

Drug and Biologic Coverage Policy



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Coverage Policy Number P0012

Pyrimethamine

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Related Coverage Resources

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. 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.

Medical Necessity Criteria

Pyrimethamine (Daraprim) is considered medically necessary for ANY of the following diagnoses:

- Treatment of toxoplasmosis when used in combination with sulfonamide
- Primary toxoplasmosis prophylaxis in combination with dapsone +/- leucovorin when there is a contraindication or intolerance to trimethoprim-sulfamethoxazole (TMP-SMX)
- Secondary prophylaxis of toxoplasmic encephalitis as chronic maintenance therapy to prevent relapse
- Treatment of cystoisosporiasis (formerly known as isosporiasis in HIV-infected individuals when there is a contraindication or failure/intolerance to trimethoprim-sulfamethoxazole (TMP-SMX)
- Prophylaxis for Pneumocystis pneumonia in adults/adolescents when there is a contraindication or intolerance to trimethoprim-sulfamethoxazole (TMP-SMX)

Pyrimethamine is considered medically necessary for continued use when the individual continues to meet the initial criteria.

Where coverage requires the use of preferred products, the following conditions of coverage apply.

For Employer Group Plans:

Daraprim (brand) tablet is considered medically necessary when the following criteria are met:

- Documented intolerance to **ONE** formulary alternative: pyrimethamine (generic Daraprim)

Initial and reauthorization is up to 12 months.

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Pyrimethamine (Daraprim) is considered experimental, investigational or unproven for ANY other use including the following:

- Malaria – Treatment or Chemoprophylaxis

Note: Receipt of sample product does not satisfy any criteria requirements for coverage.

FDA Approved Indications

FDA Approved Indication

Treatment of Toxoplasmosis:

Daraprim is indicated for the treatment of toxoplasmosis when used conjointly with a sulfonamide, since synergism exists with this combination.

Recommended Dosing

FDA Recommended Dosing

For Treatment of Toxoplasmosis:

The dosage of Daraprim for the treatment of toxoplasmosis must be carefully adjusted so as to provide maximum therapeutic effect and a minimum of side effects. At the dosage required, there is a marked variation in the tolerance to the drug. Young patients may tolerate higher doses than older individuals. Concurrent administration of folinic acid is strongly recommended in all patients.

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 of Daraprim 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 Daraprim.

Drug Availability

Supplied as 25 mg pyrimethamine tablets in bottles of 100 or 30.

Background

Pharmacology

Pyrimethamine, a folic acid antagonist, is considered to be the most effective drug against toxoplasmosis and is a standard component of therapy. (CDC, 2018) Leucovorin, a folinic acid, protects the bone marrow from the toxic effects of pyrimethamine and is often prescribed in conjunction with pyrimethamine. (CDC, 2018)

Professional Societies/Organizations

The US Department of Health and Human Services (DHHS) Guidelines for the Prevention and Treatment of Opportunistic Infections in Adults and Adolescents with Human Immunodeficiency Virus (HIV) recommend a combination of pyrimethamine plus sulfadiazine plus leucovorin as an initial therapy choice for toxoplasmic encephalitis (TE). Pyrimethamine, in combination with leucovorin and other agents, is also recommended as secondary prophylaxis of TE. Recommendations for primary prophylaxis include trimethoprim-sulfamethoxazole

(TMP-SMX) where if an individual is receiving this agent for treatment of Pneumocystis pneumonia (PCP), then no additional medications are required. (DHHS, 2017b) DHHS recommends TMP-SMX for treatment of isosporiasis as the antimicrobial agent of choice. Pyrimethamine has been used and is a treatment option for sulfa-intolerant individuals, or in those whom TMP-SMX treatment fails. (DHHS, 2015) DHHS also recommend TMP-SMX for treatment of Pneumocystis pneumonia (PCP). Pyrimethamine in combination with leucovorin (and dapsone or atovaquone) should be reserved for individuals with documented sulfa intolerance. (DHHS, 2017a)

The US Centers for Disease Control and Prevention (CDC) no longer recommend the use of pyrimethamine for the treatment or prophylaxis of malaria due to widespread resistance of Daraprim worldwide. (CDC, 2013; CDC, 2019)

Off Label Uses

AHFS Drug Information 2020 Edition supports the following off-label uses: cystoisosporiasis (formerly known as isosporiasis) and Pneumocystis pneumonia. However, pyrimethamine currently is not recommended in the following uses: malaria prevention.

References

1. Centers for Disease Control and Prevention. CDC Health Information for International Travel 2018. New York: Oxford University Press; 2019. Accessed 4/3/2020: <https://wwwnc.cdc.gov/travel/yellowbook/2018/infectious-diseases-related-to-travel/malaria#4904>
2. Centers for Disease Control and Prevention – Toxoplasmosis: August 2018. Accessed 4/3/2020. Available at: <https://www.cdc.gov/parasites/toxoplasmosis/index.html>.
3. Centers for Disease Control and Prevention. Treatment of Malaria (Guidelines For Clinicians): July 2019. Accessed 4/3/2020: <https://www.cdc.gov/malaria/resources/pdf/clinicalguidance.pdf>
4. Daraprim® [prescribing information]. New York, NY: Vyera Pharmaceuticals LLC.; August 2017.
5. Department of Health and Human Services. Guidelines for the Prevention and Treatment of Opportunistic Infections in HIV-Infected Adults and Adolescents: September 2015a. Accessed 4/3/2020: <https://aidsinfo.nih.gov/guidelines/html/4/adult-and-adolescent-opportunistic-infection/352/isosporiasis--cystoisosporiasis->
6. Department of Health and Human Services. Guidelines for the Prevention and Treatment of Opportunistic Infections in HIV-Infected Adults and Adolescents: July 2017a. Accessed 4/3/2020: <https://aidsinfo.nih.gov/guidelines/html/4/adult-and-adolescent-opportunistic-infection/321/pcp>
7. Department of Health and Human Services. Guidelines for the Prevention and Treatment of Opportunistic Infections in HIV-Infected Adults and Adolescents: July 2017b. Accessed 4/3/2020: <https://aidsinfo.nih.gov/guidelines/html/4/adult-and-adolescent-opportunistic-infection/322/toxo>
8. McEvoy GK, ed. 2020. AHFS Drug Information. Bethesda, MD: American Society of Health-System Pharmacists, Inc; 2020.

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