**MANAGEMENT AND TREATMENT OF IRIS**

- Clinicians should initiate appropriate treatment of opportunistic infections (OIs), as well as symptomatic treatment and supportive care according to the severity of immune reconstitution inflammatory syndrome (IRIS). (A3)
- Clinicians should not interrupt antiretroviral therapy (ART) except in severe, life-threatening cases of IRIS. (A3)

**Severe IRIS**

- Clinicians should consult with an experienced HIV care provider for the management of severe IRIS, including the decision of whether to interrupt ART if IRIS is severe. (A3)
- Clinicians should treat patients with severe IRIS that is not caused by either cryptococcal meningitis or Kaposi’s sarcoma (KS) with 1 to 2 mg/kg prednisone, or the equivalent, for 1 to 2 weeks, followed by a period of tapering dose that is individualized. (B3)
- Clinicians should not use corticosteroids for management of cryptococcal meningitis or in patients with KS. (A2)
- Clinicians should closely monitor patients receiving corticosteroids for the development of OIs, including cytomegalovirus (CMV) retinitis and TB disease. (A3)

**PREVENTION OF IRIS**

- ART should not be interrupted in patients with IRIS except in life-threatening cases, usually associated with CNS-IRIS, in which corticosteroids did not result in improvement.
- Steroids should not be used routinely as induction therapy in treatment of cryptococcal IRIS.
- Steroids are not effective in reducing intracranial pressure.
- Before initiating ART in patients who have TB meningitis, extrapulmonary TB, CMV retinitis, or cryptococcal infection, clinicians should consult with a care provider who is experienced in managing patients with HIV infection in the setting of active OIs.
- Finding an experienced HIV care provider: The Clinical Education Initiative (CEI) line, which is available through the New York State Department of Health, provides access to providers with experience in managing all aspects of HIV infection. Call 866-637-2342.

**ALL RECOMMENDATIONS P.3**

**PRESENTATION AND DIAGNOSIS**

- Clinicians should include immune reconstitution inflammatory syndrome (IRIS) as part of the differential diagnosis when inflammatory signs or symptoms occur following recent initiation of, re-initiation of, or a change to an antiretroviral therapy (ART) regimen. (A3)
- In assessing patients for IRIS, clinicians should exclude HIV disease progression, new infections, and drug reactions as underlying causes for inflammatory signs or symptoms. (A3)

**ALL RECOMMENDATIONS P.4**

**KEY POINTS**

- Any patient who initiates ART should be monitored closely for the development of opportunistic infections, including cytomegalovirus (CMV) retinitis and TB disease.

**HIV CLINICAL RESOURCE ¼-FOLDED GUIDE**

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**MANAGEMENT OF IMMUNE RECONSTITUTION INFLAMMATORY SYNDROME (IRIS)**

NYSDOH AIDS INSTITUTE HIV CLINICAL GUIDELINE JUNE 2017

**ALL RECOMMENDATIONS P.3**

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### SUMMARY OF RECOMMENDED TIMING OF ART INITIATION

<table>
<thead>
<tr>
<th>Opportunistic Infection (OI)</th>
<th>Timing of ART Initiation after Starting OI Treatment</th>
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</thead>
<tbody>
<tr>
<td>Cryptosporidiosis Microsporidiosis Progressive multifocal leukoencephalopathy (PML) Kaposi’s sarcoma (KS) Pneumocystis jiroveci pneumonia (formerly PCP) Hepatitis B virus (HBV) infection Hepatitis C virus (HCV) infection Pulmonary tuberculosis (TB) Other serious bacterial infections</td>
<td>Within 2 weeks of starting treatment for an OI or as soon as the patient is clinically stable</td>
</tr>
</tbody>
</table>
| Pulmonary TB | • CD4 count >50 cells/mm³: Initiate ART as soon as the patient is clinically stable after initiating TB therapy, but no more than 12 weeks later  
• CD4 count <50 cells/mm³: Initiate ART within the first 2 weeks after initiating TB therapy |
| Extrapulmonary TB | • Optimal timing has not been established; consult with an experienced HIV care provider |
| TB meningitis | • Optimal timing has not been established; consult with an experienced HIV care provider |
| Cryptococcal meningitis | • Delay 2 to 10 weeks after starting antifungal therapy  
• Optimal timing has not been established; consult with an experienced HIV care provider |
| Cryptococcal infection other than meningitis | • Delay at least 2 weeks after starting antifungal therapy  
• Optimal timing has not been established; consult with an experienced HIV care provider |
| CMV retinitis | • Immediate ART is not recommended  
• Optimal timing has not been established; consult with an experienced HIV care provider |

### MAJOR AND MINOR PRESENTATIONS OF IMMUNE RECONSTITUTION INFLAMMATORY SYNDROME (IRIS)

<table>
<thead>
<tr>
<th>Opportunistic Infection (OI)</th>
<th>IRIS Signs/Symptoms</th>
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<tbody>
<tr>
<td><strong>Major Presentations</strong></td>
<td></td>
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</table>
| Tuberculosis (TB) | • Patients responding to TB treatment may have worsening of pulmonary symptoms, X-ray findings that suggest worsening of TB disease, enlarging lymph nodes causing airway obstruction, or meningeal symptoms  
• Enlarging tuberculoma or pericardial effusions have been described [18]  
• TB-IRIS can also result in hepatotoxicity, which may be difficult to distinguish from medication-induced toxicity [54]  
• TB-IRIS may occur in patients with undiagnosed multidrug-resistant TB [55] |
| Mycobacterium avium complex (MAC) | • May present as pulmonary disease or systemic inflammation that is indistinguishable from active MAC  
• Atypical presentations, such as localized lymphadenitis or endobronchial mass lesions, may occur [56]; osteomyelitis is an atypical late manifestation [53]  
• Patients with MAC-IRIS may not be bacteremic and may have no known history of MAC diagnosis [56] |
| Cryptococcal meningitis | • Usually presents as worsening of meningitis symptoms [2,50,51,57-59], including possible rapid hearing and/or vision loss, |
| Cytomegalovirus (CMV) retiniti | • Presents as retinitis, vitritis, or uveitis (variable timing, with median time to immune reconstitution vitritis 20 weeks after ART initiation in one study) [14]:  
  - Retinitis is inflammation that is usually at the site of previous CMV retinitis lesions  
  - Uveitis and vitritis are the presence of inflammatory cells in the eye as a result of IRIS and may help to distinguish IRIS from active CMV retinitis [14]  
  - CMV-IRIS in the eye can cause rapid and permanent vision loss |
| Hepatitis B or C virus | • Transient elevations in transaminases may occur after initiation of ART with immune reconstitution and can be difficult to distinguish from drug-induced hepatitis [60-64]  
• Hepatic flares are usually mild and self-limited but can result in decompensation in someone with preexisting cirrhosis [60-64] |
| Progressive multifocal leukoencephalopathy (PML) | • PML lesions may be unmasked or worsen and could appear as new or worsening focal neurologic deficits or lesions on MRI [59,65,66] |
| Kaposi’s sarcoma (KS) | • Presents as worsening of KS  
• Cutaneous lesions are the most common presentation; other signs include lymphedema and oral, gastric, lung, genital, or conjunctival lesions [18,67]  
• Fatal cases of KS-IRIS have been reported [68,69] |
| Cerebral toxoplasmosis | • May present as cerebral abscess (also known as toxoplasmosis encephalitis) or, rarely, diffuse encephalitis or chorioretinitis [70] |
| Autoimmune diseases | • Preexisting sarcoidosis may be exacerbated [12]  
• Late presentations of Grave’s disease have been reported 8 to 33 months after ART initiation [71] |
| **Minor Presentations**       |                     |
| Herpes simplex virus (HSV) and varicella zoster virus (VZV) | • HSV and VZV can reactivate after initiation of ART, even in patients without previously diagnosed disease  
• Presentations are usually similar to non-IRIS disease; however, IRIS may worsen a patient’s symptoms |
| Nonspecific dermatologic | • A number of dermatologic manifestations, such as folliculitis and oral and genital warts, may appear or worsen during immune reconstitution |