# 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