PRIOR AUTHORIZATION POLICY

POLICY: Infectious Disease – Pyrimethamine Prior Authorization Policy
- Daraprim® (pyrimethamine tablets – Vyera, generic)

REVIEW DATE: 12/11/2024

INSTRUCTIONS FOR USE

THE FOLLOWING COVERAGE POLICY APPLIES TO HEALTH BENEFIT PLANS ADMINISTERED BY CIGNA COMPANIES. CERTAIN CIGNA COMPANIES AND/OR LINES OF BUSINESS ONLY PROVIDE UTILIZATION REVIEW SERVICES TO CLIENTS AND DO NOT MAKE COVERAGE DETERMINATIONS. REFERENCES TO STANDARD BENEFIT PLAN LANGUAGE AND COVERAGE DETERMINATIONS DO NOT APPLY TO THOSE CLIENTS. COVERAGE POLICIES ARE INTENDED TO PROVIDE GUIDANCE IN INTERPRETING CERTAIN STANDARD BENEFIT PLANS ADMINISTERED BY CIGNA COMPANIES. PLEASE NOTE, THE TERMS OF A CUSTOMER'S PARTICULAR BENEFIT PLAN DOCUMENT [GROUP SERVICE AGREEMENT, EVIDENCE OF COVERAGE, CERTIFICATE OF COVERAGE, SUMMARY PLAN DESCRIPTION (SPD) OR SIMILAR PLAN DOCUMENT] MAY DIFFER SIGNIFICANTLY FROM THE STANDARD BENEFIT PLANS UPON WHICH THESE COVERAGE POLICIES ARE BASED. FOR EXAMPLE, A CUSTOMER'S BENEFIT PLAN DOCUMENT MAY CONTAIN A SPECIFIC EXCLUSION RELATED TO A TOPIC ADDRESSED IN A COVERAGE POLICY. IN THE EVENT OF A CONFLICT, A CUSTOMER'S BENEFIT PLAN DOCUMENT ALWAYS SUPERSEDES THE INFORMATION IN THE COVERAGE POLICIES. IN THE ABSENCE OF A CONTROLLING FEDERAL OR STATE COVERAGE MANDATE, BENEFITS ARE ULTIMATELY DETERMINED BY THE TERMS OF THE APPLICABLE BENEFIT PLAN DOCUMENT. COVERAGE DETERMINATIONS IN EACH SPECIFIC INSTANCE REQUIRE CONSIDERATION OF 1) THE TERMS OF THE APPLICABLE BENEFIT PLAN DOCUMENT IN EFFECT ON THE DATE OF SERVICE; 2) ANY APPLICABLE LAWS/REGULATIONS; 3) ANY RELEVANT COLLATERAL SOURCE MATERIALS INCLUDING COVERAGE POLICIES AND; 4) THE SPECIFIC FACTS OF THE PARTICULAR SITUATION. EACH COVERAGE REQUEST SHOULD BE REVIEWED ON ITS OWN MERITS. MEDICAL DIRECTORS ARE EXPECTED TO EXERCISE CLINICAL JUDGMENT AND HAVE DISCRETION IN MAKING INDIVIDUAL COVERAGE DETERMINATIONS. COVERAGE POLICIES RELATE EXCLUSIVELY TO THE ADMINISTRATION OF HEALTH BENEFIT PLANS. COVERAGE POLICIES ARE NOT RECOMMENDATIONS FOR TREATMENT AND SHOULD NEVER BE USED AS TREATMENT GUIDELINES. IN CERTAIN MARKETS, DELEGATED VENDOR GUIDELINES MAY BE USED TO SUPPORT MEDICAL NECESSITY AND OTHER COVERAGE DETERMINATIONS.

CIGNA NATIONAL FORMULARY COVERAGE:

OVERVIEW

Pyrimethamine tablets (Daraprim, generic), a folic acid antagonist, are indicated for the treatment of **toxoplasmosis** when used conjointly with a sulfonamide, since synergism exists with this combination.[1]

Pyrimethamine tablets are considered to be the most effective drug against toxoplasmosis and are a standard component of therapy.[2] Leucovorin, a folinic acid, protects the bone marrow from the toxic effects of pyrimethamine and is prescribed in conjunction with pyrimethamine.

Guidelines

The Guidelines for the Prevention and Treatment of Opportunistic Infections in Adults and Adolescents with Human Immunodeficiency (HIV) [last updated September 2023] recommend pyrimethamine tablets as the drug of choice for treatment and chronic maintenance treatment (secondary prophylaxis) of *Toxoplasma gondii* encephalitis.[3] Pyrimethamine tablets are recommended as an option for: primary prophylaxis of *Toxoplasma gondii* encephalitis; primary prophylaxis and secondary prophylaxis (chronic maintenance treatment) of *Pneumocystis* pneumonia; and secondary prophylaxis (chronic maintenance

treatment) and treatment of cystoisosporiasis (formerly isosporiasis). The drug of choice for these conditions is trimethoprim-sulfamethoxazole.

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of pyrimethamine tablets. All approvals are provided for the duration noted below. Because of the specialized skills required for evaluation and diagnosis of patients treated with pyrimethamine tablets as well as the monitoring required for adverse events and long-term efficacy, approval requires pyrimethamine tablets to be prescribed by or in consultation with a physician who specializes in the condition being treated.

- **Daraprim® (pyrimethamine tablets – Vyera, generic) is(are) covered as medically necessary when the following criteria is(are) met for FDA-approved indication(s) or other uses with supportive evidence (if applicable):**

FDA-Approved Indication

1. **Toxoplasmosis – Treatment.** Approve for 1 year if the patient meets ALL of the following (A, B, and C):
   A) The medication is prescribed in combination with leucovorin; AND
   B) Patient meets ONE of the following (i or ii):
      i. The medication is prescribed in combination with sulfadiazine; OR
      ii. Patient meets BOTH of the following (a and b):
         a) Patient is unable to take sulfadiazine; AND
         b) Patient meets ONE of the following (1 or 2):
            1) The medication is prescribed in combination with systemic clindamycin; OR
            2) The medication is prescribed in combination with atovaquone; AND
   C) The medication is prescribed by or in consultation with an infectious diseases specialist or a physician specializing in the treatment of human immunodeficiency virus (HIV) infection.

Other Uses with Supportive Evidence

2. **Cystoisosporiasis (formerly known as isosporiasis) – Secondary Prophylaxis (Chronic Maintenance Treatment).** Approve for 1 year if the patient meets ALL of the following (A, B, and C):
   A) Patient has tried at least one other therapy for this condition; AND
   Note: Examples of other therapies used for this condition include trimethoprim-sulfamethoxazole and systemic ciprofloxacin.
   B) The medication is prescribed in combination with leucovorin; AND
   C) The medication is prescribed by or in consultation with an infectious diseases specialist or a physician specializing in the treatment of human immunodeficiency virus (HIV) infection.

3. **Cystoisosporiasis (formerly known as isosporiasis) – Treatment.** Approve for 1 year if the patient meets ALL of the following (A, B, and C):
   - **A)** Patient has tried at least one other therapy for this condition; AND
     Note: Examples of other therapies used for this condition include trimethoprim-sulfamethoxazole and systemic ciprofloxacin.
   - **B)** The medication is prescribed in combination with leucovorin; AND
   - **C)** The medication is prescribed by or in consultation with an infectious diseases specialist or a physician specializing in the treatment of human immunodeficiency virus (HIV) infection.

4. ***Pneumocystis* Pneumonia – Primary Prophylaxis.** Approve for 1 year if the patient meets ALL of the following (A, B, C, and D):
   - **A)** Patient has tried at least one other therapy for this condition; AND
     Note: Examples of other therapies used for this condition include trimethoprim-sulfamethoxazole, systemic dapsone, aerosolized pentamidine (via Respigard II™ nebulizer), and atovaquone.
   - **B)** The medication is prescribed in combination with leucovorin; AND
   - **C)** Patient meets ONE of the following (i or ii):
     - **i.** The medication is prescribed in combination with systemic dapsone; OR
     - **ii.** The medication is prescribed in combination with atovaquone; AND
   - **D.** The medication is prescribed by or in consultation with an infectious diseases specialist or a physician specializing in the treatment of human immunodeficiency virus (HIV) infection.

5. ***Pneumocystis* Pneumonia – Secondary Prophylaxis (Chronic Maintenance Therapy).** Approve for 1 year if the patient meets ALL of the following (A, B, C, and D):
   - **A)** Patient has tried at least one other therapy for this condition; AND
     Note: Examples of other therapies used for this condition include trimethoprim-sulfamethoxazole, systemic dapsone, aerosolized pentamidine (via Respigard II™ nebulizer), and atovaquone.
   - **B)** The medication is prescribed in combination with leucovorin; AND
   - **C)** Patient meets ONE of the following (i or ii):
     - **i.** The medication is prescribed in combination with systemic dapsone; OR
     - **ii.** The medication is prescribed in combination with atovaquone; AND
   - **D)** The medication is prescribed by or in consultation with an infectious diseases specialist or a physician specializing in the treatment of human immunodeficiency virus (HIV) infection.

6. ***Toxoplasma gondii* Encephalitis – Primary Prophylaxis.** Approve for 1 year if the patient meets ALL of the following (A, B, C, and D):
   - **A)** Patient has tried at least one other therapy for this condition; AND
     Note: Examples of other therapies used for this condition include trimethoprim-sulfamethoxazole and atovaquone.
   - **B)** The medication is prescribed in combination with leucovorin; AND
   - **C)** Patient meets ONE of the following (i or ii):
     - **i.** The medication is prescribed in combination with systemic dapsone; OR

ii. The medication is prescribed in combination with atovaquone; AND

D) The medication is prescribed by or in consultation with an infectious diseases specialist or a physician specializing in the treatment of human immunodeficiency virus (HIV) infection.

7. *Toxoplasma gondii* Encephalitis – Secondary Prophylaxis (Chronic Maintenance Therapy). Approve for 1 year if the patient meets ALL of the following (A, B, and C):

A) The medication is prescribed in combination with leucovorin; AND

B) Patient meets ONE of the following (i or ii):

i. The medication is prescribed in combination with sulfadiazine; OR

ii. Patient meets BOTH of the following (a and b):

a) Patient is unable to take sulfadiazine; AND

b) Patient meets ONE of the following (1 or 2):

(1) The medication is prescribed in combination with systemic clindamycin; OR

(2) The medication is prescribed in combination with atovaquone; AND

C) The medication is prescribed by or in consultation with an infectious diseases specialist or a physician specializing in the treatment of human immunodeficiency virus (HIV) infection.

CONDITIONS NOT COVERED

- **Daraprim® (pyrimethamine tablets – Vyera, generic) is(are) considered experimental, investigational or unproven for ANY other use(s) including the following (this list may not be all inclusive; criteria will be updated as new published data are available):**

1. Malaria – Chemoprophylaxis or Treatment. Pyrimethamine is no longer indicated for the treatment of acute malaria or for chemoprophylaxis of malaria.[1]

2. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Daraprim® tablets [prescribing information]. New York, NY: Vyera; August 2017.
2. Centers for Disease Control and Prevention – Toxoplasmosis. Available at: https://www.cdc.gov/parasites/toxoplasmosis/index.html. Accessed on December 5, 2024.
3. Guidelines for the prevention and treatment of opportunistic infections in adults and adolescents with HIV: recommendations from the Centers for Disease Control and Prevention, the National Institutes of Health, and the HIV Medicine Association of the Infectious Diseases Society of America. Available at: https://clinicalinfo.hiv.gov/en/guidelines/adult-and-adolescent-opportunistic-infection/whats-new-guidelines. Accessed on December 5, 2024.

HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	No criteria changes.	12/06/2023
Annual Revision	No criteria changes.	12/11/2024