Ciprofloxacin is a second-line agent that can be used for individuals with sulfa allergy and an inability to obtain pyrimethamine **(CI).** In a randomized, controlled trial in Haiti, ciprofloxacin 500 mg orally (PO) twice daily for 7 days was less effective than PO TMP-SMX but may have modest activity against *C. belli*.[31]

Special Considerations With Regard to Starting ART

There are limited data on the effectiveness of ART for *C. belli* infection in the setting of HIV coinfection.[3,23,30] Immune reconstitution with ART may result in fewer relapses of cystoisosporiasis, and immune reconstitution inflammatory syndrome (IRIS) has not been reported. Therefore, for people with HIV and cystoisosporiasis, TMP-SMX therapy and ART should both be started as soon as possible, and ART initiation should not be deferred **(AIII).**

Monitoring of Response to Therapy and Adverse Events (Including IRIS)

People treated for cystoisosporiasis should be monitored for clinical response and adverse events. In people with HIV, TMP-SMX therapy is commonly associated with side effects, such as rash, fever, leukopenia, thrombocytopenia, elevated transaminase levels, and hyperkalemia. For ciprofloxacin, side effects beyond gastrointestinal issues include prolong QT intervals and tendonitis and tendon rupture. For pyrimethamine, side effects include bone marrow suppression. As noted earlier, IRIS has not been described in this population.

Managing Treatment Failure

If symptoms worsen or persist despite approximately 5 to 7 days of TMP-SMX therapy, the possibilities of nonadherence, malabsorption, and concurrent other gastrointestinal infections or enteropathies should be considered and the TMP-SMX regimen (daily dose, duration, and mode of administration) should be reevaluated **(AIII).**[38] For people with documented sulfa intolerance or in whom treatment fails, use of a potential alternative agent (typically pyrimethamine) should be considered **(BIII).**

The effectiveness of albendazole,[37,39,40] nitazoxanide,[41,42] doxycycline,[43] and the macrolides roxithromycin and spiramycin,[33,44,45] have not been substantiated. Metronidazole, quinacrine, iodoquinol, paromomycin, and furazolidone appear to be ineffective.[14,33,34,36,44]

Preventing Recurrence

People with HIV with CD4 counts <200 cells/mm^3 should receive secondary prophylaxis (chronic maintenance therapy) with TMP-SMX **(AI),** which is also protective against *Pneumocystis jirovecii* and *Toxoplasma gondii* infections. Based on observational studies in Haiti, approximately 50% of patients who did not receive secondary prophylaxis had symptomatic recurrences approximately 2 months after completing a course of TMP-SMX therapy. These relapses rapidly responded to retreatment and secondary prophylaxis decreased the risk of another relapse.[6,7,31] In a randomized, placebo-controlled trial in Haiti, no symptomatic recurrences were noted in people who received maintenance therapy with thrice-weekly TMP-SMX (160/800 mg) **(AI).**[7] Daily TMP-SMX (160/800 mg) **(AIII)** and thrice-weekly TMP-SMX (320/1600 mg) have been effective **(BIII)**[5,16]; however, clinical and parasitological relapses despite maintenance TMP-SMX therapy and ART have been reported.[23] Many of these studies were conducted in the pre-ART era. It is unclear if recurrent *Cystoisospora* infections are due to relapse or reinfection.