**Arava®**

**Covered Medication**

Leflunomide (Arava® Tablets)

### What it does and how it is used

- **Rheumatoid arthritis (RA)** is a progressive chronic inflammatory disease that primarily affects large and small joints.
- The disease is characterized by joint deformities of the hands, wrists, neck, jaw, elbows, feet, and ankles.
- In addition to pain, patients can experience neuropathy (numbness or loss of feeling in hands or feet).
- Other conditions associated with RA include cardiac abnormalities, pulmonary fibrosis, and corneal defects.
- RA is associated with a significant amount of morbidity, which can lead to a higher risk of mortality.
- Treatment is aggressive soon after diagnosis with the goals of reducing symptoms and future damage caused by RA.
- Initial treatment is usually with a conventional Disease Modifying Antirheumatic Therapy (DMARD) (e.g., methotrexate) and/or a biologic agent (e.g., Enbrel®). DMARDs decrease pain, slow disease progression, and retard development of joint erosions.
- Leflunomide is an immunomodulatory agent that inhibits dihydroorotate dehydrogenase (an enzyme that stimulates immune cells involved in causing pain and inflammation).
- Treatment with methotrexate as initial therapy may be considered for most patients unless a patient has a contraindication to methotrexate or is unable to receive methotrexate, such as in the presence of liver disease.
- Leflunomide may be used in combination or in place of methotrexate in patients who do not respond adequately to methotrexate alone.
- For RA, leflunomide is administered as an oral loading dose of 100 mg daily for 3 days, followed by a maintenance dose of 20 mg per day.
- **Polyomavirus-associated nephropathy (PVAN)** is a complication in up to 8% of patients who receive kidney transplants. Between 35% and 65% of renal transplants will fail within one year of diagnosis of polyoma BK virus infection.
- The FDA has granted leflunomide orphan drug status for prevention of acute and chronic rejection following solid organ transplants due to its immunosuppressant and antiviral properties and since this condition affects less than 200,000 individuals in the United States.
- Immunosuppressant medications taken to prevent organ transplant rejection make patients more susceptible to infections and because there are no approved treatments for polyoma BK virus, most treatment centers reduce the dose of immunosuppressants in an effort to allow the body’s immune system to fight off the infection.
- Patients with impaired renal function eliminate leflunomide faster than the typical patient with RA, and therefore, increased doses, up to 60 mg daily, may be necessary to maintain a serum concentration of the active metabolite high enough to clear the virus.

### Benefit design

Coverage is provided immediately (without generating a coverage review process) in the presence of a prescription within the previous 18 months for a disease-modifying antirheumatic drugs (DMARDs)

In situations where a DMARD does not exist in history, coverage for leflunomide is determined through prior authorization.
## Rationale for coverage authorization

To reduce exposure to cost associated with uses of leflunomide for which efficacy is unknown or use in situations where other treatment (e.g., methotrexate) may be warranted.

## Coverage authorization criteria

Coverage is provided in accord with the following:

1. For the treatment of rheumatoid arthritis
   - In situations where methotrexate has failed to adequately treat the patient’s rheumatoid arthritis or in situations where the patient is unable to receive treatment with methotrexate (e.g., use of methotrexate is contraindicated in the patient).
2. For the treatment of established viremia after an initial trial of reduced immunosuppressant therapy

**Coverage duration:** 5 years for a quantity not to exceed 20 mg per day. Additional coverage, up to 60 mg per day, is provided for patients with established viremia after an initial trial of reduced immunosuppressant therapy who require higher dosages in order to maintain serum drug levels above 40 mcg/mL. Coverage may be renewed.

## References