann Allergy Asthma Immunol* 1998;81(5 Pt 2):478-518.
27. Van Cauwenberge P, Bachert C, Passalacqua G, et al. Consensus statement on the treatment of allergic rhinitis. *Allergy* 2000;55:116-34
28. Long A, McFadden C, DeVine D, et al. Management of Allergic and Nonallergic Rhinitis (Evidence Report/Technology Assessment No. 54 (Prepared by New England Medical Center Evidence-based Practice Center under Contract No. 290-97-0019). AHRQ Pub. No. 02-E024. Rockville, MD: Agency for Healthcare Research and Quality. May 2002.
29. Rodrigo GJ, Yanez A. The role of antileukotriene therapy in seasonal allergic rhinitis: a systematic review of randomized trials. *Ann Allergy Asthma Immunol* 2006;96:779-86.
30. American Thoracic Society/European Respiratory Society Task Force. Standards for the Diagnosis and Management of Patients with COPD [Internet]. Version 1.2. New York: American Thoracic Society; 2004 [updated 2005 September 8]. Available from: <http://www.thoracic.org/go/copd>. Accessed June 2008.
31. National Institutes of Health, National Heart, Lung, and Blood Institute. Global Initiative for Chronic Obstructive Lung Disease. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease. Updated. 2005. Available at: <http://www.goldcopd.com>. Accessed June 2008.
32. National Institute for Clinical Excellence. COPD: Management of chronic obstructive pulmonary disease in adults in primary and secondary care. Clinical Guideline 12. Developed by the National Collaborating Centre for Chronic Conditions. February 2004. Available at: [http://www.nice.org.uk/nicemedia/pdf/CG012\\_niceguideline.pdf](http://www.nice.org.uk/nicemedia/pdf/CG012_niceguideline.pdf). Accessed June 2008.
33. Baena-Cagnani CE. Safety and tolerability of treatments for allergic rhinitis in children. *Drug Safety* 2004;27:883-98.
34. Daley-Yates PT, Richards DH. Relationship between systemic corticosteroid exposure and growth velocity: Development and validation of a pharmacokinetic/pharmacodynamic model. *Clin Ther* 2004;26:1905-19.
35. Doull IF. The effect of asthma and its treatment on growth. *Arch Dis Child* 2004;89:60-3.
36. Wolthers OD et al. Inhaled corticosteroids, growth, and compliance. *N Engl J Med* 2002;347(15):1210-1.
37. Kelly HW. Potential adverse effects of the inhaled corticosteroids. *J Allergy Clin Immunol* 2003;112:469-78.
38. Randell TL, Donaghue KC, Ambler GR, et al. Safety of the newer inhaled corticosteroids in childhood asthma. *Pediatr Drugs* 2003;5(7):481-504.

39. Pedersen S. Assessing the effect of intranasal steroids on growth. *J Allergy Clin Immunol* 2001;108:S40-4.
40. The Childhood Asthma Management Program Research Group. Long-term effects of budesonide or nedocromil in children with asthma. *N Engl J Med* 2000;343(15):1054-63.
41. Wolthers OD. Impact of inhaled and intranasal corticosteroids on the growth of children. *BioDrugs* 2000;13(5):347-57.
42. Lipworth BJ. Systemic adverse effects of inhaled corticosteroid therapy: a systematic review and meta-analysis. *Arch Intern Med* 1999;159:941-55.

## Billing/Coding

CODES	NUMBER	DESCRIPTION
GPI	4450*****	Leukotriene Modulators
Type of Service	Prescription Drug	
Place of Service	Outpatient	

## Update Information

Date	Action	Reason
07/01/08	Replace PA criteria	New PA criteria

## Preauthorization Criteria History

06/26/08	Reviewed by QMC
07/01/08	Preauthorization criteria original effective date
June 2009	Next Review