Monitoring of Nonsteroidal Immunosuppressive Drugs in Patients With Lung Disease and Lung Transplant Recipients

American College of Chest Physicians
Evidence-Based Clinical Practice Guidelines

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The objective of this guideline is to provide recommendations for monitoring the use of these drugs so that clinically significant side effects can be either avoided or recognized in a timely fashion. This guideline intentionally does not provide any recommendations concerning indications for use of these drugs. Rather, it should be used exclusively to achieve maximal patient safety when these medications are prescribed. For some drugs, sufficient information related solely to treating pulmonary diseases was available. For other drugs, however, recommendations were partially or entirely abstracted from non-pulmonary studies. As the guideline focuses on common and unique side effects associated with specific drugs, it can provide important information to both physicians and patients.
ACCP Grading System

- Consensus Component – Determined by Panel
  - 1 – Strong
  - 2 – Weak

- Evidence Component – Determined by Literature
  - A – High
  - B – Moderate
  - C – Low
3.1a. For patients who will undergo anti-TNF-a therapy, a chest radiograph is recommended prior to treatment (Grade 1C).
3.1b. For patients who will undergo anti-TNF-a therapy, a tuberculin skin test is recommended to screen for latent TB prior to treatment (Grade 1C).
3.1c. For patients who will undergo anti-TNF-a therapy and present with a chest radiograph consistent with prior TB or a positive tuberculin skin test and/or are high-risk individuals, active TB infection should be excluded prior to treatment with adalimumab (Grade 1C), etanercept (Grade 1B), or infliximab (Grade 1B).
3.1d. For patients with latent Mycobacterium tuberculosis, active prophylactic treatment following published guidelines before initiation of anti-TNF-a therapy is recommended (Grade 1B).
3.1e. For patients with latent M tuberculosis who will undergo anti-TNF-a therapy, close monitoring for TB is recommended for up to 6 months after discontinuing therapy (Grade 1C).
3.1f. For patients who develop symptoms indicative of TB, prompt evaluation for active disease is recommended (Grade 1C).
3.1g. For patients with known grade III or IV New York Heart Association class heart failure, administration of adalimumab (Grade 1C), etanercept (Grade 1C), and infliximab (Grade 1B) is not recommended.
3.1h. For patients with a history of congestive heart failure (CHF) who undergo anti-TNF-a therapy, close observation for CHF exacerbation is recommended (Grade 1C).
3.1i. For patients with a history of demyelinating disease, administration of etanercept is not recommended (Grade 1C), and administration of adalimumab and infliximab is not suggested (Grade 2C).
3.1j. For patients with no history of demyelinating disease who undergo anti-TNF-a therapy and experience symptoms or display signs of a demyelinating process, discontinuation of therapy is suggested (Grade 2C).
3.1k. For patients who undergo anti-TNF-a therapy and develop symptoms of a lupus-like disorder, discontinuation of therapy is suggested (Grade 2C).
3.1. For patients who will undergo anti-TNF-α therapy and who are at risk for viral hepatitis, serologic screening for hepatitis B is recommended prior to treatment (Grade 1C).
3.1m. For patients who have hepatitis B virus infection, anti-TNF-a therapy should not be administered (Grade 1C).
3.1n. For patients who undergo anti-TNF-a therapy and develop unresolved infections, discontinuation of treatment until the infection is resolved is recommended (Grade 1B).
3.1o. For patients who are pregnant, administration of anti-TNF-a therapy is used only if alternatives are not able to be used (Grade 2C).
3.2a. For patients who will undergo CNI therapy, the monitoring of drug concentrations, BP, glucose, potassium, magnesium, lipids, CBC count, and renal function is recommended (Grade 1B).
3.2b. For patients who undergo CNI therapy, monitoring of drug levels when CYP3A4 inducers or inhibitors are added or stopped and adjusting doses are recommended when using cyclosporin A (Grade 1A) or tacrolimus (Grade 1B) therapy.
3.2c. For lung transplant recipients receiving CNI therapy who develop renal dysfunction, a reduction in the target dose concentration is suggested (Grade 2C).
3.3a. For patients who undergo antilymphocyte antibody therapy, monitoring for infusion reactions is recommended (Grade 1B).
3.3b. For patients who undergo antithymocyte globulin or muromonab therapy, monitoring of CBC counts and liver function tests is recommended during therapy (Grade 1B).
3.3c. For patients with lung disease and lung transplant recipients who will undergo anti-thymocyte globulin or muromonab therapy, laboratory evaluation for host antibodies (where available) before reinstitution of therapy is suggested (Grade 2C).
3.3d. For patients who undergo muromonab therapy, monitoring for pulmonary edema and systemic inflammatory response syndrome during therapy is recommended (Grade 1B).
3.4a. For patients who undergo IL-2 receptor antagonist therapy, monitoring for infusion reactions is recommended (Grade 1C).
3.4b. For patients who undergo IL-2 receptor antagonist therapy, monitoring of renal function, CBC counts, and infection is recommended (Grade 1C).
3.4c. For patients who undergo IL-2 receptor antagonist therapy, the simultaneous use of either basiliximab (Grade 1C) or daclizumab (Grade 1B) with antilymphocyte antibodies is not recommended.
3.5a. For patients who will undergo concurrent therapy with azathioprine and allopurinol, a reduction in dose of azathioprine is recommended (Grade 1A).
3.5b. For patients who undergo azathioprine therapy, obtaining CBC counts and renal/hepatic profiles every 1 to 3 months is recommended (Grade 1B).
3.5c. For patients who will undergo cyclophosphamide therapy, monitoring of CBC count, renal profile, and urinalysis at least monthly for dose adjustment is recommended (Grade 1B).
3.5d. For patients who will undergo cyclophosphamide therapy, increased fluid intake (eg, in addition to normal intake in adults; additional volume given to children needs to be calculated on the basis of body weight) on the days of therapy is recommended (Grade 1C).
3.5e. For patients who undergo or have undergone cyclophosphamide therapy and develop hematuria, further evaluation is recommended (Grade 1B).
3.5f. For patients who will undergo leflunomide or methotrexate therapy, screening for the use of alcohol and chronic viral hepatitis prior to treatment is recommended (Grade 2C).
3.5g. For patients who undergo methotrexate or leflunomide therapy, performance of liver function tests and CBC counts is recommended (Grade 1C).
3.5h. For patients who undergo methotrexate therapy, folic acid supplementation is recommended (Grade 1A).
3.5i. For patients who undergo leflunomide therapy and develop neuropathic symptoms, prompt consideration of discontinuing therapy and washing out with cholestyramine is recommended (Grade 1C).
3.5j. For patients who undergo methotrexate (Grade 1B) or leflunomide (Grade 1C) therapy and develop new or worsening signs or symptoms of lung disease, further evaluation is recommended.
3.5k. For patients who undergo methotrexate therapy and develop persistently elevated liver transaminases above their own baseline, cessation of treatment or evaluation by liver biopsy is recommended (Grade 1B).
3.5l. For patients with renal insufficiency, ascites, or pleural effusions who undergo methotrexate therapy, decreased methotrexate clearance may be present, and dose reduction may be required (Grade 2C).
3.5m. For patients who undergo mycophenolic acid therapy and develop adverse GI affects, including diarrhea, interruption of therapy or reduction in dose is recommended (Grade 1B).
3.5n. For patients who undergo mycophenolic acid therapy and develop signs or symptoms of progressive multifocal leukoencephalopathy, cessation of treatment is suggested (Grade 2C).
3.6a. For patients who will undergo mTOR inhibitor therapy, obtaining cholesterol and triglyceride levels prior to treatment is recommended (Grade 1B).
3.6b. For patients who present with an abnormal elevation of fasting triglycerides, avoidance of mTOR therapy or careful monitoring of triglycerides is recommended (Grade 1B).
3.6c. For patients who undergo mTOR therapy, monitoring for hyperlipidemia is recommended (Grade 1A).
3.6d. For patients who undergo mTOR therapy, monitoring of CBC counts, creatinine, and BP is recommended (Grade 1B).
3.6e. For patients who undergo sirolimus therapy, monitoring of drug concentration is recommended (Grade 1B).
3.6f. For lung transplant recipients scheduled to undergo sirolimus therapy, administration of sirolimus during the early perioperative period is contraindicated due to the risk of airway dehiscence (Grade 1A).
3.6g. For patients who undergo sirolimus therapy and are at risk for poor wound healing, consideration of dose adjustments or an alternative therapy to lower this risk is suggested (Grade 2C).
3.6h. For patients who undergo sirolimus therapy and develop new or worsening respiratory symptoms or signs, an evaluation for sirolimus-induced pulmonary toxicity is recommended (Grade 1B).
3.7a. For patients receiving hydroxychloroquine and chloroquine, an eye examination at least once per year is suggested (Grade 2B).
3.7b. For patients who undergo imatinib mesylate therapy, monitoring of CBC and hepatic function is suggested (Grade 2C).