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

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)

- **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)

- **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

- **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

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- **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

- **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

- **Toxoplasmosis-non-AIDS related:**
  - Diagnosis by an infectious disease specialist

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 $\leq$ 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:

- **Malaria Prophylaxis:** 25mg by mouth once a week. Continue for 10 weeks after exposure only for chloroquine resistant areas.

- **Malaria Treatment: monotherapy**-50mg by mouth once daily for 2 days, followed by prophylaxis therapy; **combination therapy**-25mg by mouth once daily for 2 days followed by prophylaxis therapy

- **Toxoplasmosis-Primary Prophylaxis:**
  - Pyrimethamine 50mg once a week with leucovorin (25mg once weekly) and dapsone (50mg once daily) **OR**
  - Pyrimethamine 75mg once a week with leucovorin (25mg once weekly) and dapsone (200mg once weekly) **OR**,
  - Pyrimethamine 25mg once daily with leucovorin (10mg once daily) and atovaquone (1500mg once daily)

- **Toxoplasmosis-AIDS-related CNS:**
  - 200mg by mouth for one dose, then
  - If less than 60kg: pyrimethamine 50 mg daily by mouth with sulfadiazine 1,000 mg every six hours and leucovorin 10 mg-50 mg once daily
  - If 60kg or greater: pyrimethamine 75 mg daily by mouth with sulfadiazine 1,500 mg every six hours and leucovorin 10mg -50 mg once daily
  - Treatment should be given daily for six weeks. If incomplete response at six weeks or clinical or radiological disease is extensive duration may be longer.

- **Toxoplasmosis-AIDS related-Chronic Maintenance Therapy**
  - Pyrimethamine 25 mg -50 mg once daily with sulfadiazine 2,000 mg to 4,000 mg per day (divided in two to four doses) plus leucovorin 10 mg to 25 mg once daily

- **Toxoplasmosis-non-AIDS related**
  - Pyrimethamine 50mg - 75mg by mouth once daily with sulfadiazine 1,000 mg to 4,000mg daily for one to three weeks then reduce dose for each drug by about one-half and continue for an additional four to five weeks

- **Availability:**
  - 25 mg tablets

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References:

Guidelines for the Treatment of Malaria in the United States: Available at: http://www.cdc.gov/malaria/resources/pdf/treatmenttable.pdf

Centers for Disease Control and Prevention Yellow Book Infectious Diseases Related to Travel: Available at: http://wwwnc.cdc.gov/travel/yellowbook/2016/infectious-diseases-related-to-travel/malaria#4904

Florida/Caribbean AIDS Education and Training Center: Opportunistic Infections in HIV/AIDS: Available at: http://www.fcaetc.org/treatments/OIs.pdf

AIDSinfo Guidelines for the Prevention and Treatment of Opportunistic Infections Among HIV-Exposed and HIV-Infected Children: Available at: https://aidsinfo.nih.gov/contentfiles/lvguidelines/oi_guidelines_pediatrics.pdf