Optimizing Treatment in the Patient with Rheumatoid Arthritis

The National Committee for Quality Assurance and the Center for Medicaid and Medicare Services evaluates health plans based on the Healthcare Effectiveness Data and Information Set (HEDIS®[1]). HEDIS includes a set of clinical performance measures that are reported to the public, allowing the public to have the information necessary for a comparison of health plan performance.

The *Disease-Modifying Anti-Rheumatic Drug Therapy for Rheumatoid Arthritis* HEDIS measure assesses whether patients, 18 years of age and older, diagnosed with rheumatoid arthritis (RA) have been prescribed a disease modifying anti-rheumatic drug (DMARD).

The *Disease Modifying Anti-Rheumatic Drug Therapy for Rheumatoid Arthritis* HEDIS measure is included in the following Highmark provider quality measurement programs:

- Highmark Medicare Advantage Stars Incentive Program
- Highmark True Performance Program
- Quality Blue Hospital Bundle

According to the *American College of Rheumatology Guideline for the Treatment of Rheumatoid Arthritis,* for the majority of patients, an established diagnosis of RA warrants treatment with a DMARD. For any untreated patient with persistent synovitis and joint damage, DMARD treatment should be started promptly to prevent or slow further damage.

Full texts of the referenced American College of Rheumatology recommendations are available here:
http://www.rheumatology.org/Portals/0/Files/ACR%202015%20RA%20Guideline.pdf

Important Considerations

- The Disease Modifying Anti-Rheumatic Drug Therapy for Rheumatoid Arthritis HEDIS measure uses claims information to measure performance. Incorrect claims submissions do not accurately reflect the care provided to Highmark members.
- Until a **definitive** diagnosis of rheumatoid arthritis has been confirmed, generally via x-ray and laboratory findings, claim submission should be coded based on documented signs and symptoms.
- Refer patients to a rheumatologist as appropriate for consultation and/or co-management

Table 1. HEDIS® Drug List for the Disease Modifying Anti-Rheumatic Drug Therapy for Rheumatoid Arthritis Measure

Aminosalicylates	● Sulfasalazine		
Alkylating agents	● Cyclophosphamide		
Aminoquinolines	● Hydroxychloroquine		
Anti-rheumatics	● Auranofin ● Gold sodium thiomalate	● Leflunomide ● Methotrexate	● Penicillamine
Immunomodulators	● Abatacept ● Adalimumab ● Anakinra	● Certolizumab ● Certolizumab pegol ● Infliximab	● Etanercept ● Golimumab ● Rituximab ● Tocilizumab
Immunosuppressive agents	● Azathioprine	● Cyclosporine	● Mycophenolate
Janus kinase inhibitor	● Tofacitinib		
Tetracyclines	● Minocycline		

HEDIS® is a registered trademark of the National Committee for Quality Assurance.

Classification Criteria and Diagnosis [1, 2]

The American College of Rheumatology updated the classification criteria for Rheumatoid Arthritis (RA) in 2010 to address a few limitations from the previous edition in 1987. The new criteria focus more on the earlier stage of disease as opposed to features of late-stages of the disease. With early diagnosis, therapy can be provided in order to slow disease progression and the consequent damaging effects. It is important to note that the classification criteria were designed to serve as a diagnostic tool, and there is still need for the development of diagnostic criteria.

The classification criteria for RA include the following:

- Target population for assessment
  - Patients with at least 1 joint with definite clinical synovitis
  - Patients with synovitis not better explained by another disease
- Classification criteria for RA** (4 categories)
  - Joint involvement (various ranges of large/small joints)
  - Serology (rheumatoid factor (RF) and/or anti-citrullinated protein antibody (ACPA))
  - Acute-phase reactants (C-reactive protein (CRP) and/or erythrocyte sedimentation rate (ESR))
  - Duration of symptoms (6-week marker)

**Score-based algorithm, where the scores are added in the four categories and a score of ≥6/10 is needed for classification of a patient as having definite RA*
***Criteria should only be applied to eligible patients with synovitis in at least 1 joint.*

Treatment Recommendations [1]

Treatment decisions are based on the patient's disease activity, disease duration, and current RA treatment regimen (Table 2). The 2015 ACR guidelines have further identified treatment decisions in RA patients with high-risk comorbidities (Table 3). The 2015 ACR guidelines also include recommendations for the use of vaccines in RA patients (Table 4). Disease activity is measured using a validated instrument, such as the Simplified Disease Activity Index or Clinical Disease Activity Index (Table 5). Prognosis of the disease is determined by functional limitation, extra-articular disease, positive rheumatoid factor or anticyclic citrullinated peptide antibodies, or bony erosions.

The primary goal of treatment for RA is to reduce disease activity ideally to achieve clinical remission and to minimize irreversible joint damage. The ACR guidelines recommend an aggressive treatment regimen in an attempt to prevent joint damage, preserve function, and improve long-term outcomes. Aggressive treatment means using disease modifying antirheumatic Drugs (DMARDs) as monotherapy or combination therapy, depending on disease activity and prognosis.

Table 2. ACR Summary of Treatment Decisions for Patients with Early and Established RA

Treatment Options	Examples	Early/Established RA	ACR Recommendations
Nonbiologic DMARD Monotherapy	methotrexate, leflunomide, hydroxychloroquine, sulfasalazine, and minocycline	*Early	• Monotherapy is strongly recommended over double or triple DMARD therapy for DMARD-naïve patients with early, symptomatic RA with low disease activity. • Monotherapy is conditionally recommended over double or triple DMARD therapy in DMARD-naïve patients with moderate or high disease activity. • Methotrexate is the preferred initial therapy for patients with early RA with active disease.
		**Established	• Monotherapy is strongly recommended over an anti-TNF agent for DMARD-naïve patients with low disease activity. • Monotherapy is conditionally recommended over double or triple DMARD therapy and over tofacitinib in DMARD-naïve patients with moderate or high disease activity.
Nonbiologic DMARD Combinations	methotrexate in combination with hydroxychloroquine or leflunomide or sulfasalazine	*Early	• Initiated in patients with moderate or high disease activity despite DMARD therapy (with or without glucocorticoids) with or without methotrexate, rather than continuing DMARD monotherapy alone.
		**Established	• Initiated in patients with moderate or high disease activity despite DMARD monotherapy with or without methotrexate, rather than continuing DMARD monotherapy alone.

Biologic DMARDs	anti-TNF agents such as etanercept, adalimumab, certolizumab, and golimumab	*Early	• Initiated in patients with moderate or high disease activity despite DMARD therapy with or without methotrexate, rather than continuing DMARD monotherapy alone. • Biologic therapy should be used in combination with methotrexate over biologic monotherapy, due to increased efficacy.
		**Established	• Initiated for patients with established disease of low activity with or without poor prognosis or established disease of moderate or high activity who have failed three months of DMARD therapy. • Biologic therapy should be used in combination with methotrexate over biologic monotherapy, due to increased efficacy.
	Non-TNF biologic agents such as abatacept, rituximab or tocilizumab	*Early	• Initiated in patients with moderate or high disease activity despite DMARD therapy with or without methotrexate, rather than continuing DMARD monotherapy alone. • Initiated in patients with moderate or high disease activity despite anti-TNF therapy should be tried on a non-TNF biologic agent. • Initiated in patients with moderate or high disease activity despite non-TNF biologic therapy should be tried on another non-TNF biologic agent. • Biologic therapy should be used in combination with methotrexate over biologic monotherapy, due to increased efficacy.
		**Established	• Initiated in patients with moderate or high disease activity despite DMARD monotherapy with or without methotrexate, rather than continuing DMARD monotherapy alone. • Initiated in patients with moderate or high disease activity despite anti-TNF therapy should be tried on a non-TNF biologic agent. • Initiated in patients with moderate or high disease activity despite non-TNF biologic therapy should be tried on another non-TNF biologic agent. • Biologic therapy should be used in combination with methotrexate over biologic monotherapy, due to increased efficacy.

Janus Kinase inhibitor	tofacitinib	**Established	• Initiated in patients with moderate or high disease activity despite DMARD monotherapy with or without methotrexate, rather than continuing DMARD monotherapy alone. • Initiated in patients with moderate or high disease activity despite treatment with at least one anti-TNF agent and at least one non-TNF biologic agent and treating with another non-TNF biologic are not an option (e.g., patient declines therapy due to side effects). • Initiated in patients with moderate or high disease activity despite the use of multiple (2+) anti-TNF therapies and non-TNF biologic therapy.
Low-dose glucocorticoids	≤10 mg/day of prednisone or equivalent	*Early	• Initiated in patients with moderate or high disease activity despite DMARD or biologic therapies. • May also be used in patients who require a bridge until realizing the benefits of DMARD therapy.
		**Established	• Initiated in patients with moderate or high disease activity despite DMARD or biologic therapies. • Initiated in patients that experience a RA flare while on DMARD, anti-TNF therapy, or non-TNF biologic therapy for short-term use (< 3 months of treatment) at the lowest dose and for shortest possible duration.

*Early RA: Less than 6 months RA symptom/disease duration, not the length of time since RA diagnosis.
** Established RA: Greater than or equal to 6 months RA symptom/disease duration, not the length of time since RA diagnosis.

Table 3. ACR Summary of Treatment Decisions for RA Patients with High-risk Comorbidities

High-risk comorbidity	Patient Population	ACR Recommendations
Congestive Heart Failure	• Established RA with moderate or high disease activity and New York Heart Association (NYHA) class III or IV congestive heart failure (CHF)	• Use combination DMARD therapy, a non-TNF biologic, or tofacitinib rather than an anti-TNF agent
	• Established RA with moderate or high disease activity and New York Heart Association (NYHA) class III or IV congestive heart failure (CHF) and are treated with anti-TNF therapy and their CHF worsens	• Switch to combination DMARD therapy, a non-TNF biologic, or tofacitinib

Hepatitis B	• Established RA with moderate or high disease activity and evidence of active hepatitis B infection (hepatitis surface antigen positive > 6 months), who are receiving or have received effective antiviral treatment • Natural immunity from prior exposure to hepatitis B (i.e., HB core antibody and HBS antibody positive and normal liver function tests)	• Treat the same as patients without this condition
	• Chronic hepatitis B who are untreated	• Referral for antiviral therapy prior to immunosuppressive therapy
Hepatitis C	• Established RA with moderate or high disease activity and evidence of chronic hepatitis C virus (HCV) infection, who are receiving or have received effective antiviral treatment	• Treat the same as patients without this condition
	• Chronic hepatitis C who are not requiring or receiving antiviral treatment	• Use DMARD therapy instead of anti-TNF therapy
Malignancy	• Established RA and moderate or high disease activity and a history of previously treated or untreated melanoma skin cancer	• Use DMARD therapy over biologics or tofacitinib
	• Established RA and moderate or high disease activity and a history of a previously treated lymphoproliferative disorder	• Strongly recommend use of rituximab over anti-TNF therapy • Conditionally recommend use of combination DMARD therapy, abatacept or tocilizumab over anti-TNF therapy
	• Established RA with moderate or high disease activity and previous serious infection(s)	• Use combination DMARD therapy rather than anti-TNF therapy

Table 4. ACR Summary of Recommendations for the Use of Vaccines in RA patients on DMARD and/or Biologic Therapy

Patient Population	ACR Recommendations
Early or established RA patients aged 50 and over	• Give the herpes zoster vaccine before the patient receives biologic therapy or tofacitinib

Early or established RA patients who are currently receiving biologics	• Do not give live attenuated vaccines such as the herpes zoster (shingles) vaccine • Use appropriately indicated killed/inactivated vaccines

Table 5. Instrument Used to Measure RA Disease Activity and to Define Remission [3-7]

Instrument	Instrument Description	Thresholds and corresponding disease level
Patient Activity Scale (PAS) or PAS-II (range 0–10) (3)	A composite index composed of a visual analog scale (VAS) for pain, a patient global VAS, and the Health Assessment Questionnaire (HAQ) or the HAQ II	Remission: 0–0.25 Low activity: 0.26–3.7 Moderate activity: 3.71 to <8.0 High activity: ≥8.0
Routine Assessment of Patient Index Data 3 (range 0–10) (4)	An index of the three RA core data set measures of physical function, pain, and global estimate on the multidimensional HAQ (MDHAQ)	Remission: 0–1.0 Low activity: >1.0 to 2.0 Moderate activity: >2.0 to 4.0 High activity: >4.0 to 10
Clinical Disease Activity Index (range 0–76.0) (5)	A clinical combined score of tender and swollen joint counts [28 joints] and patient and provider global assessments of disease activity	Remission: ≤2.8 Low activity: >2.8 to 10.0 Moderate activity: >10.0 to 22.0 High activity: >22
Disease Activity Score in 28 joints (range 0–9.4) (6)	A clinical assessment including a 28-swollen and tender joint count, erythrocyte sedimentation rate (ESR), and a general health assessment on a visual analog scale.	Remission: <2.6 Low activity: ≥2.6 to <3.2 Moderate activity: ≥3.2 to ≤5.1 High activity: >5.1
Simplified Disease Activity Index (range 0–86.0) (7)	A clinical assessment including tender and swollen joint count (28-joint assessment), patient and provider global assessment of disease activity with visual analog scale and level of C-reactive protein (mg/dl)	Remission: ≤3.3 Low activity: >3.3 to ≤11.0 Moderate activity: >11.0 to ≤26 High activity: >26

Table 6. Treatment Options for Rheumatoid Arthritis (RA) in Adults: Disease Modifying Anti-rheumatic Drugs (DMARDs) [8]

Generic Name	Brand Name	Typical Adult Dosing for RA	Side Effect Profile, Precautions, Warnings	Patient Education
Nonbiologic DMARDs*				
methotrexate	*Trexall®*	Severe RA : 7.5mg SQ once weekly injection Severe RA: after failure or intolerance to first-line therapy, including full-dose NSAIDs: Initial, 7.5 mg orally once weekly or 2.5 mg orally every 12 hours for 3 doses once weekly; gradually titrate to lowest effective dose.	• Hepatotoxicity • Contraindications: chronic liver disease; laboratory evidence of immunodeficiency syndromes; preexisting blood dyscrasias • Patients should not use NSAIDs prior to or concurrently with high-dose methotrexate therapy • Pregnancy Category: X	• Instruct patient to maintain adequate hydration • Drug can cause sun-sensitivity • Severe skin reactions may occur • Proton pump inhibitors (PPIs) may increase MTX levels and increase chance of toxicity and adverse events • Signs of infection should be reported (sore throat, fever etc.)
leflunomide	*Arava®*	Loading Dose: 100 mg once daily x 3 days Maintenance Dose: 10 or 20 mg once daily based on tolerability	• Adverse events include alopecia, rash, diarrhea, ulcer of mouth, dizziness, headache, respiratory tract infection • Serious adverse events may include severe skin reactions, hematologic events, hepatic toxicity and respiratory infection or lung disease • Pregnancy Category: X	• Avoid live vaccines during therapy • Severe skin reactions may occur • Signs of infection should be reported (sore throat, fever etc.)
hydroxychloroquine	*Plaquenil®*	Initial: 400-600 mg orally once daily for 4-12 weeks Maintenance Dose: 200-400 mg orally once daily	• Common adverse events may include disorders of the cornea • More serious adverse events may include hematologic disorders, hepatotoxicity, drug induced myopathy, seizures, retinopathy,	• Patient should report visual changes • Drug should be taken with food or milk to help minimize gastrointestinal side effects

			hearing loss and angioedema • Pregnancy Category: D	
sulfasalazine	*Azulfidine®*	Initial: 0.5-1 gram orally once daily or in two divided doses Maintenance Dose: 1 gram orally twice daily up to max 3 grams daily	• Common adverse events include skin reactions, gastrointestinal side effects, discoloration of urine, liver function enzyme abnormalities • More serious adverse events may include myocarditis, erythroderma, severe skin reactions, hepatotoxicity, CNS disorders, kidney disease, pneumonia and fibrosis, and sepsis • Pregnancy Category: B	• Patients at highest risk for skin/ hypersensitivity reaction during first month of therapy • Advise patient that drug may cause urine/skin to turn yellow/orange color • Signs of infection should be reported (sore throat, fever) • Advise patient to maintain adequate hydration to avoid renal complications • Advise patient to take drug in evenly divided doses after meals

Biologic DMARDs				
anti-tumor necrosis factor alpha (anti-TNF) agents				
etanercept	*Enbrel®*	Moderate to severe RA: 50mg SQ weekly	• Black Box Warning: serious infection, malignancy • Side effects include abdominal pain, vomiting, cough, rhinitis, hematologic events • CHF exacerbation • Contraindications: sepsis • Pregnancy Category: B	• Avoid live vaccines • Counsel patient about proper injection sites and rotation
infliximab*	*Remicade®*	Moderate to Severe RA: In combination with methotrexate: Induction: 3 mg/kg IV over at least 2 hours given at weeks 0, 2, and 6 in combination with methotrexate; followed by maintenance therapy	• Black Box Warning : serious infection; malignancy • Adverse events include abdominal pain, fatigue, headache, and infections • More serious adverse events may include, serious skin reactions,	• Avoid live vaccines • Instruct patient to report signs/ symptoms of a lupus-like syndrome (arthralgias, myalgias, fatigue, skin rashes) or a serum sickness-like reaction (rash,

		Maintenance: 3 mg/kg IV every 8 weeks in combination with methotrexate; may increase dose up to 10 mg/kg IV OR give 3 mg/kg IV every 4 weeks in patients with an incomplete response Maximum dose 5mg/kg/day	acute coronary syndrome, heart failure, hepatotoxicity, blood dyscrasias • Contraindications: Heart failure • Pregnancy Category: B	urticaria, arthralgia, fever, malaise, enlarged lymph nodes)
adalimumab	*Humira*®	Moderate to severe RA: 40 mg SQ every other week; may increase to 40 mg SQ every week in patients not receiving concomitant methotrexate	• Black Box Warning : serious infection, malignancy • Common adverse reactions include infections, headache and rash • Serious side effects include congestive heart failure, agranulocytosis, hepatic failure, immunologic response, and demyelinating disease, • Pregnancy Category: B	• Avoid live vaccines • Instruct patient to report signs/ symptoms of a lupus-like syndrome (e.g., arthralgias, myalgias, fatigue, skin rashes) or congestive heart failure (new onset, exacerbation) • Counsel patient about proper injection sites and rotation
certolizumab pegol*	*Cimzia*®	Active, moderate to severe RA: Initial, 400 mg SQ (as 2 SQ injections of 200 mg) once and then repeat at weeks 2 and 4; Maintenance, 200 mg SQ once every 2 weeks or 400 mg SQ (as 2 SQ injections of 200 mg) once every 4 weeks	• Black Box Warning : serious infection, malignancy • Most common adverse events include infections, rash, arthralgia • More serious adverse events include demyelinating disease, nephrotic syndrome, myocardial disorders, lupus-like reactions • Screen all patients for hepatitis B virus (HBV) infection prior to therapy initiation • Pregnancy Category: B	• Avoid live vaccines • Instruct patient to report signs/ symptoms of a lupus-like syndrome (e.g., arthralgias, myalgias, fatigue, skin rashes) or congestive heart failure (new onset, exacerbation) • Counsel patient on proper injection sites and rotations
golimumab*	*Simponi* ®	Moderate to severe RA: Active, in combination	• Black Box Warning : serious infection;	• Avoid live vaccines • Council patient on

		with methotrexate: 2 mg/kg IV infusion over 30 minutes at weeks 0 and 4, then every 8 weeks in combination with methotrexate 50 mg SQ once monthly in combination with methotrexate	malignancy • Common side effects include nasopharyngitis, injection site reactions • More serious side effects include congestive heart failure, optic neuritis, demyelinating disease of the central nervous system, • Pregnancy Category: B	appropriate injection sites, rotation and administration

non-TNF biologic agents				
abatacept*	*Orencia®*	Moderate to severe RA: Weight-based IV infusion dosing over 30 minutes <60kg: 500mg 60-100kg: 750mg >100kg: 1000mg repeat doses at 2 and 4 weeks after first infusion and every 4 weeks thereafter 125mg SQ dosing within 1 day of IV loading dose, followed by 125mg SQ once weekly 125mg SQ once weekly without IV LD can be administered	• Side effects include fever, nausea, diarrhea, abdominal pain, headaches, nasopharyngitis, cough, or upper respiratory infections • Serious side effects may include acute pyelonephritis, pneumonia, cellulitis • Maltose in solution may interfere with Diabetes glucose tolerance testing • Pregnancy Category: C	• Avoid live vaccines • Educate regarding increased risk for infection (TB, HBV) • Drug may exacerbate respiratory symptoms – advise COPD patients • Advise on proper injection site rotation
rituximab*	*Rituxan®*	Moderate to Severe RA: In combination with methotrexate, in patients who had an inadequate response to one or more tumor-necrosis-factor antagonist therapies: 1000 mg IV followed by a second 1000-mg IV dose 2 weeks later in combination with methotrexate every 24 weeks or based on clinical	• Black box warning: fatal infusion reactions, severe mucocutaneous reactions, hepatitis B virus reaction and progressive multifocal leukoencephalopathy • Cardiovascular events • Screen all patients for hepatitis B virus (HBV) prior to initiation of therapy • Monitor blood counts	• Avoid live vaccines • Recommend reliable contraception to avoid pregnancy • Patients should report signs/symptoms of infections

		evaluation; every 16 weeks	• Pregnancy Category: C	
tocilizumab*	*Actemra®*	Moderate to Severe RA with inadequate response to DMARDs: 4 mg/kg IV infusion over 1 hour every 4 weeks; increase to 8 mg/kg every 4 weeks based on clinical response. (max 800 mg per infusion) Alternate dosing: weight less than 100 kg, 162 mg SQ every other week; increase to 162 mg SQ every week based on clinical response weight 100 kg or greater, 162 mg SQ every week	• Black Box Warning: risk of serious infections • Elevated liver enzymes, hypertension, infections and injection site reactions. • Baseline absolute neutrophil count (ANC) of 2000/mm^3 or greater and a platelet count of 100,000/mm^3 or greater are required before initiation of therapy • Do not initiate tocilizumab in patients with baseline ALT or AST levels greater than 1.5 x ULN • Pregnancy Category: C	• Avoid live vaccines • Report any signs or symptoms of infection • Ensure patient is aware of proper injection technique
Tofacitinib	*Xeljanz®*	Moderate to Severe RA: In patients who had an inadequate response or intolerance to methotrexate: 5 mg orally twice daily	• Black Box Warning : serious infections and malignancies • Adverse events include diarrhea and headache • Do not initiate in patients with an absolute neutrophil count (ANC) less than 1000 cells/mm(3), a lymphocyte count less than 500 cells/mm(3), or an Hb level less than 9 g/dL • Pregnancy Category: C	• Avoid live vaccines • Report any signs or symptoms of infection • Potential for multiple drug-drug interactions, advise patient to report changes in drug therapy to doctor
Anakinra	*Kineret®*	100 mg/day SQ; administer dose at approximately the same time every day	• Injection site reaction • Serious infections • Assess patient neutrophil count prior to and during therapy • Pregnancy Category: B	• Avoid live virus vaccines during therapy

*Patients being considered for biologics, methotrexate, leflunomide, or tofacitinib should be screened and treated for tuberculosis.

Please note that for Highmark members many of these drugs require a prior authorization and in some instances, preferred agents must be tried prior to non-preferred agents.

For more information regarding the formulary status and applicable utilization management controls please access the Highmark Medicare Part D formularies:

http://client.formularynavigator.com/clients/hm/default.html

References:

1. American College of Rheumatology, 2015 American College of Rheumatology Guideline for the Treatment of Rheumatoid Arthritis.. Arthritis Care Res.. 2016 Jan;68(1):1-25.
2. Aletaha D, Neogi T, Silman AJ, et al. 2010 rheumatoid arthritis classification criteria: an American College of Rheumatology/European League Against Rheumatism collaborative initiative [published correction appears in Ann Rheum Dis. 2010;69(10):1892]. Ann Rheum Dis. 2010;69(9):1580–1588.
3. Wolfe F, Michaud K, Pincus T. A composite disease activity scale for clinical practice, observational studies, and clinical trials: the Patient Activity Scale (PAS/PAS-II). J Rheumatol 2005;32:2410–5.
4. Pincus T, Yazici Y, Bergman M. A practical guide to scoring a Multi-Dimensional Health Assessment Questionnaire (MDHAQ) and Routine Assessment of Patient Index Data (RAPID) scores in 10-20 seconds for use in standard clinical care, without rulers, calculators, websites or computers. Best Pract Res Clin Rheumatol 2007;21:755–87.
5. Aletaha D, Nell VP, Stamm T, Uffmann M, Pflugbeil S, Machold K, et al. Acute phase reactants add little to composite disease activity indices for rheumatoid arthritis: validation of a clinical activity score. Arthritis Res Ther 2005;7:R796–806.
6. Fransen J, Stucki G, van Riel PL. Disease Activity Score (DAS), Disease Activity Score-28 (DAS28), Rapid Assessment of Disease Activity in Rheumatology (RADAR), and Rheumatoid Arthritis Disease Activity Index (RADAI). Arthritis Rheum 2003;49 Suppl:S214–24.)
7. Smolen JS, Breedveld FC, Schiff MH, Kalden JR, Emery P, Eberl G, et al. A simplified disease activity index for rheumatoid arthritis for use in clinical practice. Rheumatology (Oxford) 2003;42:244–57.
8. DRUGDEX® System [Internet database]. Greenwood Village, Colo: Thomson Micromedex. Updated periodically. Accessed on August 12, 2016. Available at: <http://www.micromedexsolutions.com>