What is KESIMPTA?

Kesimpta® (ofatumumab) injection, for subcutaneous use, is approved by the US Food and Drug Administration (FDA) for the treatment of relapsing forms of multiple sclerosis (RMS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults. Kesimpta is a targeted, precisely dosed and delivered B-cell therapy that provides the flexibility of self-administration for adults with RMS.[1]

What was the approval based on?

The FDA approval was based on two Phase III ASCLEPIOS studies, which evaluated the safety and efficacy of Kesimpta versus teriflunomide in adults with RMS. ASCLEPIOS I and II found that Kesimpta showed superior efficacy with a favorable safety profile compared to teriflunomide.[1]

ASCLEPIOS I and II Primary and Secondary Endpoints Results

In the ASCLEPIOS I and II trials, Kesimpta demonstrated a significant reduction in the annualized relapse rate (ARR) (primary endpoint) by 51% (0.11 vs 0.22) and 59% (0.10 vs 0.25) compared to teriflunomide (*P*<.001 in both studies), respectively.[1] The studies also evaluated key secondary endpoints, and Kesimpta demonstrated:

- ✓ A significant reduction in the mean number of both gadolinium-enhancing (Gd+) T1 lesions (98% and 94% relative reduction in ASCLEPIOS I and II, respectively, both *P*<.001) and new or enlarging T2 lesions (82% and 85% relative reduction in ASCLEPIOS I and II, respectively, both *P*<.001) vs teriflunomide[1]
- ✓ A relative risk reduction of 34.4% (*P*=.002) in 3-month confirmed disability progression (CDP) compared with teriflunomide in a pre-specified pooled meta-analysis, as defined in ASCLEPIOS[1]
- ✓ A similar safety to teriflunomide, with the frequency of serious infections and malignancies also being similar across both treatment groups[1]
  - Upper respiratory tract infection, headache, injection-related reactions, and local injection site reactions were the most commonly observed adverse reactions with Kesimpta (incidence greater than 10%)[1]

No evidence of disease activity (NEDA-3)

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 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).[2]

Indication

KESIMPTA is a prescription medicine used to treat adults with relapsing forms of multiple sclerosis (MS) including clinically isolated syndrome (CIS), relapsing-remitting disease, and active secondary progressive disease.

It is not known if KESIMPTA is safe or effective in children.

Important Safety Information

Who should not take KESIMPTA?
Do NOT take KESIMPTA if you have active hepatitis B virus (HBV) infection.

Please see additional Important Safety Information on the following page.
Please see full Prescribing Information including Medication Guide.

How do patients take KESIMPTA?

The recommended dosage of Kesimpta is initial dosing of 20 mg by subcutaneous injection at Weeks 0, 1, and 2, followed by subsequent dosing of 20 mg by subcutaneous injection once monthly starting at Week 4.[1] Kesimpta can be self-administered at home via the Sensoready® autoinjector pen, once monthly. No premedication is required as part of the initiation of the medication.[1*]

How does KESIMPTA work?

Kesimpta is an anti-CD20 monoclonal antibody (mAb) that targets B-cells, a key target in MS pathogenesis. As shown in preclinical studies, Kesimpta is thought to work by binding to a distinct epitope on the CD20 molecule inducing potent B-cell lysis and depletion.[3]

The selective mechanism of action and subcutaneous administration of Kesimpta allows precise delivery to the lymph nodes, where B-cell depletion in MS is needed, and preclinical studies have shown that it may preserve the B-cells in the spleen.[4] Kesimpta demonstrated a median time to B-cell recovery of 40 weeks post treatment discontinuation, based on modeling and simulation data.[1]

*Initial doses of Kesimpta are given at Weeks 0, 1 and 2, with the first injection performed under the guidance of a healthcare professional.

Important Safety Information (continued)

What is the most important information I should know about KESIMPTA?
KESIMPTA can cause serious side effects such as:

- **Infections.** Serious infections can happen during treatment with KESIMPTA. If you have an active infection, your healthcare provider (HCP) should delay your treatment with KESIMPTA until your infection is gone. KESIMPTA taken before or after other medicines that weaken the immune system may increase your risk of getting infections. Tell your HCP right away if you have any infections or get any symptoms including painful and frequent urination, nasal congestion, runny nose, sore throat, fever, chills, cough, or body aches.
- **HBV reactivation.** If you have ever had HBV infection, it may become active again during or after treatment with KESIMPTA (reactivation). If this happens, it may cause serious liver problems including liver failure or death. Before starting KESIMPTA, your HCP will do a blood test to check for HBV. They will also continue to monitor you during and after treatment with KESIMPTA for HBV. Tell your HCP right away if you get worsening tiredness or yellowing of your skin or the white part of your eyes.
- **Progressive Multifocal Leukoencephalopathy (PML).** PML may happen with KESIMPTA. PML is a rare, serious brain infection caused by a virus that may get worse over days or weeks. PML can result in death or severe disability. Tell your HCP right away if you have any new or worsening neurologic signs or symptoms. These may include weakness on one side of your body, loss of coordination in arms and legs, vision problems, changes in thinking and memory, which may lead to confusion and personality changes.
- **Weakened immune system**. KESIMPTA taken before or after other medicines that weaken the immune system could increase your risk of getting infections.

Before you take KESIMPTA, tell your HCP about all your medical conditions, including if you:

- Have or think you have an infection including HBV or PML.
- Have ever taken, currently take, or plan to take medicines that affect your immune system. These medicines could increase your risk of getting an infection.
- Have had a recent vaccination or are scheduled to receive any vaccinations.
    - You should receive any required ‘live’ or ‘live-attenuated’ vaccines at least 4 weeks before you start treatment with KESIMPTA. You should not receive ‘live’ or ‘live-attenuated’ vaccines while you are being treated with KESIMPTA and until your HCP tells you that your immune system is no longer weakened.
    - Whenever possible, you should receive any ‘non-live’ vaccines at least 2 weeks before you start treatment with KESIMPTA.
    - Talk to your HCP about vaccinations for your baby if you used KESIMPTA during your pregnancy.

Please see additional Important Safety Information on the following page.
Please see full Prescribing Information including Medication Guide.

Important Safety Information (continued)

- Are pregnant, think that you might be pregnant, or plan to become pregnant. It is not known if KESIMPTA will harm your unborn baby. Females who can become pregnant should use birth control (contraception) during treatment with KESIMPTA and for 6 months after your last treatment. Talk with your HCP about what birth control method is right for you during this time.
- Are breastfeeding or plan to breastfeed. It is not known if KESIMPTA passes into your breast milk. Talk to your HCP about the best way to feed your baby if you take KESIMPTA.

Tell your HCP about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

How should I use KESIMPTA?
See the detailed Instructions for Use that comes with KESIMPTA for information about how to prepare and inject a dose of KESIMPTA and how to properly throw away (dispose of) used KESIMPTA Sensoready pens or prefilled syringes.

- Use KESIMPTA exactly as your HCP tells you to use it.
- Your HCP will show you how to prepare and inject KESIMPTA the right way before you use it for the first time.
- Do not inject into areas where the skin is tender, bruised, red, scaly or hard. Avoid areas with moles, scars, or stretch marks.

KESIMPTA may cause serious side effects including:

- **Injection-related reactions.** Injection-related reactions are a common side effect of KESIMPTA. Injecting KESIMPTA can cause injection-related reactions that can happen within 24 hours (1 day) following the first injections and with later injections. Talk with your HCP if you have any of these signs and symptoms:
  - **at or near the injection site**: redness of the skin, swelling, itching and pain or
  - **that may happen when certain substances are released in your body:** fever, headache, pain in the muscles, chills, and tiredness.
- **Low immunoglobulins.** KESIMPTA may cause a decrease in some types of antibodies. Your HCP will do blood tests to check your blood immunoglobulin levels.

The most common side effects of KESIMPTA include:

- Upper respiratory tract infection, with symptoms such as sore throat and runny nose, and headache.
- Headache.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch, or call 1-800-FDA-1088.

Please see full Prescribing Information including Medication Guide.

References

1. Kesimpta Prescribing Information. East Hanover, NJ: Novartis Pharmaceuticals Corp; August 2020.
2. 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).
3. Smith P, Kakarieka A, Wallstroem E. Ofatumumab is a fully human anti-CD20 antibody achieving potent B-cell depletion through binding a distinct epitope. Poster presentation at: ECTRIMS; September 2016; London, UK
4. Smith P, Huck C, Wegert V, et al. Low-dose, subcutaneous anti-CD20 therapy effectively depletes B-cells and ameliorates CNS autoimmunity. Poster presentation at: ECTRIMS; September 2016; London, UK.

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