Division: Pharmacy Policy	Subject: Prior Authorization Criteria
Original Development Date: Original Effective Date: Revision Date:	October 8, 2015 December 29, 2021

DARAPRIM® (pyrimethamine)

LENGTH OF AUTHORIZATION: Initial: 2 months Continuation of therapy: up to 6 months

INITIAL REVIEW CRITERIA:

- **Malaria Prophylaxis**
  - Although FDA-approved for the prophylaxis of malaria, the United States Centers for Disease Control and Prevention (CDC) does NOT recommend the use of pyrimethamine for this indication.
    - http://wwwnc.cdc.gov/travel/yellowbook/2016/infectious-diseases-related-to-travel/malaria#4904
  - Trial and failure of preferred agents (i.e., hydroxychloroquine sulfate, primaquine and mefloquine) **AND**
  - Trial and failure of generic Pyrimethamine before the use of the brand Daraprim® is required.

- **Malaria Treatment**
  - Although FDA-approved for the treatment of malaria, the CDC does NOT recommend pyrimethamine for the treatment of malaria.
    - http://www.cdc.gov/malaria/resources/pdf/treatmenttable.pdf
  - Trial and failure of preferred agents (i.e., hydroxychloroquine sulfate, primaquine and mefloquine) **AND**
  - Trial and failure of generic Pyrimethamine before the use of the brand Daraprim® is required.

- **Toxoplasmosis-Primary Prophylaxis**
  - Patient must have a diagnosis of HIV/AIDS **AND**
  - Patient must have a CD4 count <100 cells/microL **AND**
  - Patient must test positive for Toxoplasmosis gondii IgG antibodies **AND**
  - Intolerance to recommended first line agent TMP-SMX (trimethoprim-sulfamethoxazole); description of specific intolerance to TMP-SMX must be documented in progress notes **AND**
  - Documentation stating why atovaquone 1500 mg once daily is not acceptable for primary prophylaxis **AND**
  - Trial and failure of generic Pyrimethamine before the use of the brand Daraprim® is required.

- **Toxoplasmosis-AIDS associated-CNS**
  - Diagnosis made by an infectious disease specialist, neurologist or HIV specialist **AND**
  - Patient with a diagnosis of HIV/AIDS must have a CD4 count <100 cells/microL **AND**
  - Clinical syndrome of headache, fever and neurological symptoms must be present **AND**

- Submission of positive serum testing for Toxoplasmosis gondii IgG antibodies (not always present) **AND**
- Brain imaging (CT or MRI) demonstrating typical radiographic ring-enhancing lesions **AND**
- If patient is not already receiving antiretroviral treatment; orders to start antiretroviral treatment within at least two-three weeks of toxoplasmosis diagnosis **AND**
- Trial and failure of generic Pyrimethamine before the use of the brand Daraprim® is required.

- **Toxoplasmosis-AIDS related-Chronic Maintenance Therapy**
  - Patient has completed six weeks of active treatment for AIDS-related toxoplasmosis **AND**
  - CT scan or MRI documents improvement in the ring-enhancing lesions prior to initiating maintenance therapy **AND**
  - Patient has documented improvement in clinical symptoms documented in physical exam **AND**
  - Documentation that explains why a non-pyrimethamine based therapy is an inappropriate choice **AND**
  - Trial and failure of generic Pyrimethamine before the use of the brand Daraprim® is required.

- **Prevention and Treatment of Opportunistic Infections among HIV-Exposed and HIV-Infected Children**
  - Primary Prophylaxis in children with intolerance to first line SMZ-TMP: Pyrimethamine 1 mg/kg (maximum 25 mg) by mouth once daily plus either dapsone and leucovorin.
  - Secondary Prophylaxis: Pyrimethamine 1mg/kg or 15mg/m^2 (maximum 25mg) by mouth once daily plus sulfadiazine and leucovorin
  - Treatment: Pyrimethamine 2 mg/kg (maximum 50 mg) by mouth once daily for 2-3 days then 1 mg/kg (maximum 25 mg) by mouth once daily with leucovorin and sulfadiazine for up to 12 months **AND**
  - Trial and failure of generic Pyrimethamine before the use of the brand Daraprim® is required.

- **Toxoplasmosis-non-AIDS related**
  - Diagnosis by an infectious disease specialist **AND**
  - Trial and failure of generic Pyrimethamine before the use of the brand Daraprim® is required.

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CONTINUATION OF THERAPY:

- **Toxoplasmosis-Primary Prophylaxis**
  - Compliance to prescribed medication
  - Submit current CD4 counts. Once CD4 count >200 cells/microL for at least 3 months, discontinue.
    Restart primary prophylaxis if CD4 count <200 cells/microL

- **Toxoplasmosis- AIDS associated-CNS**
  - Compliance to prescribed medication
  - Improvement on brain imaging (CT or MRI)
  - Improvement of clinical symptoms

- **Toxoplasmosis-AIDS-related Chronic Maintenance Therapy**
  - Patient has a detectable HIV viral load AND
  - Patient has a CD4 count ≤ 200 cells/microL AND
  - Patient is compliant with antiretroviral treatment regimen
  - Discontinue chronic maintenance therapy when patient has no signs or symptoms of toxoplasmosis infection and CD4 count > 200 cells/microL for greater than six months while receiving an antiretroviral treatment regimen

DOSING & ADMINISTRATION:

- Refer to product labeling https://www.accessdata.fda.gov/scripts/cder/daf/
- Available as 25mg tablets.