BlueCross BlueShield of Arizona
An Independent Licensee of the Blue Cross and Blue Shield Association

PHARMACY COVERAGE GUIDELINES	**ORIGINAL EFFECTIVE DATE: 1/18/18**
SECTION: DRUGS	**LAST REVIEW DATE: 5/17/18**
	LAST CRITERIA REVISION DATE: 5/17/18
	ARCHIVE DATE:

ZYFLO® (zileuton) tablet
ZYFLO CR® (zileuton) extended-release tablet
Zileuton ER extended-release tablet

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Pharmacy Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.

This Pharmacy Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide BCBSAZ complete medical rationale when requesting any exceptions to these guidelines.

The section identified as "Description" defines or describes a service, procedure, medical device or drug and is in no way intended as a statement of medical necessity and/or coverage.

The section identified as "Criteria" defines criteria to determine whether a service, procedure, medical device or drug is considered medically necessary or experimental or investigational.

State or federal mandates, e.g., FEP program, may dictate that any drug, device or biological product approved by the U.S. Food and Drug Administration (FDA) may not be considered experimental or investigational and thus the drug, device or biological product may be assessed only on the basis of medical necessity.

Pharmacy Coverage Guidelines are subject to change as new information becomes available.

For purposes of this Pharmacy Coverage Guideline, the terms "experimental" and "investigational" are considered to be interchangeable.

This Pharmacy Coverage Guideline does not apply to FEP or other states' Blues Plans.

Information about medications that require precertification is available at www.azblue.com/pharmacy.

Some large (100+) benefit plan groups may customize certain benefits, including adding or deleting precertification requirements.

All applicable benefit plan provisions apply, e.g., waiting periods, limitations, exclusions, waivers and benefit maximums.

Precertification for medication(s) or product(s) indicated in this guideline requires completion of the request form in its entirety with the chart notes as documentation. All requested data must be provided. Once completed the form must be signed by the prescribing provider and faxed back to BCBSAZ Pharmacy Management at (602) 864-3126 or emailed to Pharmacyprecert@azblue.com. **Incomplete forms or forms without the chart notes will be returned.**

ZYFLO® (zileuton) tablet
ZYFLO CR® (zileuton) extended-release tablet
Zileuton ER extended-release tablet (cont.)

Criteria:

- **Criteria for initial therapy:** Zyflo, Zyflo CR, or Zileuton ER is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

  1. Individual is 12 years of age or older

  2. A confirmed diagnosis of asthma

  3. Individual has failure, contraindication or intolerance to a combination inhaled corticosteroid / long-acting beta-2 agonist product (e.g. Symbicort, Advair) for at least 3 months

  4. Individual has failure, contraindication or intolerance to Montelukast **AND** Zafirlukast

  5. There are **NO** contraindications.
     - Contraindications include:
       - Active liver disease or persistent hepatic function enzyme elevations ≥3x ULN
       - History of allergic reaction to zileuton or any of the ingredients of Zyflo CR or Zileuton ER

  Initial approval duration: 12 months

- **Criteria for continuation of coverage (renewal request):** Zyflo, Zyflo CR, or Zileuton ER is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

  1. Individual's condition has not worsened while on therapy
     - Worsening is defined as:
       - Frequent asthma exacerbation
       - Worsening of symptoms: shortness of breath, cough, wheezing, chest tightness
       - Use of recue inhaler more than once or twice a week

  2. Individual has been adherent with the medication

  3. Individual has not developed any contraindications or other significant level 4 adverse drug effects that may exclude continued use
     - Contraindications as listed in the criteria for initial therapy section
     - Significant adverse effect such as:
       - Liver dysfunction

  4. There are no significant interacting drugs

  Renewal duration: 12 months

ZYFLO® (zileuton) tablet
ZYFLO CR® (zileuton) extended-release tablet
Zileuton ER extended-release tablet (cont.)

Description:

Zyflo CR (zileuton extended release) and generic zileuton extended release are indicated for the prophylaxis and chronic treatment of asthma in adults and children 12 years of age and older. They are not indicated for use in the reversal of bronchospasm in an acute asthma attack.

Zileuton, is a leukotriene synthesis inhibitor. Other leukotriene inhibitors include to montelukast and zafirlukast. Leukotrienes augment neutrophil and eosinophil migration, neutrophil and monocyte aggregation, leukocyte adhesion, increased capillary permeability, and smooth muscle contraction (which contribute to inflammation, edema, mucous secretion, and bronchoconstriction in the airway of the asthmatic.)

Background:

- The goals of asthma treatment are to reduce impairment from symptoms, minimize risk of the various adverse outcomes associated with asthma (hospitalizations, loss of lung function), and minimize adverse effects from asthma medications

- Since asthma is a chronic inflammatory disorder of the airways with recurrent exacerbations, therapy for persistent asthma emphasizes efforts to suppress inflammation over the long term and prevent exacerbations

- Pharmacologic therapy varies according to asthma severity and asthma control. Asthma control is based on the current level of symptoms, FEV_1 or PEFR values, and number of exacerbations requiring oral glucocorticoids per year

- A stepwise approach to therapy is used, in which the dose of medication, the number of medications, and/or the frequency of administration are increased as necessary and decreased when possible is used to achieve control using the least number of medications

- Use of an inhaled corticosteroids (ICS) is the most effective anti-inflammatory medication for the treatment of persistent asthma
    - Most of the benefit from ICS is achieved at relatively low doses, although some patients will require higher doses to achieve a therapeutic benefit

- Addition to ICS with a long-acting beta-agonist (LABA) may achieve good asthma control without the need to increase the dose of ICS and is preferred over increasing ICS doses, especially when medium doses of ICS are used

- Leukotriene modifiers added to ICS may help reduce the dose of ICS in patients with moderate to severe asthma, but they are less effective than LABA add on therapy
    - When used alone, leukotriene modifiers are less effective than low dosages of ICS
    - They are, however, an alternative therapy option in patients with mild persistent asthma, especially those who have aspirin-sensitive asthma and ICS adherence difficulties, and who experience significant adverse effects with ICS

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- Zileuton can be used as add-on therapy to ICS for moderate-to-severe asthma, but LABAs are the preferred adjunctive therapy

Resources:

Zyflo product information accessed 04-29-18 at DailyMed: https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=aee65202-fddb-497f-9f11-17cc727cb157

Zyflo CR product information accessed 04-29-18 at DailyMed: https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=9bc08d7b-13da-444f-ac8a-3714a05176cc

Zileuton ER product information accessed 04-29-18 at DailyMed: https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=fd382540-b390-4e86-a94a-988ea89c93a8

Zyflo. Package Insert. Revised by manufacturer 05/2017. Accessed 04-11-18.

Zyflo CR. Package Insert. Revised by manufacturer 01/2017. Accessed 01-07-18.

Zileuton ER. Package Insert. Revised by manufacturer 03/2017. Accessed 01-07-18.

2017 Global Initiative for Asthma: Global Strategy for Asthma Management and Prevention. www.ginasthma.org

UpToDate: An overview of asthma management. Current through Dec 2017. https://www-uptodate-com.mwu.idm.oclc.org/contents/an-overview-of-asthma-management?search=asthma&source=search_result&selectedTitle=1~150&usage_type=default&display_rank=1#H31

UpToDate: Asthma in children younger than 12 years: Treatment of persistent asthma with controller medications. Current through Dec 2017. https://www-uptodate-com.mwu.idm.oclc.org/contents/asthma-in-children-younger-than-12-years-treatment-of-persistent-asthma-with-controller-medications?search=asthma&source=search_result&selectedTitle=7~150&usage_type=default&display_rank=8

UpToDate: Treatment of moderate persistent asthma in adolescents and adults. Current through Dec 2017. https://www-uptodate-com.mwu.idm.oclc.org/contents/treatment-of-moderate-persistent-asthma-in-adolescents-and-adults?search=asthma&source=search_result&selectedTitle=17~150&usage_type=default&display_rank=18#H24

UpToDate: Treatment of severe asthma in adolescents and adults. Current through Dec 2017. https://www-uptodate-com.mwu.idm.oclc.org/contents/treatment-of-severe-asthma-in-adolescents-and-adults?search=asthma&source=search_result&selectedTitle=16~150&usage_type=default&display_rank=17

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Fax completed prior authorization request form to 602-864-3126 or email to pharmacyprecert@azblue.com.
Call 866-325-1794 to check the status of a request.
All requested data must be provided. **Incomplete forms or forms without the chart notes will be returned.**
Pharmacy Coverage Guidelines are available at www.azblue.com/pharmacy.

Pharmacy Prior Authorization Request Form

Do not copy for future use. Forms are updated frequently.
REQUIRED: Office notes, labs, and medical testing relevant to the request that show medical justification are required.

Member Information

Member Name (first & last):	Date of Birth:	Gender:	BCBSAZ ID#:
Address:	City:	State:	Zip Code:

Prescribing Provider Information

Provider Name (first & last):	Specialty:	NPI#:	DEA#:
Office Address:	City:	State:	Zip Code:
Office Contact:	Office Phone:	Office Fax:	

Dispensing Pharmacy Information

Pharmacy Name:	Pharmacy Phone:	Pharmacy Fax:

Requested Medication Information

Medication Name:	Strength:	Dosage Form:
Directions for Use:	Quantity: / Refills:	Duration of Therapy/Use:

☐ Check if requesting **brand** only ☐ Check if requesting **generic**

☐ Check if requesting continuation of therapy (prior authorization approved by BCBSAZ expired)

Turn-Around Time For Review

☐ Standard ☐ Urgent. Sign here: _____ ☐ Exigent (requires prescriber to include a written statement)

Clinical Information

1. **What is the diagnosis? Please specify below.**

   ICD-10 Code: _____ **Diagnosis Description:** _____

2. ☐ Yes ☐ No **Was this medication started on a recent hospital discharge or emergency room visit?**

3. ☐ Yes ☐ No **There is absence of ALL contraindications.**

4. **What medication(s) has the individual tried and failed for this diagnosis? Please specify below.**
Important note: Samples provided by the provider are not accepted as continuation of therapy or as an adequate trial and failure.

Medication Name, Strength, Frequency	Dates started and stopped or Approximate Duration	Describe response, reason for failure, or allergy

5. **Are there any supporting labs or test results? Please specify below.**

Date	Test	Value

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6. Is there any additional information the prescribing provider feels is important to this review? Please specify below.
For example, explain the negative impact on medical condition, safety issue, reason formulary agent is not suitable to a specific medical condition, expected adverse clinical outcome from use of formulary agent, or reason different dosage form or dose is needed.

Signature affirms that information given on this form is true and accurate and reflects office notes

Prescribing Provider's Signature: Date:

Please note: Some medications may require completion of a drug-specific request form.

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Office notes, labs, and medical testing relevant to the request that show medical justification are required.