Leflunomide Drug Monitoring

Indications for Ordering
Therapeutic monitoring and evaluating full elimination of the drug (eg, toxicity, pregnancy)

Test Description
High-performance liquid chromatography/mass spectrometry

Tests to Consider
Leflunomide Metabolite, Serum or Plasma 2007460
- Predose (trough) concentration at steady state should be assessed
- Trade name – Arava

Disease Overview
Clinical issues
Leflunomide is used in the treatment of
- Rheumatoid arthritis
- Individuals with risk of allograft rejection due to resistant cytomegalovirus infection
- Individuals with BK virus nephropathy
- Renal transplant individuals with chronic allograft dysfunction

Physiology
- Rapidly and essentially completely converted to bioactive metabolite, teriflunomide (A77 1726)
- Teriflunomide has both immunosuppressive and antiviral effects
  - Inhibits pyrimidine production
  - Inhibits T-cell proliferation
- Following oral administration, peak levels of teriflunomide occur between 6-12 hours

Drug profile
- Pharmacokinetics are variable
  - Drug monitoring may assist in optimizing therapy
- Drug has long half-life (>2 weeks)
  - All monitoring should be performed when steady state is achieved
- Potential risk for teratogenesis
  - Pregnancy should be avoided prior to the completion of the enhanced drug elimination procedure
    - Enhanced drug elimination should be performed until results indicate plasma teriflunomide concentrations of <0.020 μg/mL on 2 separate occasions at least 14 days apart
- Liver disease
  - Leflunomide not recommended if
    - Preexisting acute or chronic liver disease is present
    - Serum alanine aminotransferase (ALT) >2 times upper limit of normal
  - Severe liver injury, including fatal liver failure, has been reported in individuals treated with leflunomide

Test Interpretation
Sensitivity/specificity
- Analytical sensitivity – 0.005 μg/mL (5.0 ng/mL)
  - Interferences from commonly used drugs and associated metabolites have not been observed

Results
- Concentration is reported
- Therapeutic and toxic ranges are not well established
  - Proposed range is 50.0-100.0 μg/mL
    - >40.0 μg/mL associated with improved individual outcome

Limitations
Adverse drug reactions (eg, diarrhea, hypertension, liver toxicity) do not correlate well with serum concentrations