LOUISIANA BLUE

Zileuton Products (Zyflo®/zileuton ER)

Policy # 00529
Original Effective Date: 01/01/2017
Current Effective Date: 10/01/2025

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc.(collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

When Services May Be Eligible for Coverage

Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Based on review of available data, the Company may consider brand/generic zileuton products (Zyflo®‡/zileuton ER) to be **eligible for coverage**** when the patient selection criterion is met.

Patient Selection Criterion

Coverage eligibility for brand/generic zileuton products (Zyflo/zileuton ER) will be considered when the following criterion is met:

- Patient has tried and failed (e.g., intolerance or inadequate response) BOTH generic montelukast and generic zafirlukast, unless there is clinical evidence or patient history that suggests BOTH generic montelukast and generic zafirlukast will be ineffective or cause an adverse reaction to the patient.

When Services Are Considered Not Medically Necessary

Based on review of available data, the Company considers the use of brand/generic zileuton products (Zyflo/zileuton ER) WITHOUT evidence that the patient has tried and failed BOTH generic montelukast and generic zafirlukast to be **not medically necessary.****

Background/Overview

Zyflo and zileuton ER are both leukotriene synthesis inhibitors that are approved for the prophylaxis and chronic treatment of asthma in adults and children 12 years of age and older. There are various alternative generic options (with a similar mechanism of action) including montelukast and zafirlukast that are a much more economical option. These generic options either include more indications or a more broad age range than Zyflo or zileuton ER offer.

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FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)

Zyflo was approved in 1996 and Zyflo CR was approved in 2007. Both carry the same indication, which is for the prophylaxis and chronic treatment of asthma in adults and children 12 years of age and older. Zyflo CR is no longer marketed, however the generic equivalent, zileuton ER, is still available. The generic products, montelukast and zafirlukast, collectively include expanded indications as well as broader age ranges.

Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. Food and Drug Administration approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, technology evaluation centers, reference to federal regulations, other plan medical policies, and accredited national guidelines.

The patient selection criterion presented in this policy takes into consideration clinical evidence or patient history that suggests BOTH generic montelukast and generic zafirlukast will be ineffective or cause an adverse reaction to the patient. Based on a review of the data, in the absence of the above mentioned caveat, there is no advantage of using brand/generic zileuton products (Zyflo/zileuton ER) over BOTH generic montelukast and generic zafirlukast.

References

1. Zylfo [package insert]. Chiesi. Cary, North Carolina. Updated March 2014.
2. Zileuton extended release [package insert]. Various Manufacturers.

Policy History

Original Effective Date: 01/01/2017
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09/08/2016	Medical Policy Committee review
09/21/2016	Medical Policy Implementation Committee approval. New policy.
09/07/2017	Medical Policy Committee review
09/20/2017	Medical Policy Implementation Committee approval. New generic available added to the policy and clarified generics that need to be tried and failed.
09/06/2018	Medical Policy Committee review
09/19/2018	Medical Policy Implementation Committee approval. Title changed from "ZyfloZyflo CR (zileuton)" to "Zileuton Products (Zyflo/Zyflo CR)". Coverage eligibility unchanged.
09/05/2019	Medical Policy Committee review
09/11/2019	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.

09/03/2020	Medical Policy Committee review
09/09/2020	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
09/02/2021	Medical Policy Committee review
09/08/2021	Medical Policy Implementation Committee approval. Removed Zyflo CR from the policy as it is no longer available. Changed Zyflo CR to zileuton ER in the policy.
09/01/2022	Medical Policy Committee review
09/14/2022	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
09/07/2023	Medical Policy Committee review
09/13/2023	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
09/05/2024	Medical Policy Committee review
09/11/2024	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
09/04/2025	Medical Policy Committee review
09/10/2025	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.

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**Medically Necessary (or "Medical Necessity") - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

A. In accordance with nationally accepted standards of medical practice;
B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, "nationally accepted standards of medical practice" means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

NOTICE: If the Patient's health insurance contract contains language that differs from the BCBSLA Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

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NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.

NOTICE: Federal and State law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage.