THERAPEUTIC DRUG MONITORING OPTIONS

FOR RHEUMATOID ARTHRITIS AND OTHER RHEUMATIC DISORDERS

LabCorp

LabCorp offers companion diagnostics to help physicians optimize **management of rheumatoid arthritis and other rheumatic disorders.**

Drug Monitoring Benefits

- Laboratory assays help monitor drug concentration levels to assist physicians in dosing and frequency of treatment.
- Testing may help identify those patients who fail therapy or have diminished response as a result of development of antibody to the drug.
- Tests to help indicate whether or not a patient has achieved an expected therapeutic level on a specific dosage protocol, and may be useful in ongoing patient management.[1]

DMARDs

One of the most common DMARDs used to treat RA and other rheumatic conditions is methotrexate (MTX).[2] It may help to decrease the pain and inflammation of arthritis, and may also help to decrease damage to joints and long-term disability.[3]

Therapeutic drug monitoring may be helpful with respect to patient compliance, individual pharmacodynamics and clinical response.[4]

Methotrexate Polyglutamates (MTXpgsRA) Test

- About 30% to 40% of RA patients do not adequately respond to methotrexate treatment.[1]
- A test indicating whether or not a patient has achieved an expected therapeutic level on a specific dosage protocol can be useful in ongoing patient management.
- It is considered important to work to attain dose optimization when treating patients on methotrexate.[5]
- Testing may be ordered at any time during therapy and should be conducted at least 36 hours after last dose of methotrexate.
- The test report includes a measure of each polyglutamate species, along with interpretive guide.

Thiopurine Drug

Thiopurine-related testing may be used to assess dosing before and during treatment, as well as to identify patients who may be at risk for drug toxicity.[6] Because of the potentially severe bone marrow toxicity that can occur even with standard thiopurine dosages in patients with TPMT enzyme deficiency, the FDA-approved label recommends consideration for testing for the most common TPMT gene mutations (genotype) or TPMT activity (phenotype) before beginning treatment.

TPMT Genetic Test

- Utilize prior to treatment to identify common mutations that cause low TPMT activity
- Clinical sensitivity approximately 95% for TPMT mutations *2, *3A, *3B, and *3C[7]
- Interpretive reports support initial dosing decisions

TPMT Activity Test

- Utilize prior to treatment as a screen for low TPMT activity
- May detect rare clinically relevant mutations that are not detected in the TPMT Genetic Test
- Interpretive reports support initial dosing decisions

Thiopurine Metabolites Test

- Utilize during treatment to help reach and maintain therapeutic goal[6]
- Assists with evaluating unresponsive patients[6]
- Monitors responsive patients to avoid potential toxicity[6]

Rheumatoid arthritis

Rheumatoid arthritis (RA) affects an estimated 1.5 million people in the United States.[3] Although treatment is multifaceted, medications play an important role in patient management. Among the therapy choices physicians may consider for treatment are disease-modifying anti-rheumatic drugs (DMARDs) and biologic therapy.[3]

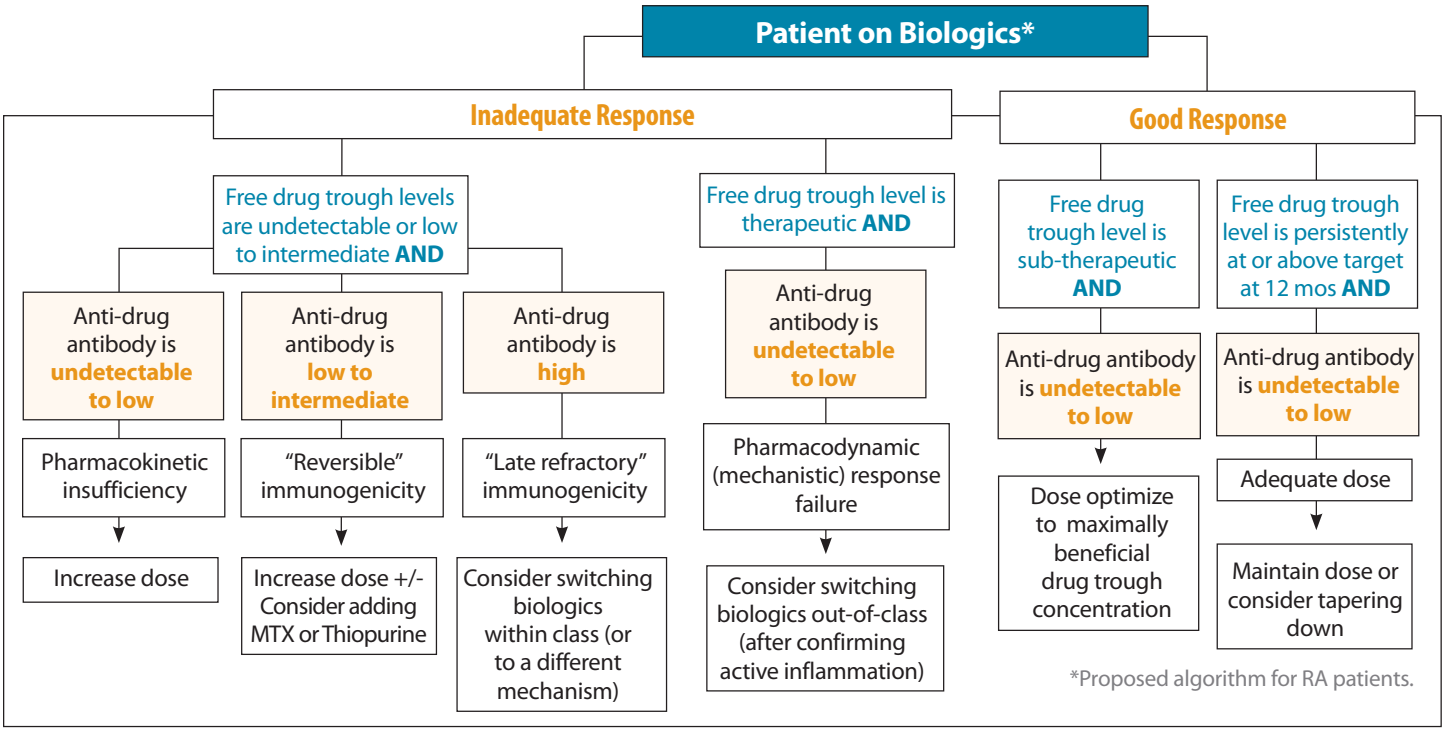
Biologic Therapy

Biologics are a class of drugs that are used to treat inflammatory conditions such as rheumatoid arthritis (RA), psoriatic arthritis (PA), plaque psoriasis (PP), ankylosing spondylitis (AS) and, juvenile idiopathic arthritis (JIA). These drugs may help to reduce inflammation and limit disease progression in RA and several other diseases.

DoseASSURE™, LabCorp's portfolio of biologics monitoring assays, offers serum measurement of drug and antibody levels for adalimumab, certolizumab, etanercept, infliximab, rituximab, golimumab, and ustekinumab. Testing may be ordered at any time during therapy.

Serum measurements of biologic drug and anti-drug antibodies can help:

- Characterize patients who maintain versus lose responsiveness to therapy[8,9]
- Optimize dosing and frequency of treatment
- Identify patients who fail therapy or have diminished response as a result of antibody development by providing clinically valid antibody results even in the presence of circulating drug.[10-13]



A consensus has yet to be reached about target ranges and maximally effective concentrations.[14]
Optimal drug concentration is patient-specific and depends on disease and desired therapeutic endpoint.

Superior Service

- Comprehensive rheumatology menu
- Broad capabilities in autoimmune testing
- Specialized assays for treatment monitoring
- Multiple connectivity options
- Extensive network of managed care health plans
- More than 1900 patient service centers nationwide

Test Name	Test No.	Reference Intervals	Methodology
Adalimumab and Anti-Adalimumab Antibody (Serial Monitor), *Dose*ASSURE™ ADL	**503890**	Concentration: <0.6 µg/mL. Results of 0.6 or higher indicates detection of adalimumab. **Note:** measures free drug concentration. Antibodies: <25 ng/mL Results of 25 or higher indicate detection of anti-adalimumab antibodies. All positive antibody results are verified by confirmatory test. <100 ng/mL Low antibody titer, no significant impact on free drug level 101-300 ng/mL Intermediate antibody titer, variable impact on free drug level. >301 ng/mL High antibody titer, significant impact on free drug level	Electrochemiluminescence Immunoassay (ECLIA)
Certolizumab and Anti-Certolizumab Antibody, *Dose*ASSURE™ CTZ	**504627**	Concentration: <1.0 ug/mL. Results of 1.0 or higher indicates detection of certolizumab. **Note:** measures free drug concentration. Antibodies: <40 ng/mL Results of 40 or higher indicate detection of anti-certolizumab andibody.	Electrochemiluminescence Immunoassay (ECLIA); Surface Plasmon Resonance (SPR)
Etanercept and Anti-Etanercept Antibody (Serial Monitor), *Dose*ASSURE™ ETN	**504245**	Concentration: <0.2 µg/mL. Results of 0.2 or higher indicates detection of etanercept. **Note:** measures free drug concentration. Antibodies: <75 ng/mL. Results of 75 or higher indicate detection of anti-etanercept antibodies.	Electrochemiluminescence immunoassay (ECLIA); enzyme-linked immunosorbent assay (ELISA)
Golimumab and Anti-Golimumab Antibody, *Dose*ASSURE™ GOL	**504563**	Concentration: <0.5 µg/mL. Results of 0.5 or higher indicate detection of golimumab. **Note:** measures free drug concentration Antibodies: <20 ng/mL. Results of 20 or higher indicate detection of anti-golimumab antibodies.	Electrochemiluminescence Immunoassay (ECLIA)
Infliximab and Anti-Infliximab Antibody (Serial Monitor), *Dose*ASSURE™ IFX	**503770** **503870**	Concentration: <0.4 µg/mL. Results of 0.4 or higher indicate detection of infliximab. Antibodies: <22ng/mL. Results of 22 or higher indicate detection of anti-infliximab antibodies. All positive antibody results are verified by confirmatory test. <200 ng/mL Low antibody titer, no significant impact on free drug level 201-1,000 ng/mL Intermediate antibody titer, variable impact on free drug level >1,001 ng/mL High antibody titer, significant impact on free drug level	Electrochemiluminescence Immunoassay (ECLIA)
Methotrexate polyglutamates	**504104**	<20 nmol/L minimal level of response >74 nmol/L level of expected response	High-pressure liquid chromatography/tandem mass spectrometry (HPLC/MS-MS)
Rituximab and Anti-Rituximab Antibody, *Dose*ASSURE™ RTX	**504355**	Concentration: <2.0 µg/mL. Results of 2.0 or higher indicates detection of rituximab. **Note:** measures free drug concentration. Antibodies: <25 ng/mL. Results of 25 or higher indicate detection of anti-rituximab antibodies.	Electrochemiluminescence immunoassay (ECLIA); chemiluminescence immunoassay (CLIA)
Thiopurine Metabolites	**503800**	**6-TGN** Suboptimal dosing: <235 pmol 6-TG/8x108 RBC Optimal dosing: 235-450 pmol 6-TG/8x108 RBC Increasing risk for myelotoxicity and leukopenia: >450 pmol 6-TGN/8x108 RBC **6-MMPN** Hepatotoxicity risk: >5700 pmol 6-MMP/8x108 RBC	Whole blood washing and red blood cell harvesting/counting. LC/MS-MS after acidic hydrolysis.
Thiopurine Methyltransferase (TPMT), Enzyme Activity, Erythrocytes	**510750**	Normal: 15.1-26.4 units/mL RBC. Heterozygous for low TPMT variant: 6.3-15.0 units/mL. RBC Homozygous for low TPMT variant: <6.3 units/mL RBC	Enzymatic endpoint/liquid chromatography/tandem mass spectrometry LC/MS-MS
Thiopurine Methyltransferase (TPMT) Genotyping	**504142**	Normal: Two TPMT*1 alleles. Heterozygous for low TPMT variant: One TPMT*1 allele and one mutant allele (TPMT*2, *3A, *3B, or *3C). Homozygous for low TPMT variant: Two mutations (TPMT*2, *3A, *3B, or *3C)	PCR and multiplex minisequencing
Ustekinumab and Anti-Ustekinumab Antibody, *Dose*ASSURE™ UST	**504594**	Concentration: <0.1 µg/mL. Results of 0.1 or higher indicate detection of ustekinumab. **Note:** measures free drug concentration Antibodies: <40 ng/mL. Results of 40 or higher indicate detection of anti-ustekinumab antibodies.	Electrochemiluminescence Immunoassay (ECLIA)

For complete test information, including specimen requirements, methodology, CPT coding, and ruo/iuo status, please visit **www.labcorp.com/testmenu.**

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