

Cromolyn Oral Solution (Gastrocrom[®], generics)

Policy # 00761

Original Effective Date: 01/01/2022

Current Effective Date: 07/01/2025

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.

Note: Cromolyn Nebulized Solution is addressed separately in medical policy 00716.

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 cromolyn oral solution (Gastrocrom[®], generics)[†] for the treatment of mastocytosis or mast cell activation syndrome to be **eligible for coverage**** when the patient selection criteria are met.

Patient Selection Criteria

Coverage eligibility for cromolyn oral solution (Gastrocrom, generics) will be considered when the following criteria are met:

- Patient has a diagnosis of mastocytosis OR mast cell activation syndrome; AND
- Patient is ≥ 2 years old.

When Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers the use of cromolyn oral solution when patient selection criteria are not met to be **investigational.***

Background/Overview

Cromolyn inhibits the release of mediators such as histamine and leukotrienes from sensitized mast cells and is used in a variety of allergic conditions. The oral solution formulation (available as brand Gastrocrom or a generic solution) is specifically indicated for the management of patients with mastocytosis. The use of cromolyn oral solution has been associated with improvement in diarrhea,

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flushing, headaches, vomiting, urticaria, abdominal pain, nausea, and itching in some patients. For mastocytosis, it should be dosed four times daily, taken one-half hour before meals and at bedtime. Patients aged 13 years and older should take two ampules (200 mg) per dose and patients aged 2-12 years should take one ampule (100 mg) per dose. This product is not recommended in patients younger than 2 years of age.

Mastocytosis is a rare disorder that occurs when mast cells accumulate in tissues. It can be limited to the skin (cutaneous mastocytosis) or involve extracutaneous tissues (systemic mastocytosis). Common cutaneous symptoms include gradual development of a characteristic rash known as maculopapular cutaneous mastocytosis/urticaria pigmentosa and a positive Darier's sign (development of rash within 5 minutes of minor skin trauma). Common systemic symptoms include episodic flushing, tachycardia, diarrhea, fatigue, or musculoskeletal pain with varying triggers. Treatment includes epinephrine for anaphylactic attacks, antihistamines for management of pruritus or urticaria, and H2-blocking antihistamines or cromolyn oral solution for the management of gastrointestinal symptoms.

Mast cell activation syndrome is a relatively new term used to classify patients with a specific set of symptoms of unknown cause. To be diagnosed with mast cell activation syndrome, patients must have episodic, objective signs and symptoms consistent with mast cell activation involving at least two organ systems; have evidence of systemic mast cell-mediator release, corresponding temporally to the presence of symptoms; and respond to medications that inhibit the actions of mast cell mediators. Although not specifically studied, cromolyn oral solution has been used in the treatment of the gastrointestinal effects of this condition.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)

Gastrocrom (cromolyn sodium oral solution [concentrate]) is indicated in the management of patients with mastocytosis.

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.

Four randomized, controlled clinical trials were conducted with cromolyn sodium oral solution in patients with either cutaneous or systemic mastocytosis; two of which utilized a placebo-controlled crossover design, one utilized an active-controlled (chlorpheniramine plus cimetidine) crossover design, and one utilized a placebo-controlled parallel group design. Due to the rare nature of this

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disease, only 36 patients qualified for study entry, of whom 32 were considered evaluable. Consequently, formal statistical analyses were not performed. Clinically significant improvement in gastrointestinal symptoms (diarrhea, abdominal pain) were seen in the majority of patients with some improvement also seen for cutaneous manifestations (urticaria, pruritus, flushing) and cognitive function. The benefit seen with cromolyn sodium 200 mg four times daily was similar to chlorpheniramine plus cimetidine for both cutaneous and systemic symptoms of mastocytosis.

Clinical improvement occurred within 2 to 6 weeks of treatment initiation and persisted for 2 to 3 weeks after treatment withdrawal. Cromolyn solution did not affect urinary histamine levels or peripheral eosinophilia, although neither of these variables appeared to correlate with disease severity.

References

1. Gastrocrom [package insert]. Meda Pharmaceuticals. Somerset, NJ. Updated October 2018.
2. Cromolyn sodium [package insert]. Micro Labs USA. Basking Ridge, NJ. Updated June 2018.
3. Mastocytosis (cutaneous and systemic) in adults: Epidemiology, pathogenesis, clinical manifestations, and diagnosis. UpToDate. Updated July 2021.
4. Mast cell disorders: An overview. UpToDate. Updated April 2020.

Policy History

Original Effective Date: 01/01/2022

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10/07/2021 Medical Policy Committee review

10/13/2021 Medical Policy Implementation Committee approval. New policy.

06/02/2022 Medical Policy Committee review

06/08/2022 Medical Policy Implementation Committee approval. Updated criteria to include coverage for mast cell activation syndrome.

06/01/2023 Medical Policy Committee review

06/14/2023 Medical Policy Implementation Committee approval. Coverage eligibility unchanged.

06/06/2024 Medical Policy Committee review

06/12/2024 Medical Policy Implementation Committee approval. Coverage eligibility unchanged.

06/05/2025 Medical Policy Committee review

06/11/2025 Medical Policy Implementation Committee approval. Coverage eligibility unchanged.

Next Scheduled Review Date: 06/2026

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*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

- A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
- B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
 - 1. Consultation with technology evaluation center(s);
 - 2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
 - 3. Reference to federal regulations.

**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.

‡ Indicated trademarks are the registered trademarks of their respective owners.

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.