LOUISIANA BLUE

propranolol (Hemangeol®)

Policy # 00992
Original Effective Date: 01/01/2027
Current Effective Date: 01/01/2027

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.

Investigational or experimental services are not covered. This includes any drug, device, procedure, or service provided under the investigational arm of a clinical trial or clinical study. These services are excluded from coverage under benefits.

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 propranolol (Hemangeol®)‡ for the treatment of proliferating infantile hemangioma requiring systemic therapy to be **eligible for coverage.****

Patient Selection Criteria

Coverage eligibility for propranolol (Hemangeol) will be considered when the following criteria are met:

Initial

- Patient has a diagnosis of proliferating infantile hemangioma requiring systemic therapy due to at least one of the following: potential for disfigurement, life-threatening complications, functional impairment, ulceration, or underlying abnormalities; AND
  *(Note: The additional requirements described above define the specific circumstances under which the need for systemic therapy is considered medically necessary and are considered an additional Company requirement for eligibility. Requests for systemic therapy that do not meet these requirements will be denied as not medically necessary**.)*
- Patient is greater than or equal to 5 weeks and less than or equal to 5 months of age at treatment initiation; AND
- For premature infants, corrected age is greater than or equal to 5 weeks; AND
- Patient weighs greater than or equal to 2 kg; AND
- Patient does not have pheochromocytoma; AND
- Patient has tried and failed (e.g., intolerance or inadequate response) GENERIC propranolol solution unless there is clinical evidence or patient history that suggests GENERIC propranolol solution will be ineffective or cause an adverse reaction to the patient; AND
  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*

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- Prescriber attests that:
  - The starting dose will not exceed 0.15 mL/kg (0.6 mg/kg) twice daily; AND
  - Titration will occur according to FDA-approved labeling; AND
- The maintenance dose will not exceed 0.4 mL/kg (1.7 mg/kg) twice daily.

Continuation

- Patient met initial approval criteria, including initiation of treatment when the patient was greater than or equal to 5 weeks and less than or equal to 5 months of age; AND
- Patient has demonstrated clinical benefit from therapy, as evidenced by:
  - Reduction in hemangioma size; OR
  - Prescriber attestation of clinical improvement; AND

  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*
- Patient is less than or equal to 12 months of age; AND
- Prescriber attests therapy remains consistent with FDA-approved dosing recommendations.

When Services Are Considered Not Medically Necessary

Based on review of available data, the Company considers the use of propranolol (Hemangeol) when the patient's need for systemic therapy is NOT due to at least one of the following: potential for disfigurement, life-threatening complications, functional impairment, ulceration, or underlying abnormalities to be **not medically necessary.****

Based on review of available data, the Company considers the use of propranolol (Hemangeol) when the patient has not tried and failed GENERIC propranolol solution to be **not medically necessary.****

Based on review of available data, the Company considers the continued use of propranolol (Hemangeol) when the patient has not demonstrated a beneficial response to the drug to be **not medically necessary.****

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 propranolol (Hemangeol) when the patient selection criteria are not met (except for those noted to be **not medically necessary****) to be **investigational.***

Background/Overview

Hemangeol oral solution contains propranolol hydrochloride, a beta-adrenergic blocker indicated for the treatment of proliferating infantile hemangioma requiring systemic therapy. Treatment should be initiated in patients 5 weeks to 5 months of age. The recommended starting dosage is 0.15 mL/kg (0.6 mg/kg) twice daily, with doses administered at least 9 hours apart. After 1 week, the dosage should be increased to 0.3 mL/kg (1.1 mg/kg) twice daily. After 2 weeks of treatment, the dosage should be increased to 0.4 mL/kg (1.7 mg/kg) twice daily and continued for 6 months. The dose should be readjusted periodically as the child's weight increases. Blood pressure and heart rate

should be monitored for 2 hours after treatment initiation or any dosage increase. Hemangeol is supplied with an oral dosing syringe and should preferably be administered directly into the child's mouth. If needed, the product may be diluted in a small quantity of milk or fruit juice and given in a baby's bottle. To reduce the risk of hypoglycemia, Hemangeol should be administered during or immediately after feeding. Doses should be skipped if the child is not eating or is vomiting.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)

Hemangeol oral solution is a beta-adrenergic blocker indicated for the treatment of proliferating infantile hemangioma requiring systemic therapy.

The safety and effectiveness for infantile hemangioma have not been established in pediatric patients greater than 1 year of age.

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 regulations, other plan medical policies, and accredited national guidelines.

A randomized, double-blind study in 460 infants, aged 35 days to 5 months at inclusion, with proliferating infantile hemangiomas (IH) requiring systemic therapy (excluding life-threatening IH, function-threatening IH, and ulcerated IH with pain and lack of response to simple wound care measures) compared four regimens of Hemangeol (1.2 or 3.4 mg/kg/day in twice daily divided doses for 3 or 6 months; N = 99-103 per group) to placebo (N = 55). Clinical efficacy was evaluated by counting complete or nearly complete resolution of the target hemangioma, which was evaluated by blinded centralized independent assessments of photographs at Week 24 compared to baseline.

The main reason for treatment discontinuation was treatment inefficacy, which happened in 58% of patients randomized to placebo, 25-30% of patients randomized to Hemangeol for 3 months (mainly after the switch to placebo), and 7-9% of patients randomized to Hemangeol for 6 months.

Overall, 2 out of 55 patients (4%) in the placebo arm and 61 out of 101 patients (60%) on Hemangeol 3.4 mg/kg/day for 6 months had complete or nearly complete resolution of their hemangioma at Week 24 ($p < 0.0001$).

Of patients on Hemangeol 3.4 mg/kg/day for 6 months who were considered successes, 10% required retreatment for recurrence of hemangiomas.

A second uncontrolled study in 23 patients with proliferating IH included function-threatening IH, IH in certain anatomic locations that often leave permanent scars or deformity, large facial IH, smaller IH in exposed areas, severe ulcerated IH, pedunculated IH. Target lesions resolved in 36% of patients by 3 months.

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References

1. Hemangeol [package insert]. Eton Pharmaceuticals, Inc. Deer Park, Illinois. June 2021.

Policy History

Original Effective Date: 01/01/2027
Current Effective Date: 01/01/2027
10/01/2026 Pre Pharmacy & Therapeutics Committee review
10/07/2026 Pharmacy & Therapeutics Committee approval. New policy.
Next Scheduled Review Date: 10/2027

*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.

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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.

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.

NOTICE: If an authorization for an ongoing course of treatment has been provided to a member and the member changes from one health plan to another health plan (e.g., a member moves from carrier A to Louisiana Blue), Louisiana Blue may honor the previous health plan's authorization for the same service under the same type of in-network benefit for a 90-day transition period. Documentation of the authorization for the ongoing course of treatment from the previous health plan must be provided to us by the member or their provider and the services provided for the course of treatment must otherwise be a covered service under the Louisiana Blue health plan. This provision does not apply to medications covered under the plan's pharmacy benefit.