KESIMPTA® [ke-SIMP-ta] (ofatumumab) [ofa-tu-mu-mab]
Clinical Summary for Formulary Review
Please utilize in conjunction with accompanying Prescribing Information

Indications and Usage[1]: Kesimpta is a CD20-directed cytolytic antibody indicated for the treatment of relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults.

Mechanism of Action[1]: Prior to initating Kesimpta, perform Hepatitis B virus (HBV) screening and perform testing for quantitiative serum immunoglobulins. The precise mechanism by which ofatumumab exerts its therapeutic effects in MS is unknown, but is presumed to involve binding to CD20, a cell surface antigen present on pre-B and mature B lymphocytes. Following cell surface binding to B lymphocytes, ofatumumab results in antibody-dependent cellular cytolysis and complement-mediated lysis.

Dosage and Administration[1]: The recommended dose is 20 mg administered by subcutaneous (SC) injection with initial dosing at Weeks 0, 1, and 2 followed by subsequent once monthly dosing, starting at Week 4. The first injection should be performed under the guidance of a healthcare professional. If an injection is missed, it should be administered as soon as possible without waiting until the next scheduled dose. Subsequent doses should be administered at the recommended intervals. See the Full ***Prescribing Information***

Efficacy[1, 2]: The efficacy of Kesimpta were evaluated in two randomized, double-blind, active-controlled Phase III pivotal trials of identical design [Study 1 (ASCLEPIOS I) and Study 2 (ASCLEPIOS II)] in patients with RMS. Patients were randomized 1:1 to receive either ofatumumab 20 mg SC injections every 4 weeks (following an initial loading regimen of three 20 mg SC doses per week at days 1, 7, and 14) or teriflunomide 14 mg capsules orally once daily for up to 30 months. Primary efficacy endpoint of both trials was the annualized relapse rate (ARR) based on an Expanded Disability Status Scale (EDSS). Additional outcome measures included: 1) the time to 3-month confirmed disability progression (CDP) for the pooled populations, 2) the number of T1 gadolinium-enhancing (GdE) lesions per MRI scan, and 3) the annualized rate of new or enlarging T2 MRI lesions. Demographics and disease characteristics were balanced across treatment arms in both trials.The following provides a brief summary of the two trials:

- *Kesimpta significantly lowered the ARR compared to teriflunomide.*
  - Study 1 randomized 927 patients (n=465 to Kesimpta, n=462 to teriflunomide). ARR was significantly lower in patients treated with Kesimpta (0.11) than in patients treated with teriflunomide (0.22); relative rate reduction 51% ($p<0.001$).
  - Study 2 randomized 955 patients (n=481 to Kesimpta, n=474 to teriflunomide). ARR was significantly lower in patients treated with Kesimpta (0.10) than in patients treated with teriflunomide (0.25); relative rate reduction 59% ($p<0.001$).
- *Kesimpta significantly reduced the risk of 3-month CDP compared to teriflunomide.*
  - 3-month CDP demonstrated a relative risk reduction of 34.4% (10.9% vs. 15.0%; p=0.002).
- *Kesimpta significantly reduced the number of T1 GdE lesions and the rate of new or enlarging T2 lesions.*
  - In Study 1, Kesimpta significantly reduced the mean number of T1 GdE lesions per MRI scan compared to teriflunomide (0.01 vs. 0.45; relative reduction 98%), as well as the number of new or enlarging T2 lesions (0.72 vs. 4.00; relative reduction 82.0%); ($p<0.001$ for each)
  - In Study 2, Kesimpta significantly reduced the mean number of T1 GdE lesions per MRI scan compared to teriflunomide (0.03 vs. 0.51; relative reduction 94%), as well as the number of new or enlarging T2 lesions (0.64 vs. 4.15; relative reduction 85%); ($p<0.001$ for each).

A separate post hoc analysis demonstrated that the odds of achieving no evidence of disease activity (NEDA-3; no relapses, no MRI lesions, and no 6-month disability worsening combined) with Kesimpta versus teriflunomide were >3-fold higher at Months 0–12 (47.0% vs 24.5% of patients) and >8-fold higher at Months 12–24 (87.8% vs 48.2% of patients).[3]

Adverse Event Profile[1]: Most common adverse reactions (incidence >10%) upper respiratory tract infection, headache, injection- related reactions, and local injection site reactions.

Contraindications[1]: Active hepatitis B virus infection.

Warnings and Precautions[1]:

- Infections: Delay Kesimpta administration in patients with an active infection until the infection is resolved. Vaccination with live-attenuated or live vaccines is not recommended during treatment with Kesimpta and after discontinuation, until B-cell repletion.
- Injection-Related Reactions: Management for injection-related reactions depends on the type and severity of the reaction.
- Reduction in Immunoglobulins: Monitor the level of immunoglobulins at the beginning, during, and after discontinuation of treatment with Kesimpta until B-cell repletion. Consider discontinuing Kesimpta if a patient develops a serious opportunistic infection or recurrent infections if immunoglobulin levels indicate immune compromise.

- Fetal Rrisk: May cause fetal harm based on animal data. Advise females of reproductive potential of the potential risk to a fetus and to use an effective method of contraception during treatment and for 6 months after stopping Kesimpta.

References:

1. KESIMPTA® (ofatumumab) [prescribing information]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; August 2020.
2. Hauser SL, Bar-Or A, Cohen J, et al. Efficacy and Safety of Ofatumumab Versus Teriflunomide in RMS: Phase 3 ASCLEPIOS I and II Trials. *N Engl J Med.* 2020; 383:546−57.
3. Hauser S, Bar-Or A, Cohen J, et al. Ofatumumab versus teriflunomide in relapsing multiple sclerosis: analysis of no evidence of disease activity (NEDA-3) from ASCLEPIOS I and II trials. Eur J Neurol. 2020;27(S1).