Medication Policy Manual

Policy No: dru129

Topic: Orencia®, abatacept

Date of Origin: March 2006

Committee Approval Date: May 8, 2015

Next Review Date: January 2016

Effective Date: May 8, 2015

IMPORTANT REMINDER

This Medical Policy has been developed through consideration of medical necessity, generally accepted standards of medical practice, and review of medical literature and government approval status.

Benefit determinations should be based in all cases on the applicable contract language. To the extent there are any conflicts between these guidelines and the contract language, the contract language will control.

The purpose of medical policy is to provide a guide to coverage. Medical Policy is not intended to dictate to providers how to practice medicine. Providers are expected to exercise their medical judgment in providing the most appropriate care.

Description

Abatacept (Orencia) inhibits the activity of T cells, which reduces inflammation caused by the immune system. It is available in intravenous and subcutaneous formulations and is used to treat diseases that may be caused or worsened by an overactive immune system such as rheumatoid arthritis.
Policy/Criteria

I. Most contracts require prior authorization approval of abatacept (Orencia) prior to coverage.

A. Intravenous abatacept (Orencia) may be considered medically necessary when criteria 1 AND 2 below are met

1. Alternative Site of Care - for Washington, Oregon, and Idaho commercial, fully insured members only (does not apply to Medicare)

Abatacept (Orencia) is administered in a non-hospital outpatient setting (also referred to as an “alternative site of care”; such as a provider’s office, an infusion center, or home infusion), unless both of the following criteria a. and b. below are met:

a. All non-hospital outpatient settings are greater than 10 miles further from the member’s home than the hospital outpatient setting.

AND

b. The member’s home is not eligible for home infusion services (such as home is not within the service area or is deemed unsuitable for care by the home infusion provider).

NOTE: Alternative Site of Care criteria will be waived for payment of the first dose, to allow for adequate transition time to arrange for a non-hospital outpatient setting for the infusion.

AND

2. At least one of the following diagnostic criterion a. or b. below is met:

a. A diagnosis of juvenile idiopathic arthritis (JIA) and both of criteria i. and ii. are met.

i. Diagnosis is established by or in consultation with a specialist in rheumatology.

AND

ii. There is clinical documentation that an oral DMARD (such as methotrexate) was not effective after at least a 6 to 12 week treatment course based on one or more of the assessment components listed in Appendix 1, or that an oral DMARD was not tolerated or all oral DMARDs are contraindicated (see Appendix 4).

OR

b. A diagnosis of rheumatoid arthritis (RA) when established by or in consultation with a specialist in rheumatology (see Appendix 2), and both criteria i. and ii. below are met.

i. There is clinical documentation that an oral DMARD (such
as methotrexate) was not effective after at least a 6 to 12 week treatment course based on one or more of the assessment components listed in Appendix 1, or that an oral DMARD was not tolerated or all oral DMARDs are contraindicated (see Appendix 4).

AND

ii. There is clinical documentation that treatment with infliximab (Remicade) or intravenous golimumab (Simponi Aria) was not effective after at least a 12-week treatment course unless each were not tolerated or are contraindicated.

B. Subcutaneous abatacept (Orencia) may be considered medically necessary when all of criteria 1 through 3 below are met.

a. A diagnosis of rheumatoid arthritis (RA) when established by or in consultation with specialist in rheumatology (see Appendix 2).

AND

b. There is clinical documentation that an oral DMARD (such as methotrexate) was not effective after at least a 6 to 12 week treatment course based on one or more of the assessment components listed in Appendix 1, or that an oral DMARD was not tolerated or all oral DMARDs are contraindicated (see Appendix 4).

AND

c. There is clinical documentation that treatment with two preferred biologic therapies were each not effective after at least a 12-week treatment course unless each were not tolerated or were contraindicated (see Appendix 3).

II. Administration, Quantity Limitations, and Authorization Period

A. Administration

1. OmedaRx does not consider intravenous abatacept (Orencia) to be a self-administered medication.

2. OmedaRx considers subcutaneous abatacept (Orencia) to be a self-administered medication.

B. When prior authorization is approved, abatacept (Orencia) may be covered in the following quantities:

1. Intravenous abatacept (Orencia)

   a. Initial authorization – A maximum of 8 infusions in a 6 month period in a non-hospital outpatient setting, unless waived per criteria I.A.1. above.
NOTE: Alternative Site of Care criteria will be waived for payment of the first dose, to allow for adequate transition time to arrange for a non-hospital outpatient setting for the infusion.

b. Continued authorization – A maximum of 13 infusions in a 1 year period based on a recommended infusion interval of every 4 weeks.

2. Subcutaneous abatacept (Orencia)
   a. 125 mg every week
   b. A single intravenous loading dose of abatacept (Orencia) may be authorized if required.

C. Authorization review
   1. Intravenous abatacept (Orencia)
      a. Initial authorization **shall** be reviewed at 6 months.
      b. Continued authorization or re-authorization (after the initial 6 month period) **shall** be reviewed at least annually, and clinical documentation indicating that there is disease stability or improvement must be provided.
   2. Subcutaneous abatacept (Orencia) – Authorization **may** be reviewed at least annually to confirm that current medical necessity criteria are met and that the medication is effective.

III. For Washington, Oregon, and Idaho commercial, fully insured members only (does not apply to Medicare)

Intravenous abatacept (Orencia) is considered not medically necessary when administered in a hospital outpatient setting when an alternative site of care (non-hospital outpatient setting) is a treatment option (see Section I. Alternative Site of Care).

IV. Abatacept (Orencia) is considered investigational when used for all other conditions, including but not limited to:
   A. Use in combination with another biologic response modifier (see Appendix 3), apremilast (Otezla), or tofacitinib (Xeljanz)
   B. Conditions other than rheumatoid arthritis (RA) for subcutaneous abatacept (Orencia)
   C. Diabetes mellitus
   D. Diffuse systemic sclerosis (scleroderma)
   E. Inflammatory bowel disease [e.g. Crohn’s disease (CD), ulcerative colitis (UC)]
   F. Psoriatic arthritis (PsA)
   G. Systemic lupus erythematosus (SLE)
Position Statement

- There are many treatments for chronic inflammatory conditions that are effective, have known long-term safety profiles, and are recommended by national treatment guidelines.
- Non-medical therapies, such as prescribed exercise therapy, physical therapy, weight loss, and smoking cessation are important treatment plan components for patients suffering from many chronic inflammatory conditions.
- When a systemic medication therapy is needed to manage a chronic inflammatory condition, generic oral therapies usually offer the best value.
- When non-medical therapies and oral medications are inadequate, a biologic medication may be appropriate.
- Preferred/formulary biologic medications for the treatment of chronic inflammatory conditions include: adalimumab (Humira), etanercept (Enbrel), infliximab (Remicade), golimumab IV (Simponi Aria) and ustekinumab (Stelara).
- No studies have shown that any one biologic medication is more effective than another in the treatment of chronic inflammatory conditions; however, the data for some individual products is of sufficient quality that indirect comparison can be made.
  * Indirect comparison is made base on the calculated number needed to treat (NNT) which describes the average number of patients that need to be treated for one patient to benefit.
  * The lower the NNT, the more likely the medication will have a benefit.
  * Products with similar NNTs can be considered to have comparable efficacy.
- When there is no demonstrated difference in safety or efficacy, the medication with the lowest cost often provides the best value for members.
- Individual responses and tolerability are unpredictable and may vary between patients. If one biologic agent provides an inadequate response, another biologic may yet be effective.
- Due to the potential for development of antibodies with anti-TNF therapies (see Table 1) which may result in loss of efficacy, clinical practice guidelines generally recommend a trial with no more than two anti-TNF therapies. [1-3] For those who have an inadequate response or intolerance to two anti-TNF therapies, it is reasonable to consider a biologic with an alternative mechanism of action and proven efficacy for the patient’s diagnosis [e.g. abatacept (Orencia), tocilizumab (Actemra), rituximab (Rituxan), or ustekinumab (Stelara)].
- All biologics (both anti-TNFs and non-anti-TNFs) carry a risk of severe infections. There is no conclusive evidence that any one biologic option has a superior safety profile.
- There is significant variation in recommended dosing across indications for individual medications; therefore, when multiple dosage forms of a biologic agent are available, coverage can be provided for those indications where the dosage form has been evaluated in randomized controlled trials, the dosage form has been proven safe and effective, and for which the dosage form has an established dose. For all other indications, the specific dosage form will be considered investigational.
- New technologies and pharmaceuticals allow therapeutic services, such as infusion therapy, to be administered safely, effectively, and much less costly outside of the
hospital outpatient setting. Alternative sites of care (such as doctor’s offices, infusion centers, and home infusion) are well-established, accepted by physicians, and reduce the overall cost of care.

**Clinical Efficacy**

**Background**

- Treatments for rheumatic conditions may include non-medical therapies, medications for the management of symptoms, and medications that modify the disease course such as oral or biologic disease modifying anti-rheumatic drugs (DMARD), including the first-in-class phosphodiesterase 4 (PDE4) inhibitor, apremilast (Otezla), and the Janus kinase (JAK) inhibitor, tofacitinib (Xeljanz).
- Medications to control inflammation such as nonsteroidal antiinflammatory medications (e.g. ibuprofen, indomethacin, and naproxen) and glucocorticoids (oral or injected into the joint) are effective for the management of symptoms, particularly during the early stages of disease.
- Generic, orally administered DMARDs, including methotrexate (MTX), hydroxychloroquine, leflunomide, and sulfasalazine are effective for decreasing symptoms and slowing disease progression, have a proven track record, and have been the standard of care for many years.
  * Methotrexate (MTX) is considered effective in the treatment of rheumatoid arthritis (RA) and is the standard reference DMARD to which newer oral and biologic DMARDs are compared for efficacy.
  * Generic oral therapies have known potential risks. The management of these risks is well established.
- The biologic agents can also decrease symptoms, help preserve joint functioning, and slow the progression of chronic inflammatory conditions; however, these medications also have significant risks.
- There is no comparative safety data within the biologics class that indicates one medication or mechanism of action is safer than alternatives, including anti-TNFs compared to non-anti-TNF medications.
- In RA, the best response is seen when MTX is used concomitantly with any of the biologics. Infliximab (Remicade) and golimumab (Simponi, Simponi Aria) have been shown to be effective only when used with MTX. Treatment options other than infliximab (Remicade) or golimumab (Simponi, Simponi Aria) should be considered for patients who cannot take MTX.
- Inhibiting PDE4 is a novel mechanism in the treatment of rheumatic conditions. PDE4 is a protein present in immune cells and is associated with inflammation.
- JAK inhibition is a novel mechanism in the treatment of rheumatic conditions. JAKs are enzymes that stimulate hematopoiesis and promote immune cell function.

**Juvenile Idiopathic Arthritis (JIA); Juvenile Rheumatoid Arthritis (JRA)**

- Several biologic agents have been shown to be effective in the treatment of JIA including:
  * Abatacept (Orencia) intravenous
* Adalimumab (Humira)
* Etanercept (Enbrel)
* Tocilizumab (Actemra) intravenous

Due to lack of high quality data, the comparative efficacy for these agents in the treatment of JIA is uncertain.

**Efficacy of abatacept (Orencia) in juvenile idiopathic arthritis (JIA); juvenile rheumatoid arthritis (JRA)** [4]
- The safety and efficacy of abatacept (Orencia) in 190 patients with JIA were assessed in one three-part study including an open-label extension. During the double-blind randomized withdrawal phase, patients treated with abatacept (Orencia) experienced significantly fewer disease flares compared to placebo-treated patients (20% vs 53%) and the risk of disease flare among patients continuing on abatacept (Orencia) was less than one-third of that for patients who withdrew from treatment (hazard ratio = 0.31; 95% CI: 0.16, 0.59).
- Abatacept (Orencia), with or without a concomitant oral DMARD, is administered intravenously for the treatment of JIA. Dosing is based on a patient’s weight, and following induction infusions at 0, 2, and 4 weeks, maintenance infusions should be given every four weeks.

**Rheumatoid Arthritis (RA)**
- Several biologic and newer oral agents have been shown to be effective in the treatment of RA including the following:
  * Abatacept (Orencia) intravenous and subcutaneous
  * Adalimumab (Humira)
  * Anakinra (Kineret)
  * Etanercept (Enbrel)
  * Certolizumab pegol (Cimzia)
  * Golimumab (Simponi, Simponi Aria)
  * Infliximab (Remicade)
  * Rituximab (Rituxan)
  * Tocilizumab (Actemra) intravenous and subcutaneous
  * Tofacitinib (Xeljanz)
- All of these agents, with the exception of tocilizumab (Actemra) subcutaneous and tofacitinib (Xeljanz) have high quality data in the treatment of RA (see Table 1) and, therefore, can be indirectly compared based on their calculated NNTs (see Table 2).
- With the exception of anakinra (Kineret), and those products without high quality data, the efficacy of these agents in the treatment of RA is similar.

**Efficacy of abatacept (Orencia) in rheumatoid arthritis (RA)**
- There is evidence that abatacept (Orencia) in combination with MTX reduces pain and inflammation and improves quality of life in patients who did not respond to an anti-TNF therapy or MTX monotherapy. [4-9]
- Abatacept (Orencia), with or without a concomitant oral DMARD, can be administered intravenously or subcutaneously for the treatment of RA. [4]
* Intravenous dosing is based on a patient’s weight. Following induction infusions at 0, 2, and 4 weeks, maintenance infusions should be given every four weeks.
* Subcutaneous dosing may or may not be preceded by a single intravenous loading dose with a 125 mg subcutaneous injection within a day. Maintenance dosing consists of 125 mg injections once weekly.

**Other Conditions**
Abatacept (Orencia) has been studied in a variety of other conditions. Due to lack of published data, lack of high quality data, or lack of positive data these conditions are considered investigational. Details of select investigational uses are reported below.

**Diabetes mellitus**
- One double-blind, randomized controlled trial evaluated the use of abatacept (Orencia) in 112 patients with type 1 diabetes mellitus. While treatment with abatacept (Orencia) slowed reduction in B-cell function, the duration of response is uncertain. Additional high quality data evaluating clinically relevant outcomes are needed to confirm these results. [10]

**Diffuse systemic sclerosis (scleroderma)**
- No randomized controlled trials have been published evaluating the use of abatacept (Orencia) in patients with diffuse systemic sclerosis/scleroderma.

**Inflammatory bowel disease (e.g. Crohn’s disease, ulcerative colitis)**
- In a review of four clinical trials evaluating the use of abatacept (Orencia) in the treatment of Crohn’s disease and ulcerative colitis, the authors concluded that abatacept (Orencia) was not efficacious for these conditions. [11]

**Psoriatic arthritis (PsA)**
- One small, phase II, randomized, placebo-controlled trial evaluated the use of abatacept (Orencia) in patients with psoriatic arthritis. [12]
* At 6 months, response as measured by the proportion of patients achieving a 20% improvement in ACR20 was significantly higher than placebo for two of the three groups treated with abatacept (Orencia). There was no statistically significant difference between these two dosage regimens; although, the study was not powered to detect a difference between groups receiving active medication.
* While suggestive of benefit as measured by ACR20 response, larger randomized controlled trials are needed to establish the optimum dose, and the safety and efficacy of abatacept (Orencia) in this condition.

**Systemic lupus erythematosus (SLE)** [13]
- One small randomized, placebo-controlled trial evaluated the use of abatacept (Orencia) in patients with non–life-threatening SLE and polyarthritis, discoid lesions, or pleuritis and/or pericarditis.
The study did not reach statistical significance with the primary endpoint (proportion of patients with a new flare of SLE), but was suggestive of a positive effect in certain exploratory measures. Further study is needed to establish the safety and efficacy of abatacept (Orencia) in SLE.

Safety Summary
- All biologic and non-biologic DMARDs have an adequate track record of clinical experience (≥ 3 years) with the exception of tofacitinib (Xeljanz), vedolizumab (Entyvio) and golimumab (Simponi Aria); however, the compound golimumab has been available as Simponi since 2009.
- All biologics (both anti-TNFs and non-anti-TNFs) carry a risk of severe infections. There is no conclusive evidence that any one biologic option has a superior safety profile.
- Apremilast (Otezla) has a short track record of clinical experience (< 1 year) in the U.S. for the treatment of PsA. It has been approved in Europe for the treatment of Behçet’s disease since August 2013.
- Immune suppression and subsequent increased risk of infection or malignancy is a potential risk with all biologic and non-biologic DMARDs. Serious infections such as tuberculosis and fungal infections should be considered prior to starting any of these therapies.
- Branded DMARDs are not recommended to be given concomitantly, should be used with caution when given concomitantly with other immunosuppressive therapies, and may interfere with live vaccines.

Safety of abatacept (Orencia) [4]
- The most commonly reported adverse events (≥ 10%) with abatacept (Orencia) in clinical trials were headache, upper respiratory tract infection, nasopharyngitis, and nausea.
- The administration of abatacept (Orencia) has been associated with anaphylaxis/anaphylactoid reactions.
- Caution should be used when administering abatacept (Orencia) to patients with chronic obstructive pulmonary disorder (COPD) due to a potential for more frequent respiratory adverse events (e.g. COPD exacerbation, cough, rhonchi, and dyspnea).
- Administration of abatacept (Orencia) to patients with RA receiving background biologic agents was associated with a greater frequency of serious adverse events (22.3%) than in other subgroups (11.7 to 12.5%, p-values not reported).

Alternative Site of Care:
- Use of an alternative site of care, including non-hospital outpatient infusion centers and home infusion services, is an accepted standard medical practice. These alternative sites of care offer high-quality services for patients and reduce the overall cost of care, as compared to a hospital-based infusion center.
- All medications infused outside of a hospital setting (at an alternative site of care) have undergone an evaluation for safe infusion and development of infusion standards, including adverse drug reaction (ADR) management and reporting algorithms.
- For use of an alternative site of care, every patient undergoes a patient assessment during the intake process by the infusion provider, which includes evaluation of individual clinical assessment parameters. These parameters may include, but are not limited to, previous tolerance of products (such as IVIG), assessment of kidney function, risk factors for developing thromboembolic events, and venous access.
- For use of home infusion services, an assessment is conducted to determination whether or not the home is a safe, appropriate site of care, with adequate support for infusion in the home.
- Because these “alternative site of care” providers need time to arrange for assessment and coordinate the first dose of each new medication, the first dose of infused medications may be covered in a hospital-based infusion center, if needed, to allow adequate time for a seamless transition of care. This may include arranging for delivery of medications and/or patient education, such as for self-administration of medications such as subcutaneous immune globulin (SCIG).
### Table 1. Summary of Evidence Quality by Indication for Select Disease Modifying Anti-Rheumatic Drugs (DMARD)

<table>
<thead>
<tr>
<th>Generic (brand) [Original FDA-approval Date]</th>
<th>Route/Site of Administration</th>
<th>Mechanism of action</th>
<th>Rheumatoid Arthritis</th>
<th>Psoriatic Arthritis</th>
<th>Ankylosing Spondylitis</th>
<th>Juvenile Idiopathic Arthritis</th>
<th>Systemic Juvenile Idiopathic Arthritis</th>
<th>Chronic Plaque Psoriasis</th>
<th>Crohn’s Disease</th>
<th>Ulcerative Colitis</th>
</tr>
</thead>
<tbody>
<tr>
<td>infliximab (Remicade) [8/1998]</td>
<td>IV/HCP</td>
<td>TNF antagonist (anti-TNF)</td>
<td>✔ ✔ ✔</td>
<td>✔ ✔ ✔</td>
<td>✔</td>
<td>✔ ✔ ✔</td>
<td>✔ ✔ a ✔ ^</td>
<td>x</td>
<td></td>
<td></td>
</tr>
<tr>
<td>etanercept (Enbrel) [11/1998]</td>
<td>SC/Pat</td>
<td>TNF antagonist (anti-TNF)</td>
<td>✔ ✔ ✔</td>
<td>✔ ✔ x</td>
<td>✔</td>
<td>✔ ✔ ✔</td>
<td>✔</td>
<td>✔ ✔ a ✔ ^</td>
<td></td>
<td></td>
</tr>
<tr>
<td>adalimumab (Humira) [12/2002]</td>
<td>SC/Pat</td>
<td>TNF antagonist (anti-TNF)</td>
<td>✔ ✔ ✔</td>
<td>✔ ✔ ✔</td>
<td>✔</td>
<td>✔ ✔ ✔</td>
<td>✔</td>
<td>✔ ✔ a ✔ ^</td>
<td></td>
<td></td>
</tr>
<tr>
<td>certolizumab pegol (Cimzia) [4/2008]</td>
<td>SC/Pat</td>
<td>TNF antagonist (anti-TNF)</td>
<td>✔ x x</td>
<td>x</td>
<td>✔</td>
<td>✔ ✔ ✔</td>
<td>✔</td>
<td>x</td>
<td></td>
<td></td>
</tr>
<tr>
<td>golimumab (Simponi) [4/2009]</td>
<td>SC/Pat</td>
<td>TNF antagonist (anti-TNF)</td>
<td>✔ ✔ ✔</td>
<td>✔ ✔ ✔</td>
<td>✔</td>
<td>✔ ✔ ✔</td>
<td>x</td>
<td>✔</td>
<td></td>
<td></td>
</tr>
<tr>
<td>golimumab (Simponi Aria) [7/2013]</td>
<td>IV/HCP</td>
<td>TNF antagonist (anti-TNF)</td>
<td>✔ ✔ ✔</td>
<td>✔ ✔ ✔</td>
<td>✔</td>
<td>✔ ✔ ✔</td>
<td>x</td>
<td>✔</td>
<td></td>
<td></td>
</tr>
<tr>
<td>rituximab (Rituxan) [11/1997]</td>
<td>IV/HCP</td>
<td>B-lymphocyte depleter</td>
<td>✔</td>
<td></td>
<td>✔</td>
<td>✔ ✔ ✔</td>
<td>✔</td>
<td>✔</td>
<td></td>
<td></td>
</tr>
<tr>
<td>anakinra (Kineret) [11/2001]</td>
<td>SC/Pat</td>
<td>IL-1 receptor antagonist</td>
<td>✔</td>
<td></td>
<td>✔</td>
<td>✔ ✔ ✔</td>
<td>✔</td>
<td>✔</td>
<td></td>
<td></td>
</tr>
<tr>
<td>canakinumab (Ilaris) [6/2009]</td>
<td>SC/Pat</td>
<td>IL-1β receptor antagonist</td>
<td>✔</td>
<td></td>
<td>✔</td>
<td>✔ ✔ ✔</td>
<td>✔</td>
<td>✔</td>
<td></td>
<td></td>
</tr>
<tr>
<td>tocilizumab (Actemra) [1/2010]</td>
<td>IV/HCP</td>
<td>IL-6 receptor antagonist</td>
<td>✔</td>
<td></td>
<td>✔</td>
<td>✔ ✔ ✔</td>
<td>✔</td>
<td>✔</td>
<td></td>
<td></td>
</tr>
<tr>
<td>tocilizumab (Actemra) [10/2013]</td>
<td>SC/Pat</td>
<td>IL-6 receptor antagonist</td>
<td>✔</td>
<td></td>
<td>✔</td>
<td>✔ ✔ ✔</td>
<td>✔</td>
<td>✔</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ustekinumab (Stelara) [9/2009]</td>
<td>SC/Pat, HCP</td>
<td>IL-12,-23 receptor antagonist</td>
<td>✔</td>
<td></td>
<td>✔</td>
<td>✔ ✔ ✔</td>
<td>✔</td>
<td>✔</td>
<td></td>
<td></td>
</tr>
<tr>
<td>natalizumab (Tysabri) [11/2004]</td>
<td>IV/HCP</td>
<td>Integrin inhibitor</td>
<td>✔</td>
<td></td>
<td>✔</td>
<td>✔ ✔ ✔</td>
<td>✔</td>
<td>✔</td>
<td></td>
<td></td>
</tr>
<tr>
<td>vedolizumab (Entyvio) [5/2014]</td>
<td>IV/HCP</td>
<td>Integrin inhibitor</td>
<td>✔</td>
<td></td>
<td>✔</td>
<td>✔ ✔ ✔</td>
<td>✔</td>
<td>✔</td>
<td></td>
<td></td>
</tr>
<tr>
<td>abatacept (Orencia) [12/2005]</td>
<td>IV/HCP</td>
<td>T-lymphocyte inhibitor</td>
<td>✔</td>
<td></td>
<td>✔</td>
<td>✔ ✔ ✔</td>
<td>✔</td>
<td>✔</td>
<td></td>
<td></td>
</tr>
<tr>
<td>abatacept (Orencia) [12/2011]</td>
<td>SC/Pat</td>
<td>T-lymphocyte inhibitor</td>
<td>✔</td>
<td></td>
<td>✔</td>
<td>✔ ✔ ✔</td>
<td>✔</td>
<td>✔</td>
<td></td>
<td></td>
</tr>
<tr>
<td>tofacitinib (Xeljanz) [11/2012]</td>
<td>PO/Pat</td>
<td>JAK inhibitor</td>
<td>✔</td>
<td></td>
<td>✔</td>
<td>✔ ✔ ✔</td>
<td>✔</td>
<td>✔</td>
<td></td>
<td></td>
</tr>
<tr>
<td>apremilast (Otezla) [3/2014]</td>
<td>PO/Pat</td>
<td>PDE-4 inhibitor</td>
<td>✔</td>
<td></td>
<td>✔</td>
<td>✔ ✔ ✔</td>
<td>✔</td>
<td>✔</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

HCP = healthcare provider administered; IL = interleukin; IV = intravenous; JAK = Janus kinases; Pat = patient (self) administered; PDE = phosphodiesterase; PO = oral; SC = subcutaneous; TNF = tumor necrosis factor; ✔ = FDA-approved indication and high confidence data; ✔ ✔ = FDA-approved indication and less than high confidence data; ❌ = not FDA-approved, but specifically recommended by clinical practice guidelines

* Refers to data for induction therapy only. Data for maintenance therapy is less than high confidence.

a Refers to data for induction therapy only. Data for maintenance therapy is less than high confidence.
b = FDA approved, but evidence has not undergone complete appraisal.
<table>
<thead>
<tr>
<th>Condition</th>
<th>Ankylosing Spondylitis</th>
<th>Psoriatic Arthritis</th>
<th>Rheumatoid Arthritis</th>
<th>Chronic Plaque Psoriasis</th>
<th>Crohn’s Disease</th>
<th>Ulcerative Colitis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Description of symptom improvement</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Medication</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>abatacept (Orencia)</td>
<td>N/A</td>
<td>N/A</td>
<td>NNT = 4 (Range 3-4)</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>adalimumab (Humira)</td>
<td>NNT = 4 (Range 3-4)</td>
<td>NNT = 3</td>
<td>NNT = 3 (Range 2-4)</td>
<td>NNT = 3 (Range 2-4)</td>
<td>Initial treatment: NNT = 7 (Range 5-8) Ongoing treatment: Uncertain</td>
<td>Initial treatment: NNT = 11 Ongoing treatment: Uncertain</td>
</tr>
<tr>
<td>anakinra (Kineret)</td>
<td>N/A</td>
<td>N/A</td>
<td>NNT = 7</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>apremilast (Otezla)</td>
<td>N/A</td>
<td>NNT = 6 (Range 4-8)</td>
<td>N/A</td>
<td>N/A</td>
<td>Uncertain at this time</td>
<td>Uncertain at this time</td>
</tr>
<tr>
<td>certolizumab pegol (Cimzia)</td>
<td>Uncertain</td>
<td>Uncertain</td>
<td>NNT = 3 (Range 2-4)</td>
<td>N/A</td>
<td>Uncertain</td>
<td>N/A</td>
</tr>
<tr>
<td>etanercept (Enbrel)</td>
<td>NNT = 4 (Range 3-4)</td>
<td>NNT = 3</td>
<td>NNT = 3 (Range 2-4)</td>
<td>NNT = 3 (Range 2-4)</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>golimumab (Simponi)</td>
<td>NNT = 3</td>
<td>NNT = 3</td>
<td>NNT = 4 (Range 3-5)</td>
<td>N/A</td>
<td>N/A</td>
<td>Uncertain</td>
</tr>
<tr>
<td>infliximab (Remicade)</td>
<td>NNT = 4 (Range 3-4)</td>
<td>NNT = 3</td>
<td>NNT = 3 (Range 2-4)</td>
<td>NNT = 3 (Range 2-4)</td>
<td>Initial treatment: NNT = 3 Ongoing treatment: Uncertain</td>
<td>Initial treatment: Uncertain Ongoing treatment: Uncertain</td>
</tr>
<tr>
<td>natalizumab (Tysabri)</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>Uncertain</td>
<td>N/A</td>
</tr>
<tr>
<td>rituximab (Rituxan)</td>
<td>N/A</td>
<td>N/A</td>
<td>NNT = 3</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>tocilizumab (Actemra)</td>
<td>N/A</td>
<td>N/A</td>
<td>NNT = 4 (Range 3-5)</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>tofacitinib (Xeljanz)</td>
<td>N/A</td>
<td>N/A</td>
<td>Uncertain</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>ustekinumab (Stelara)</td>
<td>N/A</td>
<td>NNT = 4 (Range 4-5)</td>
<td>N/A</td>
<td>NNT = 3 (Range 2-4)</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>vedolizumab (Entyvio)</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>Initial treatment: Uncertain Ongoing treatment: Uncertain</td>
<td>Initial treatment: Uncertain Ongoing treatment: Uncertain</td>
</tr>
</tbody>
</table>

ACR = American College of Rheumatology; ASAS = Assessment in Ankylosing Spondylitis International Working Group Criteria; PASI = Psoriasis Area Severity Index

* In select conditions. Likelihood of symptom improvement relative to placebo after three to six months of treatment based on number needed to treat (NNT). An NNT represents the average number of patients that need to be treated for one patient to benefit and can be calculated only where there is high confidence data.
Appendix 1: American College of Rheumatology (ACR) Classification Criteria for Establishing the Diagnosis of Rheumatoid Arthritis (RA) [14,15]

| 1. Morning stiffness in and around joints lasting more than 1 hour. |
| 2. Arthritis in at least 1 area in a wrist or proximal interphalangeal (PIP) joint (hands or fingers) for > 6 weeks. |
| 3. Simultaneous swelling or fluid accumulation in 3 or more joints for > 6 weeks. |
| 4. Symmetric (bilateral joint) involvement for > 6 weeks. |
| 5. Presence of rheumatoid nodules. |
| 6. Positive serum rheumatoid factor. |
| 7. Radiographic changes typical of RA (erosion or unequivocal bony decalcification in or adjacent to the involved joint) on hand and wrist present. |

Appendix 2: American College of Rheumatology (ACR) Assessment Components for Improvement in Rheumatoid Arthritis (RA) [16]

- Tender joint count.
- Swollen joint count.
- Patient's assessment of pain.
- Patient's global assessment of disease activity.
- Physician's global assessment of disease activity.
- Patient's assessment of physical function.
- Acute phase reactant measures (erythrocyte sedimentation rate or C-reactive protein levels.)
Appendix 3: Select Biologic Response Modifiers

- Actemra®, tocilizumab
- Cimzia®, certolizumab pegol
- Enbrel®, etanercept*
- Entyvio®, vedolizumab
- Humira®, adalimumab*
- Kineret®, anakinra
- Orencia®, abatacept
- Remicade®, infliximab*
- Rituxan®, rituximab
- Simponi®, golimumab
- Simponi Aria®, golimumab*
- Stelara®, ustekinumab
- Tysabri®, natalizumab

* Preferred/formulary biologics for the treatment of rheumatologic conditions

Appendix 4: Select List of Oral Disease Modifying Anti-rheumatic Drugs (DMARD)

Oral DMARDS for Rheumatic Conditions

<table>
<thead>
<tr>
<th>azathioprine (Imuran)</th>
<th>methotrexate (oral, injectable)</th>
</tr>
</thead>
<tbody>
<tr>
<td>cyclosporine (Gengraf, Neoral, Sandimmune)</td>
<td>mycophenolate (CellCept, Myfortic)</td>
</tr>
<tr>
<td>hydroxychloroquine (Plaquenil)</td>
<td>sulfasalazine (Azulfidine)</td>
</tr>
<tr>
<td>leflunomide (Arava)</td>
<td></td>
</tr>
</tbody>
</table>

© 2015. OmedaRx. All rights reserved.
<table>
<thead>
<tr>
<th>Cross References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Actemra®, tocilizumab dru209</td>
</tr>
<tr>
<td>Cimzia®, certolizumab dru160</td>
</tr>
<tr>
<td>Enbrel®, etanercept dru035</td>
</tr>
<tr>
<td>Entyvio®, vedolizumab dru356</td>
</tr>
<tr>
<td>Humira®, adalimumab dru081</td>
</tr>
<tr>
<td>Kineret®, anakinra dru049</td>
</tr>
<tr>
<td>Rituxan®, rituximab dru214</td>
</tr>
<tr>
<td>Simponi®, golimumab dru183</td>
</tr>
<tr>
<td>Stelara®, ustekinumab dru193</td>
</tr>
<tr>
<td>Tysabri®, natalizumab dru111</td>
</tr>
<tr>
<td>Xeljanz®, tofacitinib dru289</td>
</tr>
<tr>
<td>Codes</td>
</tr>
<tr>
<td>-------</td>
</tr>
<tr>
<td>CPT</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>HCPCS</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
</tbody>
</table>
References


3. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs. [cited 09/13/2013]; Available from: http://ard.bmj.com/content/early/2010/05/04/ard.2009.126532.abstract


