Clinical Policy: pyrimethamine (Daraprim®)

Reference Number: ERX.NSMN.27
Effective Date: 12/15
Last Review Date: 09/16

Revision Log

Clinical policies are intended to be reflective of current scientific research and clinical thinking. This policy is current at the time of approval, may be updated and therefore is subject to change. This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members.

Description

The intent of the criteria is to ensure that patients follow selection elements established by Envolve Pharmacy Solutions for the use of pyrimethamine (Daraprim®).

Policy/Criteria

It is the policy of health plans affiliated with Envolve Pharmacy Solutions® that pyrimethamine (Daraprim®) is **medically necessary** for members meeting the following criteria:

Initial Approval Criteria

I. Initial Therapy for Toxoplasmosis Infection – Active Disease (must meet all):
- **A.** Prescribed by or in consultation with an infectious disease specialist;
- **B.** Documented diagnosis of toxoplasmosis;
- **C.** Member meets one of the following:
  a. Age < 18 years;
  b. Failure of trimethoprim/sulfamethoxazole (TMP/SMX) as evidenced by lack of clinical improvement within 10-14 days or radiological deterioration during the first week despite compliant use, unless TMP/SMX is contraindicated;
- **D.** Daraprim is prescribed with sulfadiazine or clindamycin, along with leucovorin;
- **E.** Request does not exceed FDA approved maximum recommended dose and health plan approved daily quantity limit.

Approval duration: Immunocompromised member: 6 weeks
Immunocompetent member: 4 weeks

II. Primary Prophylaxis for Toxoplasmosis – Preventing 1st Episode (must meet all):
- **A.** Prescribed by or in consultation with an infectious disease specialist;

B. Request is for prevention for toxoplasmosis;
C. Member is HIV-infected with CD4 counts < 100 cells/mm^3 and positive for *Toxoplasma gondii* IgG;
D. Documented contraindication to TMP/SMX;
E. Daraprim is prescribed with leucovorin and dapsone;
F. Request does not exceed FDA approved maximum recommended dose and health plan approved daily quantity limit.

Approval duration: 6 months

III. Malaria and Malaria Prophylaxis: This agent is not covered for these indications. *Daraprim is indicated for both treatment and prophylaxis of malaria. In the treatment of malaria, FDA-labeling recommends its use with fast-acting schizonticides (chloroquine or quinine). However, resistance to pyrimethamine is prevalent worldwide. Pyrimethamine is not recommended for use by the CDC treatment guidelines for the treatment or prophylaxis of malaria.*

Continued Approval Criteria

I. Chronic Maintenance – Following Initial Therapy for Active Disease (must meet all):
A. Previously received medication via health plan benefit or member has previously met all initial approval criteria;
B. Documentation of positive response to Daraprim;
C. Adherence to antiretroviral therapy (ART) as evidenced by pharmacy claims history or office notes;
D. Member is HIV-infected with CD4 counts < 200 cells/mm^3 at any time in the previous 6 months;
E. Daraprim is prescribed with sulfadiazine or clindamycin, along with leucovorin;
F. Request does not exceed FDA approved maximum recommended dose and health plan approved daily quantity limit.

Approval duration: 6 months

II. Primary Prophylaxis for Toxoplasmosis – Preventing 1st Episode (must meet all):
A. Previously received medication via health plan benefit or member has previously met all initial approval criteria;
B. Member is HIV-infected with CD4 counts < 200 cells/mm^3 at any time in the previous 3 months;
C. Daraprim is prescribed with leucovorin and dapsone;
D. Request does not exceed FDA approved maximum recommended dose and health plan approved daily quantity limit.

Approval duration: 3 months

Workflow Document

USS.NSMN.27
pyrimethamine (Dara

Background

Description/Mechanism of Action

Pyrimethamine is a folic acid antagonist. The rationale for its therapeutic action is based on the differential requirement between host and parasite for nucleic acid precursors involved in growth. This activity is highly selective against plasmodia and *Toxoplasma gondii*. Pyrimethamine possesses blood schizonticidal and some tissue schizonticidal activity against malaria parasites of humans.

Although TMP/SMX is approved for pediatric patients 2 months of age and older, use in the treatment of toxoplasmosis is only indicated for adults > 18 years of age based on the study supporting its use for this condition.

FDA Approved Indications

Daraprim is FDA approved for the treatment of toxoplasmosis, treatment of acute malaria, and chemoprophylaxis of malaria.

References

1. Daraprim® [package insert]. Raleigh, NC: Salix Pharmaceuticals, Inc.; October 2015.
2. Panel on Opportunistic Infections in HIV-infected Adults and Adolescents. Guidelines for prevention and treatment of opportunistic infections in HIV-infected adults and adolescents: 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. Department of Health and Human Services. https://aidsinfo.nih.gov/guidelines/html/4/adult-and-adolescent-oi-prevention-and-treatment-guidelines/0. Updated May 3, 2016. Accessed July 6, 2016.
3. Global Health - Division of Parasitic Diseases and Malaria. Treatment of malaria: guidelines for clinicians (United States). Centers for Disease Control and Prevention. http://www.cdc.gov/malaria/diagnosis_treatment/treatment.html. Updated July 2013. Accessed July 6, 2016.
4. Bactrim™ [package insert]. Philadelphia, PA: Mutual Pharmaceutical Company, Inc.; March 2005.
5. Sulfamethoxazole/trimethoprim. In: DRUGDEX® System [Internet database]. Greenwood Village, Colo: Thomson Micromedex. Updated periodically. Accessed September 28, 2015.
6. Pyrimethamine Drug Monograph. Clinical Pharmacology. Accessed October 2015. http://www.clinicalpharmacology-ip.com
7. Heller, HM. Toxoplasmosis in immunocompetent hosts. Weller PF (Ed), UpToDate, Waltham, MA. Accessed October 2015.

8. Gandhi RT. Toxoplasmosis in HIV-infected patients. Bartlett JG (Ed), UpToDate, Waltham, MA. Accessed October 2015
9. Torre D, Casari S, Speranza F, et al. Randomized trial of trimethoprim-sulfamethoxazole versus pyrimethamine sulfadiazine for therapy of toxoplasmic encephalitis in patients with AIDS. Italian Collaborative Study Group. Antimicrob Agents Chemother. 1998; 42(6): 1346-1349.

Reviews, Revisions, and Approvals	Date	Approval Date
Policy created.	11/15	11/15
No major content changes. Created workflow document. Updated references.	07/16	09/16