Clinical Policy: Pyrimethamine (Daraprim)

Reference Number: PA.CP.PMN.44
Effective Date: 01/18
Last Review Date: 07/17/19

Coding Implications
Revision Log

Description
Pyrimethamine (Daraprim®) is a folic acid antagonist.

FDA approved indication
Daraprim is indicated for the treatment of toxoplasmosis when used conjointly with a sulfonamide.

Policy/Criteria
** Provider must submit documentation (including office chart notes and lab results) supporting that member has met all approval criteria **

It is the policy of Pennsylvania Health and Wellness® that Daraprim is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Initial Therapy for Toxoplasmosis Infection – Active Disease (must meet all)**:**

1. Diagnosis of toxoplasmosis;
2. Prescribed by or in consultation with an infectious disease or HIV specialist;
3. Member meets one of the following (a or b):
   a. Age < 18 years;
   b. Failure of ≥ 10 days, or radiological deterioration within 7 days, of trimethoprim/sulfamethoxazole (TMP/SMX) at maximum indicated doses, unless member experiences clinically significant adverse effects or has contraindication(s) to TMP/SMX;
4. Daraprim is prescribed with sulfadiazine, clindamycin, atovaquone, or azithromycin and leucovorin;
5. Doses does not exceed (a or b):
   a. Immunocompromised member: initial loading dose of 200 mg, followed by ≤ 75 mg per day for treatment duration;
   b. Immunocompetent member: initial loading dose of 100 mg, followed by ≤ 50 mg per day for treatment duration.

Approval duration: duration of request or 8 weeks (whichever is less)

B. Primary Prophylaxis for Toxoplasmosis – Preventing 1st Episode (off-label) (must meet all)**:**

1. Diagnosis of HIV infection;
2. Prescribed by or in consultation with an infectious disease or HIV specialist;
3. Request is for prevention for toxoplasmosis;
4. CD4 count < 100 cells/mm^3 (*for age ≥ 6 years*) or CD4 cell percentage < 15% (*for age < 6 years*);
5. Seropositive for *Toxoplasma gondii* IgG or IgM;
6. Member is contraindicated or has clinically significant adverse effects to TMP/SMX;

7. Daraprim is prescribed with leucovorin and dapsone;
8. Dose does not exceed 75 mg per week.

Approval duration: 6 months

C. Other diagnoses/indications – Refer to PA.CP.PMN.53 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized)

II. Continued Therapy

A. Chronic Maintenance – Following Initial Therapy for Active Disease (off-label) (must meet all)**:**

1. Currently receiving medication via Pennsylvania Health and Wellness benefit or member has previously met initial approval criteria, or the Continuity of Care policy applies (*see PA.LTSS.PHAR.01*);
2. Member is HIV-infected with CD4 counts ≤ 200 cells/mm^3 at any time in the previous 6 months;
3. Adherence to antiretroviral therapy (ART) as evidenced by pharmacy claims history or office notes, or medical justification as to why the member is not being treated with ART;
4. Request does not exceed 50 mg per day.

Approval duration: 6 months

B. Primary Prophylaxis for Toxoplasmosis – Preventing 1st Episode (off-label) (must meet all)**:**

1. Currently receiving medication via Pennsylvania Health and Wellness benefit or member has previously met initial approval criteria, or the Continuity of Care policy applies (*see PA.LTSS.PHAR.01*);
2. Member is HIV-infected with CD4 counts ≤ 200 cells/mm^3 at any time in the previous 3 months;
3. Adherence to antiretroviral therapy (ART) as evidenced by pharmacy claims history or office notes, or medical justification as to why the member is not being treated with ART;
4. Daraprim is prescribed with leucovorin and dapsone;
5. Requested dose is ≤ 75 mg per week.

Approval duration: 3 months

C. Other diagnoses/indications (must meet 1 or 2)**:**

1. Currently receiving medication via Pennsylvania Health and Wellness benefit and documentation supports positive response to therapy, or the Continuity of Care policy applies (*see PA.LTSS.PHAR.01*); or
2. Refer to CP.PMN.53 if requested indication is NOT listed under section III (Diagnoses/Indications for which coverage is NOT authorized)

Approval duration: duration of request or 6 months (whichever is shorter)

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off-label use policy – CP.PMN.53 or evidence of coverage documents
B. Malaria

IV. Appendices/General Information

Appendix A: Abbreviation Key
ART: antiretroviral therapy
CDC: Centers for Disease Control and Prevention
HHS: Department of Health and Human Services
HIV: human immunodeficiency virus
TMP/SMX: trimethoprim/sulfamethoxazole

V. Dosage and Administration

VI. Indication	Dosing Regimen	Maximum Dose
Treatment of toxoplasmosis	Administered in combination with a sulfonamide; recommended dosing regimen varies per guideline referenced: <u>FDA labeling</u> Adults: 50-75 mg daily for 1-3 weeks depending on the response of the patient and tolerance to therapy, followed by one-half of the initial dose continued for an additional 4 to 5 weeks Pediatrics: 1 mg/kg/day divided into 2 equal daily doses for 2-4 days, followed by one-half of the initial dose continued for approximately 1 month <u>HHS guidelines</u> [*HIV-infected patients*] Initial loading dose of 200 mg, followed by 50 mg/day (if body weight ≤ 60 kg) or 75 mg/day (if body weight > 60 kg) for the remainder of treatment duration <u>CDC guidelines</u> [*immunocompetent patients*] Adult: Initial loading dose of 100 mg, followed by 25-50 mg/day for the remainder of treatment duration Pediatric: Initial loading dose of 2 mg/kg, followed by 1 mg/kg/day for the remainder of treatment duration	300 mg/day
Primary prophylaxis of toxoplasmosis*	50-75 mg/week PO in combination with a sulfonamide	75 mg/week

VI. Indication	Dosing Regimen	Maximum Dose
	Recommended treatment regimen is Daraprim 50 mg per week plus dapsone 50 mg once daily plus leucovorin 25 mg per week or Daraprim 75 mg plus dapsone 200 mg plus plus leucovorin 25 mg weekly	
Chronic maintenance therapy (secondary prophylaxis of toxoplasmosis)*	25-50 mg/day PO in combination with a sulfonamide	50 mg/day

**Off-label uses recommended by the HHS guidelines for prevention and treatment of opportunistic infections in HIV-infected adults and adolescents*

VII. Product Availability

Tablets: 25 mg

VIII. References

1. Daraprim Prescribing Information. Raleigh, NC: Salix Pharmaceuticals, Inc.; August 2017. Available at: www.daraprimdirect.com. Accessed April 2, 2018.
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 – Toxoplasma gondii encephalitis: 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. Available at https://aidsinfo.nih.gov/guidelines/html/4/adult-and-adolescent-opportunistic-infection/322/toxo. Updated July 25, 2017. Accessed April 2, 2018.
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 April 2, 2018.
4. Sulfamethoxazole/trimethoprim. In: DRUGDEX® System [Internet database]. Greenwood Village, Colo: Thomson Micromedex. Updated periodically. Accessed April 2, 2018.
5. 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.
6. Global Health - Division of Parasitic Diseases and Malaria. Resources for health professionals: toxoplasmosis. Centers for Disease Control and Prevention. Available at http://www.cdc.gov/parasites/toxoplasmosis/health_professionals/index.html. Updated April 10, 2017. Accessed April 2, 2018.

Reviews, Revisions, and Approvals	Date	Approval Date
4Q 2018 annual review: no significant changes; HIV specialist added as prescriber option; removed recommended regimens from continued criteria; references reviewed and updated.	08/18	

Reviews, Revisions, and Approvals	Date	Approval Date
3Q 2019 annual review: No changes per Statewide PDL implementation 01-01-2020	07/17/19	