09-J2000-48

Original Effective Date: 01/15/16

Reviewed: 11/13/24

Revised: 12/15/24

Subject: Pyrimethamine (Daraprim)

THIS MEDICAL COVERAGE GUIDELINE IS NOT AN AUTHORIZATION, CERTIFICATION, EXPLANATION OF BENEFITS, OR A GUARANTEE OF PAYMENT, NOR DOES IT SUBSTITUTE FOR OR CONSTITUTE MEDICAL ADVICE. ALL MEDICAL DECISIONS ARE SOLELY THE RESPONSIBILITY OF THE PATIENT AND PHYSICIAN. BENEFITS ARE DETERMINED BY THE GROUP CONTRACT, MEMBER BENEFIT BOOKLET, AND/OR INDIVIDUAL SUBSCRIBER CERTIFICATE IN EFFECT AT THE TIME SERVICES WERE RENDERED. THIS MEDICAL COVERAGE GUIDELINE APPLIES TO ALL LINES OF BUSINESS UNLESS OTHERWISE NOTED IN THE PROGRAM EXCEPTIONS SECTION.

DESCRIPTION:

Pyrimethamine (Daraprim), a synthetic antiparasitic agent, was approved by the U.S. Food and Drug Administration (FDA) in 1953 for the treatment of malaria and toxoplasmosis and for the prophylaxis of malaria. Pyrimethamine is chemically and pharmacologically similar to trimethoprim, a component of co-trimoxazole. Pyrimethamine should not be used alone to treat acute malaria. Due to widespread resistance and availability of faster acting agents, use of pyrimethamine for both the treatment and prophylaxis of malaria is no longer recommended by the CDC.

POSITION STATEMENT:

Comparative Effectiveness

The Food and Drug Administration has deemed the drug(s) or biological product(s) in this coverage policy to be appropriate for self-administration or administration by a caregiver (i.e., not a healthcare professional). Therefore, coverage (i.e., administration) in a provider-administered setting such as an outpatient hospital, ambulatory surgical suite, or emergency facility is not considered medically necessary.

Initiation pyrimethamine (Daraprim) **meets the definition of medical necessity** when used for one of the following indications and **ALL** of the following criteria are met:

1. Treatment of toxoplasmosis (including toxoplasmic encephalitis)
    a. Member is diagnosed with toxoplasmosis – documentation from the medical record must be provided

b. If brand Daraprim is requested, the member has tried and had intolerable adverse effects to generic pyrimethamine and **ALL** of the following must be submitted:
    i. The specific intolerance(s) and rationale for using brand Daraprim must be specified
    ii. Completed Medwatch reporting form (FDA 3500) – https://www.fda.gov/safety/medical-product-safety-information/forms-reporting-fda
    iii. Completed Naranjo Adverse Drug reaction probability scale - https://assets.guidewell.com/m/2736e82ff52fe22d/original/mcg-naranjoalgorithm.pdf
c. Dose does not exceed (dosage will be achieved using the fewest number of tablets per day):
    i. Loading dose: 200 mg (1 dose)
    ii. Maintenance dose: 75 mg/day

2. Prophylaxis of toxoplasmosis
    a. Member is immunocompromised (e.g., HIV-positive, solid organ transplant receipt/donor) – documentation from the medical record must be provided
    b. **ONE** of the following:
        i. Use is for chronic maintenance therapy
        ii. Member had persistent, intolerable adverse effects with use of trimethoprim-sulfamethoxazole
        iii. Member has a contraindication to trimethoprim-sulfamethoxazole
        iv. Member was previously approved for pyrimethamine by another health plan – documentation of a recent (within 90 days prior to authorization request) health plan-paid claim for pyrimethamine must be provided
    c. If brand Daraprim is requested, the member has tried and had intolerable adverse effects to generic pyrimethamine and **ALL** of the following must be submitted:
        i. The specific intolerance(s) and rationale for using brand Daraprim must be specified
        ii. Completed Medwatch reporting form (FDA 3500) – https://www.fda.gov/safety/medical-product-safety-information/forms-reporting-fda
        iii. Completed Naranjo Adverse Drug reaction probability scale - https://assets.guidewell.com/m/2736e82ff52fe22d/original/mcg-naranjoalgorithm.pdf
    d. Dose does not exceed (dosage will be achieved using the fewest number of tablets per day):
        i. If dosing daily: 25 mg/day
        ii. If dosing weekly: 75 mg/week

3. Prophylaxis of pneumocystis pneumonia (PCP)

a. Member is immunocompromised (e.g., HIV-positive, solid organ transplant receipt/donor) – documentation from the medical record must be provided

b. **ONE** of the following:

   i. Member had persistent, intolerable adverse effects with use of trimethoprim-sulfamethoxazole

   ii. Member has a contraindication to trimethoprim-sulfamethoxazole

   iii. Member was previously approved for pyrimethamine by another health plan **–** documentation of a recent (within 90 days prior to authorization request) health plan-paid claim for pyrimethamine must be provided

c. If brand Daraprim is requested, the member has tried and had intolerable adverse effects to generic pyrimethamine and **ALL** of the following must be submitted:

   i. The specific intolerance(s) and rationale for using brand Daraprim must be specified

   ii. Completed Medwatch reporting form (FDA 3500) – https://www.fda.gov/safety/medical-product-safety-information/forms-reporting-fda

   iii. Completed Naranjo Adverse Drug reaction probability scale - https://assets.guidewell.com/m/2736e82ff52fe22d/original/mcg-naranjoalgorithm.pdf

d. Dose does not exceed (dosage will be achieved using the fewest number of tablets per day):

   i. If dosing daily: 25 mg/day

   ii. If dosing weekly: 75 mg/week

4. Treatment of cystoisosporiasis (also known as isosporiasis)

   a. Member is immunocompromised (e.g., HIV-positive, solid organ transplant receipt/donor) – documentation from the medical record must be provided

   b. **ONE** of the following:

      i. Member had persistent, intolerable adverse effects with use of trimethoprim-sulfamethoxazole

      ii. Member has a contraindication to trimethoprim-sulfamethoxazole

      iii. Member was previously approved for pyrimethamine by another health plan **–** documentation of a recent (within 90 days prior to authorization request) health plan-paid claim for pyrimethamine must be provided

   c. If brand Daraprim is requested, the member has tried and had intolerable adverse effects to generic pyrimethamine and **ALL** of the following must be submitted:

      i. The specific intolerance(s) and rationale for using brand Daraprim must be specified

      ii. Completed Medwatch reporting form (FDA 3500) – https://www.fda.gov/safety/medical-product-safety-information/forms-reporting-fda

iii. Completed Naranjo Adverse Drug reaction probability scale - https://assets.guidewell.com/m/2736e82ff52fe22d/original/mcg-naranjoalgorithm.pdf

d. Dose does not exceed 75 mg/day (dosage will be achieved using the fewest number of tablets per day)

5. Prophylaxis of cystoisosporiasis (also known as isosporiasis)

   a. Member is immunocompromised (e.g., HIV-positive, solid organ transplant receipt/donor) – documentation from the medical record must be provided

   b. **ONE** of the following:

      i. Member had persistent, intolerable adverse effects with use of trimethoprim-sulfamethoxazole

      ii. Member has a contraindication to trimethoprim-sulfamethoxazole

      iii. Member was previously approved for pyrimethamine by another health plan **–** documentation of a recent (within 90 days prior to authorization request) health plan-paid claim for pyrimethamine must be provided

   c. If brand Daraprim is requested, the member has tried and had intolerable adverse effects to generic pyrimethamine and **ALL** of the following must be submitted:

      i. The specific intolerance(s) and rationale for using brand Daraprim must be specified

      ii. Completed Medwatch reporting form (FDA 3500) – https://www.fda.gov/safety/medical-product-safety-information/forms-reporting-fda

      iii. Completed Naranjo Adverse Drug reaction probability scale - https://assets.guidewell.com/m/2736e82ff52fe22d/original/mcg-naranjoalgorithm.pdf

   d. Dose does not exceed (dosage will be achieved using the fewest number of tablets per day):

      i. If dosing daily: 25 mg/day

      ii. If dosing weekly: 75 mg/week

Approval duration: 6 months

Continuation of pyrimethamine (Daraprim) **meets the definition of medical necessity** when **ALL** of the following criteria are met:

1. Authorization/reauthorization has been previously approved by Florida Blue in the past two years, OR the member has previously met all indication-specific initiation criteria
2. Dose does not exceed 75 mg/day – dosage will be achieved using the fewest number of tablets per day

Approval duration: 6 months

Pyrimethamine **meets the definition of medical necessity** when used for treatment of the following designated Orphan Drug indication when the maximum FDA-approved dose is not exceeded:

1. Treatment of GM-2 gangliosidoses (Tay-Sachs disease and Sandhoff disease).

Approval duration: 6 months

DOSAGE/ADMINISTRATION:

THIS INFORMATION IS PROVIDED FOR INFORMATIONAL PURPOSES ONLY AND SHOULD NOT BE USED AS A SOURCE FOR MAKING PRESCRIBING OR OTHER MEDICAL DETERMINATIONS. PROVIDERS SHOULD REFER TO THE MANUFACTURER'S FULL PRESCRIBING INFORMATION FOR DOSAGE GUIDELINES AND OTHER INFORMATION RELATED TO THIS MEDICATION BEFORE MAKING ANY CLINICAL DECISIONS REGARDING ITS USAGE.

FDA-approved

For Treatment of Toxoplasmosis

- The adult starting dose is 50 to 75 mg of the drug daily, together with 1 to 4 g daily of a sulfonamide of the sulfapyrimidine type, e.g., sulfadoxine. This dosage is ordinarily continued for 1 to 3 weeks, depending on the response of the patient and tolerance to therapy. The dosage may then be reduced to about one half that previously given for each drug and continued for an additional 4 to 5 weeks.
- The pediatric dosage is 1 mg/kg/day divided into 2 equal daily doses; after 2 to 4 days this dose may be reduced to one half and continued for approximately 1 month. The usual pediatric sulfonamide dosage is used in conjunction with pyrimethamine.

Dose Adjustments

- Please refer to product label

Drug Availability

- Tablet: 25 mg

PRECAUTIONS:

Boxed Warning

- None

Contraindications

- Known hypersensitivity to pyrimethamine or to any component of the formulation
- Megaloblastic anemia due to folate deficiency

Precautions/Warnings

- Data in 2 humans indicate that pyrimethamine may be carcinogenic; a 51-year-old female who developed chronic granulocytic leukemia after taking pyrimethamine for 2 years for toxoplasmosis and a 56-year-old patient who developed reticulum cell sarcoma after 14 months of pyrimethamine for toxoplasmosis

- In patients receiving high dosage, as for the treatment of toxoplasmosis, semiweekly blood counts, including platelet counts, should be performed

BILLING/CODING INFORMATION:

The following codes may be used to describe:

HCPCS Coding

J8499	Prescription drug, oral, non-chemotherapeutic, Not Otherwise Specified

ICD-10 Diagnosis Codes That Support Medical Necessity

A07.3	Isosporiasis
B58.00 – B58.0	Toxoplasma oculopathy
B58.1	Toxoplasma hepatitis
B58.2	Toxoplasma meningoencephalitis
B58.3	Pulmonary toxoplasmosis
B58.81 – B58.89	Toxoplasmosis with other organ involvement
B58.9	Toxoplasmosis, unspecified
P37.1	Congenital toxoplasmosis
Z92.25	Personal history of immunosuppression therapy

REIMBURSEMENT INFORMATION:

Refer to section entitled **POSITION STATEMENT**.

PROGRAM EXCEPTIONS:

Federal Employee Program (FEP): Follow FEP guidelines.

State Account Organization (SAO): Follow SAO guidelines.

Medicare Part D: Florida Blue has delegated to Prime Therapeutics authority to make coverage determinations for the Medicare Part D services referenced in this guideline.

Medicare Advantage: No National Coverage Determination (NCD) and/or Local Coverage Determination (LCD) were found at the time of the last guideline revised date.

DEFINITIONS:

None

RELATED GUIDELINES:

None

OTHER:

None

REFERENCES:

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COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Pharmacy Policy Committee on 11/13/24.

GUIDELINE UPDATE INFORMATION:

01/15/16	New Medical Coverage Guideline.
01/15/17	Review and revision to guideline consisting of updating position statement and references.
01/15/18	Review and revision to guideline consisting of updating position statement and references.
01/15/19	Review and revision to guideline consisting of updating references.
12/15/19	Revision to position statement.
01/15/20	Review and revision to guideline consisting of updating references and coding.

01/15/21	Review and revision to guideline consisting of updating the position statement and references.
12/15/21	Review and revision to guideline consisting of updating position statement and references
12/15/22	Review and revision to guideline consisting of updating references
12/15/23	Review and revision to guideline consisting of updating position statement and references
12/15/24	Review and revision to guideline consisting of updating position statement and references