Kesimpta (ofatumumab)

NEW PRODUCT SLIDESHOW

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Introduction

- **Brand name:** Kesimpta
- **Generic name:** Ofatumumab
- **Pharmacologic class:** CD20-directed cytolytic monoclonal antibody
- **Strength and Formulation:** 20mg/0.4mL; solution for subcutaneous injection; preservative-free
- **Manufacturer:** Novartis
- **How supplied:** Single-dose Sensoready pen—1; Single-dose prefilled syringe—1
- **Legal Classification:** Rx

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Kesimpta

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Indication

- Relapsing forms of **multiple sclerosis** (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults.

Dosage and Administration

- Prior to initiating, perform hepatitis B virus screening, test for quantitative serum immunoglobulins, and administer all immunizations according to guidelines.
- First injection should be performed by healthcare professional; subsequent injections can be self-administered by patient.
- Give by SC inj into abdomen, thigh, or outer upper arm.
- Initially 20mg at weeks 0, 1, 2, followed by 20mg once monthly starting at week 4.

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Considerations for Specific Populations

- **Pregnancy:** No adequate data on developmental risk.
- **Females of childbearing potential:** Use effective contraception during and for 6 months after the last treatment.
- **Nursing mothers:** No data on the presence of ofatumumab in human milk.
- **Pediatric**: Not established.
- **Geriatrics**: Clinical studies did not include sufficient numbers to determine difference from younger patients.
- **Renal impairment**: Not studied.
- **Hepatic impairment**: Not studied.

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Contraindications

Active HBV infection

- Fatal infections caused by HBV in patients who have not been previously infected have occurred in patients being treated with ofatumumab for chronic lymphocytic leukemia (at higher IV doses than the recommended dose in MS but for a shorter duration of treatment).
- Screening should include Hepatitis B surface antigen (HBsAg) and Hepatitis B Core Antibody (HBcAb) testing, at a minimum.

Warnings and Precautions

- Increased risk of infections; delay treatment in patients with active infection.
- Consult liver disease experts prior to and during treatment for patients who are negative for HBsAg and positive for HBcAb or are carriers of HBV.
- Withhold at first sign/symptom of progressive multifocal leukoencephalopathy (PML) and perform a diagnostic evaluation; discontinue if confirmed.

Warnings and Precautions

- Complete all immunizations according to guidelines ≥4 weeks prior to treatment for live or live-attenuated vaccines and ≥2 weeks prior to treatment initiation for inactivated vaccines.
- Vaccination with live or live-attenuated vaccines: not recommended during treatment and after discontinuation until B-cell repletion.
- Infants born to mothers treated during pregnancy:
  - Do not administer live or live-attenuated vaccines before confirming B-cell recovery.
  - Inactivated vaccines may be administered but an assessment of vaccine immune response should be considered.

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Warnings and Precautions

- Perform testing for quantitative serum immunoglobulins prior to initiation; monitor during and after discontinuation until B-cell repletion.
- Consult immunology experts prior to initiation for patients with low serum immunoglobulins.
- Consider discontinuing Kesimpta if patient with low immunoglobulins develops serious opportunistic or recurrent infection, or if prolonged hypogammaglobulinemia requires treatment with IV immunoglobulins.

Interactions

- Concomitant live or live-attenuated vaccines: not recommended during treatment and after discontinuation until B-cell repletion.
- May interfere with the effectiveness of inactivated vaccines.
- Concomitant use with immunosuppressants, including systemic corticosteroids, may increase risk of infection.
- Consider additive immune system effects when coadministering immunosuppressive therapies.

Adverse Reactions

- **Most common (>10%)**: Upper respiratory tract infection, headache, injection-related reactions, local injection site reactions
- **Others**: Reduction in immunoglobulins
- Potential for immunogenicity

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Mechanism of Action

- The precise mechanism by which **ofatumumab** exerts its therapeutic effects in multiple sclerosis 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.

Pharmacokinetics

- Ofatumumab is a protein for which the expected metabolic pathway is degradation to small peptides and amino acids by ubiquitous proteolytic enzymes.
- Eliminated in 2 ways:
  - A target-independent route as with other IgG molecules.
  - A target-mediated route that is related to binding to B-cells.
- Half-life: ~16 days (at steady state).

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Clinical Trials

- Efficacy was based on 2 randomized, double-blind, double-dummy, active comparator-controlled clinical trials (Study 1 [NCT02792218] and Study 2 [NCT02792231]) in 1882 adult patients with relapsing forms of MS.
- Patients had at least 1 relapse in the previous year, 2 relapses in the previous 2 years, or the presence of a T1 gadolinium-enhancing (GdE) lesion in the previous year.
- Patients were required to have an Expanded Disability Status Scale (EDSS) score from 0 to 5.5.

Clinical Trials

- Patients were randomized 1:1 to receive either Kesimpta 20mg SC on days 1, 7, and 14, then 20mg every 4 weeks thereafter starting at week 4 with a daily oral placebo, or teriflunomide 14mg orally once daily with a placebo administered SC on days 1, 7, 14, and every 4 weeks thereafter.

- The **primary end point** of both trials was the annualized relapse rate (ARR) over the treatment period.

Clinical Trials

- **Patient demographics (Study 1)**
  - Mean age: 38 years; 89% White; 69% female.
  - Mean time since MS diagnosis: 5.7 years.
  - Median EDSS score: 3.0; 60% received nonsteroid MS therapy.
  - At baseline, mean number of relapses in the previous year was 1; mean number of T1 GdE lesions on MRI scan was 1.5.
- **Patient demographics (Study 2)**
  - Mean age: 38 years; 87% White; 67% female.
  - Mean time since MS diagnosis: 5.5 years.
  - Median EDSS score: 2.5; 61% received nonsteroid MS therapy.
  - At baseline, mean number of relapses in the previous year was 1.3; mean number of T1 GdE lesions on MRI scan was 1.6.

Clinical Trials

- Results from both studies showed:
  - Kesimpta significantly lowered the ARR compared with teriflunomide.
  - Kesimpta significantly reduced the risk of 3-month confirmed disability progression compared with teriflunomide, as well as the number of T1 GdE lesions and the rate of new or enlarging T2 lesions.

Clinical Trials

- **Study 1**
  - ARR: 0.11 with Kesimpta vs 0.22 with teriflunomide
    - Relative reduction: 51% (*P* <.001)
  - Proportion of patients with 3-month confirmed disability progression: 10.9% with Kesimpta vs 15.0% with teriflunomide
    - Relative risk reduction: 34.4% (*P* =.002)
  - Mean number of T1 GdE lesion per MRI scan: 0.01 with Kesimpta vs 0.45 with teriflunomide
    - Relative reduction: 98% (*P* <.001)
  - Number of new or enlarging T2 lesions per year: 0.72 with Kesimpta vs 4.00 with teriflunomide
    - Relative reduction: 82% (*P* <.001)

Clinical Trials

- **Study 2**
  - ARR: 0.10 with Kesimpta vs 0.25 with teriflunomide
    - Relative reduction: 59% (*P* <.001)
  - Proportion of patients with 3-month confirmed disability progression: 10.9% with Kesimpta vs 15.0% with teriflunomide
    - Relative risk reduction: 34.4% (*P* =.002)
  - Mean number of T1 GdE lesion per MRI scan: 0.03 with Kesimpta vs 0.51 with teriflunomide
    - Relative reduction: 94% (*P* <.001)
  - Number of new or enlarging T2 lesions per year: 0.64 with Kesimpta vs 4.15 with teriflunomide
    - Relative reduction: 85% (*P* <.001)

New Product Monograph

- For more information view the product monograph available at:

  https://www.empr.com/drug/kesimpta/