pyrimethamine (Daraprim®, generic)

Policy # 00530
Original Effective Date: 01/01/2017
Current Effective Date: 08/12/2024

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 pyrimethamine (Daraprim®, generic)‡ for various infectious conditions to be **eligible for coverage.****

Patient Selection Criteria

Coverage eligibility for pyrimethamine (Daraprim, generic) will be considered when the following criteria are met:

- For Daraprim brand requests: Patient has tried and failed (e.g. intolerance or inadequate response) the generic equivalent pyrimethamine unless there is clinical evidence or patient history that suggests the generic equivalent 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)*
- Patient meets any of the following diagnoses AND their subsequent requirements (if any):
  - Daraprim or its generic is being used for the treatment of acute malaria due to susceptible strains of plasmodia∞; AND

- Patient has tried and failed (e.g. intolerance or inadequate response) TWO other malaria treatment regimens (including, but not limited to atovaquone/proguanil, artemether/lumefantrine [Coartem®]‡, chloroquine, hydroxychloroquine, chloroquine plus primaquine, quinine plus clindamycin, quinidine plus doxycycline) (CDC); OR
  *(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)*

- Daraprim or its generic is being used for the prophylaxis of malaria due to susceptible strains of plasmodia∞; AND
  - Patient has tried and failed (e.g. intolerance or inadequate response) TWO other malaria treatment regimens (including, but not limited to atovaquone/proguanil, artemether/lumefantrine [Coartem], chloroquine, hydroxychloroquine, chloroquine plus primaquine, quinine plus clindamycin, quinidine plus doxycycline) (CDC); OR
    *(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)*
- Daraprim or its generic is being used for the treatment of toxoplasmosis∞; AND
  - Patient is using Daraprim or its generic in combination with a sulfonamide unless contraindicated, not tolerated, or has been tried and had an inadequate response; OR
- Daraprim or its generic is being used for the prevention of an initial episode of toxoplasmosis in HIV infected patients (AHFS); AND
  - Patient has an intolerance or contraindication to trimethoprim-sulfamethoxazole (CDC/NIH/IDSA); OR
    *(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)*
- Daraprim or its generic is being used to prevent a recurrence of toxoplasmosis in HIV infected patients (AHFS); OR
  *(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)*

- Daraprim or its generic is being used to treat or prevent a recurrence of cystoisosporiasis in HIV infected patients (AHFS); AND
  - Patient has an intolerance or contraindication to trimethoprim-sulfamethoxazole (CDC/NIH/IDSA); OR
    *(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)*
- Daraprim or its generic is being used to prevent an initial episode or recurrence of Pneumocystis jiroveci pneumonia in HIV infected patients (AHFS); AND
  - Patient has an intolerance or contraindication to trimethoprim-sulfamethoxazole (CDC/NIH/IDSA).
    *(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)*

Abbreviations: NIH=National Institutes of Health, CDC=Centers for Disease Control and Prevention, IDSA=Infectious Diseases Society of America, AHFS=American Hospital Formulary Services, HIV=Human Immunodeficiency Virus

∞FDA Approved

When Services Are Considered Not Medically Necessary

Based on review of available data, the Company considers the use of pyrimethamine (Daraprim, generic) WITHOUT meeting the criteria denoted in the above section as **not medically necessary**** (e.g. trial, intolerance, contraindications of previous drugs, etc) to be **not medically necessary.****

Based on review of available data, the Company considers the use of brand Daraprim without a trial and failure of generic pyrimethamine to be **not medically necessary.****

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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 pyrimethamine (Daraprim, generic) for any indication other than its respective FDA approved indication (except those allowed in the patient selection criteria above) to be **investigational.***

Background/Overview

Daraprim is a drug that has been around for quite some time. It has only recently garnered press due to the pricing practices of Turing Pharmaceuticals. Daraprim is approved for the treatment of toxoplasmosis, the treatment of acute malaria, and the chemoprophylaxis of malaria. Specifically, for the treatment of toxoplasmosis, the package insert states that the product should be used along with a sulfonamide. For the treatment of acute malaria, the package insert notes that fast acting schizonticides (such as chloroquine or quinine) are indicated and preferable for the treatment of acute malaria. For the chemoprophylaxis of malaria, the package insert states that resistance to Daraprim is prevalent worldwide, and that it is not a suitable prophylactic agent for travelers to most areas. Other organizations such as the Infectious Diseases Society of America, the Centers for Disease Control and Prevention, the National Institutes of Health, and the American Hospital Formulary Services have formulated recommendations for appropriate off-label uses for Daraprim as well as recommended therapies for certain conditions in which Daraprim is approved (or recommended off-label to treat). Those uses are noted in the patient selection criteria and are denoted by the organization's initials for which the recommendation originated. In 2020, a generic formulation of Daraprim became available.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)

Daraprim was originally approved in early 1953 for the treatment of toxoplasmosis, the treatment of acute malaria, and the chemoprophylaxis of malaria. As of early 2020, there is generic availability of pyrimethamine.

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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 rationale behind this policy is to ensure that Daraprim and its generic are being appropriately utilized based on FDA approvals and guideline recommendations. This policy also ensures that the generic product is utilized, where possible.

References

1. Daraprim [package insert]. Turing Pharmaceuticals. New York, New York. Updated October 2015.
2. Centers for Disease Control and Prevention. www.cdc.gov.
3. National Institutes of Health. www.NIH.gov
4. Infectious Diseases Society of America. www.idsociety.org
5. American Hospital Formulary Service. www.ahfsdruginformation.com.

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. No change to coverage.
09/06/2018	Medical Policy Committee review
09/19/2018	Medical Policy Implementation Committee approval. No change to coverage.
09/05/2019	Medical Policy Committee review
09/11/2019	Medical Policy Implementation Committee approval. No change to coverage.
07/02/2020	Medical Policy Committee review

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07/08/2020	Medical Policy Implementation Committee approval. Added the newly available generic pyrimethamine to the policy. Added "generic" to the title. Also, updated to require use of the generic pyrimethamine first.
07/01/2021	Medical Policy Committee review
07/14/2021	Medical Policy Implementation Committee approval. No change to coverage.
07/07/2022	Medical Policy Committee review
07/13/2022	Medical Policy Implementation Committee approval. No change to coverage.
07/06/2023	Medical Policy Committee review
07/12/2023	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
07/02/2024	Medical Policy Committee review
07/10/2024	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.

Next Scheduled Review Date: 07/2025

*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.

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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.

‡ 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.

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.