Product Monograph

Including Patient Medication Information

PrKESIMPTA®

ofatumumab injection

Produced in murine cell lines (NS0) by recombinant DNA technology

Solution, 20 mg / 0.4 mL, for subcutaneous use

Professed Standard

Selective immunomodulator

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Recent Major Label Changes

4 Dosage and Administration, 4.1 Dosing Considerations	2026-08
7 Warnings and Precautions, Hepatic/Biliary/Pancreatic	2026-08
7.0 Warnings and Precautions, 7.1.1 Pregnancy	2026-11

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Part 1: Healthcare Professional Information

1. Indications

KESIMPTA® (ofatumumab injection) is indicated for:

- the treatment of adult patients with relapsing remitting multiple sclerosis (RRMS) with active disease defined by clinical and imaging features (see 14 Clinical Trials).

KESIMPTA treatment should be initiated and supervised by healthcare professionals experienced in the treatment of patients with MS and who are familiar with the efficacy and safety profile of KESIMPTA (see 7 Warnings and Precautions).

1.1. Pediatrics

Pediatrics (< 18 years of age): The safety and efficacy of KESIMPTA in pediatric MS patients below the age of (< 18 years of age) have not been studied. KESIMPTA is not authorized for pediatric use.

1.2. Geriatrics

Geriatrics: Ofatumumab was not studied in patients ≥ 55 years of age.

2. Contraindications

KESIMPTA is contraindicated in patients:

- Who are hypersensitive to this drug or to any ingredient in the formulation, including any non-medicinal ingredient, or component of the container. For a complete listing, see 6 Dosage Forms, Strengths, Composition and Packaging.
- With active HBV infection (see 4.1 Dosing Considerations and 7 Warnings and Precautions, Infections)
- With severe, active infections (see 7 Warnings and Precautions, Infections)
- Who have or have had confirmed progressive multifocal leukoencephalopathy (PML) (see 7 Warnings and Precautions, Infections)
- Who are in a severely immunocompromised state (see 7 Warnings and Precautions, General)
- With known active malignancies

4. Dosage and Administration

4.1. Dosing Considerations

KESIMPTA is intended for patient self-administration by subcutaneous injection. Administration should be performed by an individual who has been trained to administer the product.

The first injection of KESIMPTA should be performed under the guidance of an experienced healthcare professional (see 7 Warnings and Precautions, General).

Assessment Prior to First Dose of KESIMPTA

Hepatitis B Virus Screening

Prior to initiating KESIMPTA, perform Hepatitis B virus (HBV) screening. KESIMPTA is contraindicated in patients with active HBV confirmed by positive results for HBsAg and anti-HBV tests. For patients who are negative for surface antigen [HBsAg] and positive for HB core antibody [HBcAb+] or are carriers of HBV [HBsAg+], consult liver disease experts before starting and during treatment (see 7 Warnings and Precautions, Infections).

Serum Immunoglobulins

Prior to initiating KESIMPTA, perform testing for quantitative serum immunoglobulins (see 7 Warnings and Precautions, General). For patients with low serum immunoglobulins, consult immunology experts before initiating treatment with KESIMPTA.

Vaccinations

Because vaccination with live-attenuated or live vaccines is not recommended during treatment and after discontinuation until B-cell repletion, administer all necessary immunizations according to immunization guidelines at least 4 weeks prior to initiation of KESIMPTA for live or live-attenuated vaccines, and whenever possible, at least 2 weeks prior to initiation of KESIMPTA for inactivated vaccines (see 7 Warnings and Precautions, Immune and 10 Clinical Pharmacology).

Liver Function Tests

Prior to initiating KESIMPTA, obtain serum aminotransferases (alanine aminotransferase [ALT] and aspartate aminotransferase [AST]), alkaline phosphatase, and bilirubin levels (see 7 Warnings and Precautions, Hepatic/Biliary/Pancreatic).

Assessment before every injection

Infection Assessment

In case of active infection, delaying injection of KESIMPTA should be considered until the infection resolves (see 7 Warnings and Precautions, Infections).

Premedication

The decision to initiate or continue premedication should be made on an individual patient basis (see 7 Warnings and Precautions, General).

4.2. Recommended Dose and Dosage Adjustment

The recommended dosage of KESIMPTA is:

- initial dosing of 20 mg by subcutaneous injection at weeks 0, 1 and 2, followed by
- subsequent monthly dosing of 20 mg by subcutaneous injection, starting at week 4.

Special populations

The pharmacokinetics of ofatumumab have not been studied in patients with renal or hepatic impairment, pediatric and geriatric patients (see 10 Clinical Pharmacology, Special population).

4.4. Administration

The usual sites for subcutaneous injections are the abdomen, the thigh and the upper outer arm.

Prior to administration, allow KESIMPTA to reach room temperature for about 15 to 30 minutes.

Visually inspect for particulate matter prior to administration. Do not use if the solution contains visible particles or is cloudy.

Do not freeze. Do not shake.

Comprehensive instructions for the administration of KESIMPTA are provided in the Patient Medication Information.

4.5. Missed Dose

If an injection of KESIMPTA is missed, it should be administered as soon as possible without waiting until the next scheduled dose. Subsequent doses should be reset to administer the next sequential dose at the recommended once a month intervals.

5. Overdose

No cases of overdose have been reported in RMS clinical studies.

Doses up to 700 mg have been administered intravenously in clinical studies with MS patients without dose-limiting toxicity. In the event of overdose, it is recommended that the patient be monitored for any signs or symptoms of adverse reactions and appropriate symptomatic treatment be instituted as necessary.

For the most recent information in the management of a suspected drug overdose, contact your regional poison control centre or Health Canada's toll-free number, 1-844 POISON-X (1-844-764-7669).

6. Dosage Forms, Strengths, Composition, and Packaging

To help ensure the traceability of biologic products healthcare professionals should record both the brand name and the non-proprietary (active ingredient) name as well as other product-specific identifiers such as the Drug Identification Number (DIN) and the batch/lot number of the product supplied.

Table 1 – Dosage Forms, Strengths, and Composition

Route of Administration	Dosage Form/ Strength/Composition	Non-Medicinal Ingredients
Subcutaneous injection	Solution for injection in Pre-filled syringe Pre-filled Sensoready® pen / 20 mg/0.4 mL	disodium edetate dihydrate; hydrochloric acid; L-arginine; polysorbate 80; sodium acetate trihydrate; sodium chloride and water for injection

Description

The single-use solution for injection is sterile, preservative-free, clear to slightly opalescent, and colorless to slightly brownish-yellow.

KESIMPTA is supplied as follows:

- 20 mg/0.4 mL Solution for injection in a pre-filled syringe*
- 20 mg/0.4 mL Solution for injection in a pre-filled Sensoready pen

Each pre-filled syringe and pre-filled Sensoready pen contains 20 mg ofatumumab solution for injection (0.4 mL of 50 mg/mL solution).

*Pre-filled syringes are not available in Canada

7. Warnings and Precautions

General

Injection-related reactions

Injection site reaction (local) symptoms observed in clinical studies included erythema, swelling, itching and pain.

Injection-related reactions with systemic symptoms observed in clinical studies occurred predominantly within 24 hours of the first injection, but were also observed with later injections. Symptoms observed include fever, headache, myalgia, chills and fatigue and were predominantly (99.8%) mild to moderate in severity. There were no life-threatening injection reactions in RMS clinical studies.

Additional systemic injection-related reactions (SIRRs) reported in the post-marketing setting include rash, urticaria, dyspnea, angioedema (e.g., tongue, pharyngeal or laryngeal swelling), and rare cases which were reported as anaphylaxis. Most of the cases were non-serious and occurred with first injection. While there were some cases which were serious and resulted in discontinuation of KESIMPTA treatment, there were also cases where patients were able to continue KESIMPTA treatment.

Some SIRR symptoms may be clinically indistinguishable from Type 1 acute hypersensitivity reactions (IgE-mediated). Patients should be informed that SIRRs generally occur within 24 hours and predominantly following the first injection. SIRRs can be managed with symptomatic treatment, should they occur.

A hypersensitivity reaction may present with any injection, although typically would not present with the first injection. For subsequent injections, more severe symptoms than previously experienced, or new severe symptoms, should prompt consideration of a potential hypersensitivity reaction. Patients with known IgE mediated hypersensitivity to KESIMPTA must not be treated with KESIMPTA (see 2 Contraindications).

Ofatumumab-treated patients who received premedication with methylprednisolone (or an equivalent steroid) experienced fewer symptoms such as fever, myalgia, chills, and nausea. However, in some patients, the use of steroid premedication increased the occurrence of flushing, chest discomfort, hypertension, tachycardia, and abdominal pain even in the absence of ofatumumab treatment (i.e. in patients receiving placebo injections). Therefore, the decision to initiate or continue premedication should be made on an individual patient basis (see 4.1 Dosing Considerations).

The first injection of KESIMPTA should be performed under the guidance of an appropriately trained healthcare professional.

Possible Increased Risk of Immunosuppressant Effects with other Immunosuppressants

When initiating KESIMPTA after immunosuppressive therapy or initiating immunosuppressive therapy after KESIMPTA, consider the potential for increased immunosuppressive effects (see 9.2 Drug Interactions Overview and 10 Clinical Pharmacology).

Hepatic/Biliary/Pancreatic

Liver Injury

Clinically significant liver injury, without findings of viral hepatitis, has been observed in the postmarketing setting in patients treated with KESIMPTA. Signs of liver injury, including markedly elevated serum hepatic enzymes with elevated total bilirubin, have occurred from days to months after treatment initiation.

Liver function tests should be performed before initiation of treatment with KESIMPTA, and patients should be monitored for signs and symptoms of any hepatic injury during treatment. Serum aminotransferases, alkaline phosphatase, and bilirubin levels should be measured in patients who report symptoms that may indicate liver injury, including new or worsening fatigue, anorexia, nausea, vomiting, right upper abdominal discomfort, dark urine, or jaundice.

If liver injury is confirmed, discontinue KESIMPTA. If an alternative etiology is identified, treatment with KESIMPTA can be resumed only when the event has been fully resolved.

Immune

Vaccinations

Healthcare professionals should review the immunization status of patients before starting treatment with KESIMPTA. All immunizations should be administered according to immunization guidelines at least 4 weeks prior to initiation of KESIMPTA for live or live-attenuated vaccines and, whenever possible, at least 2 weeks prior to initiation of KESIMPTA for inactivated vaccines.

KESIMPTA may interfere with the effectiveness of inactivated vaccines (see 9.2 Drug Interactions Overview).

The safety of immunization with live or live-attenuated vaccines following KESIMPTA therapy has not been studied. Vaccination with live or live-attenuated vaccines is not recommended during treatment and after discontinuation until B-cell repletion (see 10.1 Mechanism of Action).

Vaccination of infants born to mothers treated with KESIMPTA during pregnancy

Due to the potential depletion of B cells in infants of mothers treated with KESIMPTA during pregnancy, live or live-attenuated vaccines should not be administered before confirming the B-cell count is within normal range. Depletion of B-cells in these infants may increase the risks from live or live-attenuated vaccines (see 16 Non-Clinical Toxicology and 10 Clinical Pharmacology).

Inactivated vaccines may follow the local immunization schedule, but healthcare professionals should assess whether a protective immune response was mounted. Healthcare professionals may consult vaccination experts as the efficacy of the vaccination of an infant may be decreased following KESIMPTA exposure (see 9.2 Drug Interactions Overview and 7.1.1 Pregnancy).

Infections

Delay KESIMPTA administration in patients with an active infection until the infection is resolved.

It is recommended to evaluate the patient's immune status prior to initiating therapy (see 4.1 Dosing Considerations).

An increased risk of infections has been observed with other anti – CD20 B-cell depleting therapies. KESIMPTA has the potential for an increased risk of infections, including serious bacterial, fungal, and new or reactivated viral infections; some of these infections have been fatal in patients treated with other anti-CD20 antibodies.

In Study G2301 and Study G2302, the proportion of patients with infections and serious infections was similar in the ofatumumab and the teriflunomide treatment groups (51.6% vs 52.7%, and 2.5 vs 1.8%, respectively).

Progressive Multifocal Leukoencephalopathy

Progressive multifocal leukoencephalopathy (PML) is an opportunistic viral infection of the brain caused by the John Cunningham virus (JCV) that typically only occurs in patients who are immunocompromised, and that usually leads to death or severe disability.

Although no cases of PML have been reported for KESIMPTA in the RMS clinical studies, PML resulting in death has occurred in patients being treated with ofatumumab for CLL (at substantially higher intravenous doses than the recommended dose in MS but for a shorter duration of treatment). In addition, JCV infection resulting in PML has also been observed in patients treated with other anti-CD20 antibodies and other MS therapies. At the first sign or symptom suggestive of PML, withhold KESIMPTA and perform an appropriate diagnostic evaluation. MRI findings may be apparent before clinical signs or symptoms. Typical symptoms associated with PML are diverse, progress over days to weeks, and include progressive weakness on one side of the body or clumsiness of limbs, disturbance of vision, and changes in thinking, memory, and orientation leading to confusion and personality changes.

If PML is confirmed, discontinue treatment of KESIMPTA.

Hepatitis B Virus Reactivation

No cases of hepatitis B virus (HBV) reactivation were identified in KESIMPTA RMS clinical studies. However, HBV reactivation has occurred in patients treated with anti-CD20 antibodies, which in some cases resulted in fulminant hepatitis, hepatic failure and death.

Patients with active hepatitis B disease should not be treated with KESIMPTA (see 2 Contraindications). HBV screening should be performed in all patients before initiation of treatment with KESIMPTA (see 4.1 Dosing Considerations). At minimum screening should include Hepatitis B surface antigen (HBsAg) and Hepatitis B Core Antibody (HBcAb) testing. These can be complemented with other appropriate markers as per local guidelines. For patients who are negative for HBsAg and positive for HB core antibody [HBcAb+] or are carriers of HBV [HBsAg+], consult liver disease experts before starting, and during, treatment with KESIMPTA. These patients should be monitored and managed following local medical standards to prevent hepatitis B reactivation.

In the event of HBV reactivation, KESIMPTA and concomitant medications should be discontinued until the active infection is resolved.

Reproductive Health

Females of childbearing potential should use effective contraception (methods that result in less than 1% pregnancy rates) while receiving KESIMPTA and for 6 months after the last treatment of KESIMPTA.

7.1. Special Populations

7.1.1. Pregnancy

Human IgG is known to cross the placental barrier; therefore, KESIMPTA may be transmitted from the mother to the developing fetus. In humans, IgG transport across the placenta is an active process mediated by the neonatal Fc receptor (FcRn), which is low in the first trimester and increases progressively from the early second trimester.

In the ongoing KESIMPTA Pregnancy Registry and the KESIMPTA PRegnancy outcomes Intensive Monitoring (PRIM) study, over 1000 prospective pregnancy cases with maternal exposure during pregnancy were retrieved including approximately 500 cases with known pregnancy outcomes. As the studies are ongoing, data are not yet sufficient to draw conclusions on pregnancy and infant outcomes.

The majority of patients were treated with KESIMPTA pre-conception and/or during the first trimester of pregnancy. Experience with administration during the second and third trimesters is limited.

Treatment with KESIMPTA is not recommended during pregnancy unless the potential benefit to the mother outweighs the potential risk to the fetus. Females of reproductive potential should use contraception during treatment with KESIMPTA and for 6 months following treatment (see 7 Warnings and Precautions, Reproductive health; 10.3 Pharmacokinetics).

Animal studies have shown that ofatumumab may cross the placenta and causes fetal B-cell depletion in monkeys. In addition, in monkeys, in utero exposure to ofatumumab resulted in incidences of B-cell depletion, infection, and deaths in infant monkeys. Ofatumumab was also detected in infant monkey blood (see 16 Non-Clinical Toxicology).

Transient peripheral B-cell depletion and lymphocytopenia have been reported in infants born to mothers exposed to other anti-CD20 antibodies during pregnancy. The potential duration of B-cell depletion in infants exposed to ofatumumab in utero, and the impact of B-cell depletion on the safety and effectiveness of vaccines, are unknown (see 7 Warnings and Precautions, Immune and 10 Clinical Pharmacology).

7.1.2. Breastfeeding

There are no data on the presence of KESIMPTA in human milk, the effects on the breastfed infant, or the effects on human milk production. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for KESIMPTA and any potential adverse effects on the breastfed infant from KESIMPTA.

7.1.3. Pediatrics

Pediatrics (< 18 years of age): The safety and efficacy of KESIMPTA in pediatric MS patients below the age of 18 years have not been studied. KESIMPTA is not authorized for pediatric use.

7.1.4. Geriatrics

No studies have been performed in elderly MS patients. Ofatumumab was studied in patients with RMS aged 18 to 55 years.

8. Adverse Reactions

8.1. Adverse Reaction Overview

Approximately 1500 (n=1420 at the date of submission) patients with RMS received ofatumumab in clinical studies. In the two Phase 3 pivotal studies, 1882 patients with RMS were randomized, 946 of whom were treated with ofatumumab for a median duration of 85 weeks; 33% (n=312) of patients receiving ofatumumab were treated for more than 96 weeks (see 14 Clinical Trials).

The proportion of patients with adverse events (AEs) (83.6% versus 84.2%) and the AEs leading to drug discontinuation (5.7% versus 5.2%) were similar in the ofatumumab and teriflunomide groups.

The most common adverse reactions occurring in >10% of patients treated with KESIMPTA, and more frequently than in patients treated with teriflunomide, were upper respiratory tract infections, injection-related reactions (systemic), headache, and injection-site reactions (local). The most common cause of discontinuation in patients treated with KESIMPTA was low immunoglobulin M (3.3%), defined in trial protocols as IgM at 10% below the lower limit of normal (LLN).

8.2. Clinical Trial Adverse Reactions

Clinical trials are conducted under very specific conditions. Therefore, the frequencies of adverse reactions observed in the clinical trials may not reflect frequencies observed in clinical practice and should not be compared to frequencies reported in clinical trials of another drug.

Table 2 – Summary of Adverse Reactions associated with KESIMPTA with an incidence of ≥1% and higher than teriflunomide

Adverse drug reactions	Ofatumumab 20 mg n = 946 (%)	Teriflunomide 14 mg n = 936 (%)
Gastrointestinal disorders		
Constipation	24 (2.5)	14 (1.5)
General disorders and administration site conditions		
Injection site reaction (local)	103 (10.9)	52 (5.6)[2]
Pyrexia	37 (3.9)	26 (2.8)
Influenza like illness	21 (2.2)	10 (1.1)

Adverse drug reactions	Ofatumumab 20 mg n = 946 (%)	Teriflunomide 14 mg n = 936 (%)
Infections and infestations		
Nasopharyngitis	170 (18.0)	156 (16.7)
Urinary tract infection	97 (10.3)	78 (8.3)
Injury, poisoning and procedural complications		
Injection related reaction (systemic)	195 (20.6)	143 (15.3)[2]
Investigations		
Blood immunoglobulin M decreased	56 (5.9)	21 (2.2)
Immunoglobulins decreased	15 (1.6)	2 (0.2)
Musculoskeletal and connective tissue disorders		
Back pain	72 (7.6)	58 (6.2)
Muscular weakness	23 (2.4)	13 (1.4)
Psychiatric disorders		
Anxiety	43 (4.5)	33 (3.5)

[1)] Pooled data from treatment epochs of G2301 and G2302 (safety set)

[2)] Teriflunomide group received matching placebo injections

Description of selected adverse drug reactions

Upper Respiratory Tract Infections

A higher proportion of ofatumumab-treated patients experienced upper respiratory tract infections compared to teriflunomide-treated patients. In the RMS clinical studies, 39.4% of ofatumumab-treated patients experienced upper respiratory tract infections* compared to 37.8% of teriflunomide-treated patients. The infections were predominantly mild to moderate and mostly consisted of nasopharyngitis, upper respiratory tract infection and influenza.

*Grouping of preferred terms (PTs) was considered for adverse drug reactions frequency determination and includes the following: nasopharyngitis, upper respiratory tract infection, influenza, sinusitis, pharyngitis, rhinitis, viral upper respiratory infection, tonsillitis, acute sinusitis, pharyngotonsillitis, laryngitis, pharyngitis streptococcal, viral rhinitis, sinusitis bacterial, tonsillitis bacterial, viral pharyngitis, viral tonsillitis, chronic sinusitis, nasal herpes, tracheitis.

Injection related reactions and injection site reactions

In patients treated with ofatumumab in the RMS Phase 3 clinical studies, injection related reactions (systemic) and injection-site reactions (local) were reported in 20.6% and 10.9% of patients treated with ofatumumab, respectively.

The incidence of injection-related reactions was highest with the first injection (14.4%), decreasing significantly with subsequent injections (4.4% with second, <3% from third injection). Injection-related reactions were mostly (99.8%) mild to moderate in severity. Only two (0.2%) ofatumumab-treated MS patients reported serious injection-related reactions. There were no life-threatening injection-related reactions. The most frequently reported symptoms (≥2%) included fever, headache, myalgia, chills, and fatigue.

Local reactions at the administration site were very common. Injection-site reactions were all mild to moderate in severity and non-serious in nature. The most frequently reported symptoms (≥2%) included erythema, pain, itching, and swelling (see 7 Warnings and Precautions, General).

8.3. Less Common Clinical Trial Adverse Reactions

In RMS clinical trials, there are no adverse reactions that occurred at an incidence rate of <1%.

8.4. Abnormal Laboratory Findings: Hematologic, Clinical Chemistry, and Other Quantitative Data

Clinical Trial Findings

Immunoglobulins

In Study G2301 and Study G2302, a decrease in mean level of immunoglobulin M (IgM) was observed in KESIMPTA-treated patients, but was not associated with risk of infections. In 14.3% of patients in Study G2301 and Study G2302, treatment with KESIMPTA resulted in a decrease in a serum IgM that reached a value below 0.34 g/L. KESIMPTA was associated with a decrease of 4.3% in mean IgG levels after 48 weeks of treatment and an increase of 2.2% after 96 weeks.

Neutropenia

The overall incidence of neutropenia-related AEs was low in ofatumumab group (9 patients, 1.0%), as compared to 32 patients (3.4%) in the teriflunomide group and were mostly grade 1 or 2 and transient in nature. Causality to KESIMPTA has not been established.

8.5. Post-Market Adverse Reactions

The following adverse drug reactions have been derived from postmarketing experience with KESIMPTA via spontaneous case reports and literature cases. Because these reactions are reported voluntarily from a population of uncertain size, it is not possible to reliably estimate their frequency which is therefore categorized as not known.

Immune system disorders: Hypersensitivity reaction (see 7 Warnings and Precautions, General).

Hepatobiliary disorders: Liver injury (see 7 Warnings and Precautions, Hepatic/Biliary/Pancreatic)

9. Drug Interactions

9.2. Drug Interactions Overview

Ofatumumab does not share a common clearance pathway with chemical drugs that are metabolized by the cytochrome P450 system or other drug metabolizing enzymes. Additionally, there is no evidence that CD20 monoclonal antibodies (mAbs) are involved in the regulation of the expression of drug metabolizing enzymes. Interactions between KESIMPTA and other medicinal products have not been investigated in formal studies.

Vaccinations

The safety of and the ability to generate a primary or anamnestic (recall) response to immunization with live, live-attenuated or inactivated vaccines during ofatumumab treatment has not been investigated. The response to vaccination could be impaired when B-cells are depleted. It is recommended that patients complete immunizations prior to the start of KESIMPTA therapy (see 7 Warnings and Precautions, Immune).

Other Immunosuppressive or Immune-Modulating Therapies

Concomitant use of KESIMPTA with immunosuppressant drugs, including systemic corticosteroids, may increase the risk of infections. Consider the risk of additive immune system effects when co-administering immunosuppressive therapies with KESIMPTA.

When switching from therapies with prolonged immune effects, such as ocrelizumab, cladribine, fingolimod, natalizumab, teriflunomide, mitoxantrone, or dimethyl fumarate, the duration and mode of action of these therapies should be taken into account because of potential additive immunosuppressive effects when initiating KESIMPTA.
Patients in a severely immunocompromised state must not be treated until the condition resolves (see 2 Contraindications).

9.4. Drug-Drug Interactions

Interactions with other drugs have not been established.

9.5. Drug-Food Interactions

Interactions with food have not been established.

9.6. Drug-Herb Interactions

Interactions with herbal products have not been studied.

9.7. Drug-Laboratory Test Interactions

Interference of KESIMPTA with laboratory and/or diagnostic tests has not been studied.

10. Clinical Pharmacology

10.1. Mechanism of Action

B-cells play an important role in MS pathogenesis due to production of pro-inflammatory cytokines, release of auto-reactive antibodies and activation of pathogenic T cells. Ofatumumab is a human monoclonal antibody (IgG1κ) that binds specifically to a distinct epitope encompassing both the small and large extracellular loops of the CD20 molecule. The CD20 molecule is a transmembrane phosphoprotein expressed on B lymphocytes from the pre-B to mature B lymphocyte stage. The CD20 molecule is also expressed on a small fraction of activated T cells.
The binding of ofatumumab to CD20 induces lysis of CD20+ B-cells primarily through complement-dependent cytotoxicity (CDC) and to a lesser extent, through antibody-dependent cell-mediated cytotoxicity (ADCC). Ofatumumab has also been shown to induce cell lysis in both high and low CD20-expressing cells. CD20-expressing T cells are also depleted by ofatumumab.

10.2. Pharmacodynamics

B-cell depletion

For B-cell counts, assays for CD-19+ B-cells are used because the presence of KESIMPTA interferes with CD20 assay. In Study G2301 and Study G2302, KESIMPTA administered as recommended, resulted in a reduction of CD19+ B-cells to below the LLN in 77% and 78.8% of patients, respectively, one week after treatment initiation, and 95% and 95.8% of patients, respectively, two weeks after treatment initiation (see 4 Dosage and Administration and 14 Clinical Trials). In Study G2301 and Study G2302, at week 12, 99.3% to 99.5% of patients had CD19+B-cell counts below LLN. The CD19+B-cell counts remained below LLN for approximately 97% of patients in Study G2301 and 92% of patients in Study G2302 from 12 weeks through 120 weeks while on KESIMPTA treatment.

In a study of bioequivalence using the same dosing regimen as in Study G2301 and Study G2302, before initiation of the maintenance phase, total CD19+B-cell levels below the defined threshold of 10 cells/µL were achieved in 94% of patients starting week 4 and 98% of patients at week 12.

B-cell repletion

Data from the two RMS Phase 3 studies indicate a median time to B-cell recovery to either LLN or baseline value of 24.6 weeks post treatment discontinuation. PK and PD (B-cell) modelling and simulation for B-cell repletion corroborate these data, predicting median time to B-cell recovery to LLN of 23 weeks post treatment discontinuation.

10.3. Pharmacokinetics

Ofatumumab exhibits a long half-life and low volume of distribution similar to that of other monoclonal antibodies. Ofatumumab is eliminated through a non-linear target-mediated

route as well as a target-independent route mediated by non-specific endocytosis followed by intracellular catabolism. Higher baseline B-cell count results in greater component of target-mediated elimination clearance and shorter ofatumumab half-life at the start of therapy. Subsequent ofatumumab dosing leads to potent depletion of B-cells resulting in reduced overall clearance.

Absorption

A monthly subcutaneous dose of 20 mg leads to a mean AUCtau of 483 µg·h/mL and a mean Cmax of 1.43 µg/mL at steady state.

After subcutaneous administration, ofatumumab is believed to be predominantly absorbed via the lymphatic system similarly to other therapeutic monoclonal antibodies.

Distribution

The volume of distribution at steady-state was estimated to be 5.42 L following subcutaneous administration of repeated KESIMPTA 20 mg dose.

Metabolism

Ofatumumab is a protein for which the expected metabolic pathway is degradation to small peptides and amino acids by ubiquitous proteolytic enzymes.

Elimination

Ofatumumab is eliminated by a target-independent catabolic pathway and a target (i.e. B-cell)-mediated pathway. At the beginning of ofatumumab treatment, the B-cells counts at baseline result in a greater component of B-cell-mediated clearance of ofatumumab. Following depletion of B-cells by ofatumumab administration, the overall clearance is reduced as it is primarily driven by the catabolic pathway. The half-life at steady state was estimated to be approximately 11 days following repeated subcutaneous administration of KESIMPTA at a dose of 20 mg.

Special populations and conditions

- **Pediatrics:** No studies have been conducted to investigate the pharmacokinetics in pediatric patients below the age of 18 years.
- **Geriatrics:** No studies have been performed in elderly MS patients. Ofatumumab was studied in patients with RMS aged 18 to 55 years.
- **Sex:** Gender had a modest (12%) effect on ofatumumab central volume of distribution in a cross-study population analysis, with higher C_{max} and AUC values observed in female patients (48% of the patients in this analysis were male and 52% were female); these effects are not considered to have a significant change in the pharmacokinetics of ofatumumab.
- **Hepatic Insufficiency:** No formal pharmacokinetic study has been conducted. Since hepatic metabolism of monoclonal antibodies such as ofatumumab is negligible,

hepatic impairment is not expected to impact its pharmacokinetics.

- **Renal Insufficiency:** No formal pharmacokinetic study has been conducted. Ofatumumab is not excreted via urine; therefore, no significant change in the pharmacokinetics of ofatumumab is expected in patients with renal impairment.

10.4. Immunogenicity

All therapeutic proteins have the potential for immunogenicity.

As a fully human monoclonal antibody, ofatumumab has a low potential of inducing anti-drug antibodies (ADA). In RMS Phase 3 studies, the overall incidence of ADAs was very low: treatment induced ADA were detected in 2 of 914 ofatumumab treated patients and no patients with treatment enhancing or neutralizing ADA were identified. There was no impact of positive ADA titers on PK, safety profile or B-cell kinetics in any patient.

11. Storage, Stability, and Disposal

Store between 2°C to 8°C.

Do not freeze. Do not shake.

Store in the original carton to protect from light.

If necessary, KESIMPTA may be stored unrefrigerated for a single period of up to 7 days at room temperature (not above 30°C). If not used during this period, KESIMPTA can then be returned to the refrigerator for a maximum of 7 days.

KESIMPTA must be kept out of the reach and sight of children.

12. Special Handling Instructions

Any unused product or waste material should be disposed of in accordance with local regulations.

Part 2: Scientific Information

13. Pharmaceutical Information

Drug Substance

Non-proprietary name of the drug substance:	Ofatumumab
Chemical name:	Fully human monoclonal immunoglobulin G1 antibody (IgG1-kappa) against human CD20
Molecular formula and molecular mass:	$C_{6480}H_{10022}N_{1742}O_{2020}S_{44}$ 146062 Da
Structural formula:	Ofatumumab consists of two IgG1 heavy chains and two kappa light chains. Both heavy chains of Ofatumumab contain oligosaccharide chains linked to the protein backbone at Asn302.
Physicochemical properties:	The drug substance (DS) is a clear to opalescent, colorless to pale yellow aqueous solution of Ofatumumab. The pH of the aqueous solution is in the range of 5.3 – 5.7.

Product Characteristics:

Ofatumumab is a recombinant fully human monoclonal immunoglobulin G1 (IgG1) antibody against human CD20 expressed on B-cells. Ofatumumab is produced in a murine cell line (NS0) by recombinant DNA technology.

14. Clinical Trials

The efficacy and safety of KESIMPTA were evaluated in two randomized, double-blind, double-dummy, active-controlled Phase 3 pivotal studies of identical design (G2301 (ASCLEPIOS I) and G2302 (ASCLEPIOS II)) in patients with relapsing forms of MS (RMS), aged 18 to 55 years, a disability status at screening with an Expanded Disability Status Scale (EDSS) score from 0 to 5.5, and who had experienced at least one documented relapse during the previous year or two relapses during the previous two years or a positive gadolinium (Gd)-enhancing MRI scan during the previous year.

14.1. Clinical Trials by Indication

Table 3 - Summary of Trial Design and patient demographics for clinical trials in RMS

	Study COMB157G2301 (ASCLEPIOS I)		**Study COMB157G2302 (ASCLEPIOS II)**	
Study Summary				
Trial Design	Double-blind, double-dummy, active-comparator controlled, parallel-group, multi-center study evaluating efficacy and safety of ofatumumab vs teriflunomide in patients with RMS			
Dosage and Route of Administration	Ofatumumab 20 mg/0.4 mL s.c. injections on Days 1, 7, 14 (loading dose regimen) and every 4 weeks thereafter starting at Week 4 (maintenance dose regimen) Comparator: teriflunomide 14 mg capsules orally once daily			
Study Duration	Up to 30 months			
Study Subjects (n)	Ofatumumab: n = 465 Teriflunomide: n = 462		Ofatumumab: n = 481 Teriflunomide: n = 474	
Baseline characteristics	Ofatumumab (N=465)	Teriflunomide (N=462)	Ofatumumab (N=481)	Teriflunomide (N=474)
Mean age (years)	38.9	37.8	38.0	38.2
Age range (years)	19 - 55	18 - 55	18 - 55	18 - 55
Female (%)	68.4	68.6	66.3	67.3
Mean/Median duration of MS since first symptoms (years)	8.36 / 6.41	8.18 / 6.69	8.20 / 5.70	8.19 / 6.30
Mean/Median duration of MS since diagnosis (years)	5.77 / 3.94	5.64 / 3.49	5.59 / 3.15	5.48 / 3.10
Previously treated with DMTs (%)	58.9	60.6	59.5	61.8
Number of relapses in last 12 months (mean)	1.2	1.3	1.3	1.3
Mean/Median EDSS score	2.97 / 3.00	2.94 / 3.00	2.90 / 3.00	2.86 / 2.50
Mean total T2 lesion volume (cm^3)	13.2	13.1	14.3	12.0

Patients free of Gd+ T1 lesions (%)	62.6	63.4	56.1	61.4
Number of Gd+ T1 lesions (mean)	1.7	1.2	1.6	1.5

In the two studies, 927 and 955 patients with RMS, respectively, were randomized 1:1 to receive either KESIMPTA 20 mg subcutaneous injections every 4 weeks starting at Week 4 after an initial dosing regimen of three weekly 20 mg doses in the first 14 days (on Days 1, 7 and 14) or teriflunomide 14 mg capsules orally once daily. Patients also received matching placebo corresponding to the other treatment arm to ensure blinding (double-dummy design). The treatment duration for individual patients was variable based on when the end of study criteria were met. The maximal duration of treatment for an individual patient was 120 weeks. Neurologic evaluations were performed at baseline, every 3 months during blinded treatment, and at the time of a suspected relapse. Brain MRI scans were performed at baseline, 1 and 2 years.

In Study G2301, a total of 927 patients were randomized to receive KESIMPTA (n = 465) or teriflunomide (n = 462). Of those randomized to KESIMPTA, 89.5% completed the study; of those randomized to teriflunomide, 81.4% completed the study. In Study G2302, a total of 955 patients were randomized to receive KESIMPTA (n = 481) or teriflunomide (n = 474). Of those randomized to KESIMPTA, 82.5% completed the study; of those randomized to teriflunomide, 82.1% completed the study.

Patients with active disease were enrolled in the studies. These included both newly diagnosed patients and patients switching from their current treatment due to lack of efficacy, safety or tolerability considerations. Demographics and baseline characteristics were well-balanced across treatment arms and both studies (Table 3).

The primary efficacy endpoint of both studies was the annualized rate of confirmed relapses (ARR) based on EDSS. Key secondary efficacy endpoints included the time to disability worsening on EDSS (confirmed at 3 months and 6 months), defined as an increase in EDSS of ≥1.5, ≥1, or ≥0.5 in patients with a baseline EDSS of 0, 1 to 5, or ≥5.5, respectively. Further key secondary endpoints were the number of Gd-enhancing T1 lesions per MRI scan, and the annualized rate of new or enlarging T2 lesions. Disability-related key-secondary endpoints were evaluated in a pooled analysis of combined data from studies G2301 and G2302, as defined in the study protocols.

In both studies, KESIMPTA significantly lowered the ARR compared to teriflunomide.

KESIMPTA significantly reduced the risk of 3-month confirmed disability worsening and 6-month confirmed disability worsening compared to teriflunomide based on a pooled analysis of both studies.

In both studies, KESIMPTA significantly reduced the number of Gd-enhancing T1 lesions and the rate of new or enlarging T2 lesions.

The efficacy results for both studies are summarized in Table 4 and Figure 1.

Table 4 – Results of Key Clinical and MRI Endpoints from the Phase 3 studies in RMS

Endpoints	Study G2301 (ASCLEPIOS I)		Study G2302 (ASCLEPIOS II)	
	Ofatumumab 20 mg (n=465)	Teriflunomide 14 mg (n=462)	Ofatumumab 20 mg (n=481)	Teriflunomide 14 mg (n=474)
Endpoints based on separate studies				
Annualized relapse rate (ARR) (Primary Endpoint)[1]	0.11	0.22	0.10	0.25
ARR ratio (95% CI)[2]	0.495 (0.375, 0.655)		0.416 (0.309, 0.560)	
Rate reduction	50.5% (p<0.001)		58.4% (p<0.001)	
Mean number of T1 Gd-enhancing lesions per MRI scan	0.0115	0.4555	0.0317	0.5172
Rate ratio (95% CI)[3]	0.025 (0.013, 0.049)		0.061 (0.037, 0.101)	
Relative Reduction	97.5% (p<0.001)		93.9% (p<0.001)	
Number of new or enlarging T2 lesions per year	0.72	4.00	0.64	4.16
Rate ratio (95% CI)[4]	0.18 (0.15, 0.22)		0.15 (0.13, 0.19)	
Relative Reduction	81.9% (p<0.001)		84.6% (p<0.001)	
Endpoints based on pre-specified pooled analyses				
Proportion of patients with 3-month confirmed disability worsening[5] Hazard ratio (95% CI)[6] Risk reduction	10.9% ofatumumab vs. 15.0% teriflunomide 0.657 (0.5000,0.863) 34.3% (p=0.003)			
Proportion of patients with 6-month confirmed disability worsening[5] Hazard ratio (95% CI)[6] Risk reduction	8.1% ofatumumab vs. 12.0% teriflunomide 0.676 (0.498, 0.917) 32.4% (p=0.012)			

[1] confirmed relapses (accompanied by a clinically relevant change in the EDSS)

[2] estimated from a negative binomial regression model with log-link to the number of relapses, adjusted for treatment and region as factors, number of relapses in previous year, baseline EDSS, baseline number of Gd-enhancing lesions and the patient's age at baseline as covariates. The natural log of the time-in-study was used as offset to annualize the relapse rate.

[3] estimated from a negative binomial regression model with log-link to the total number of Gd-enhancing lesions, adjusted for treatment and region as factors, baseline number of Gd-enhancing lesions and patient's age at baseline as covariates. The natural log of the number of MRI-scans with evaluable Gd-enhancing lesion counts was used as the offset to obtain the lesion rate per scan.

[4] estimated from a negative binomial regression model with log-link to the number of new or enlarging T2 lesions, adjusted for treatment and region as factors, baseline volume of T2 lesions and patient's age at baseline as covariates. The natural log of the time (in years) from the screening scan to the last scheduled scan was used as the offset.

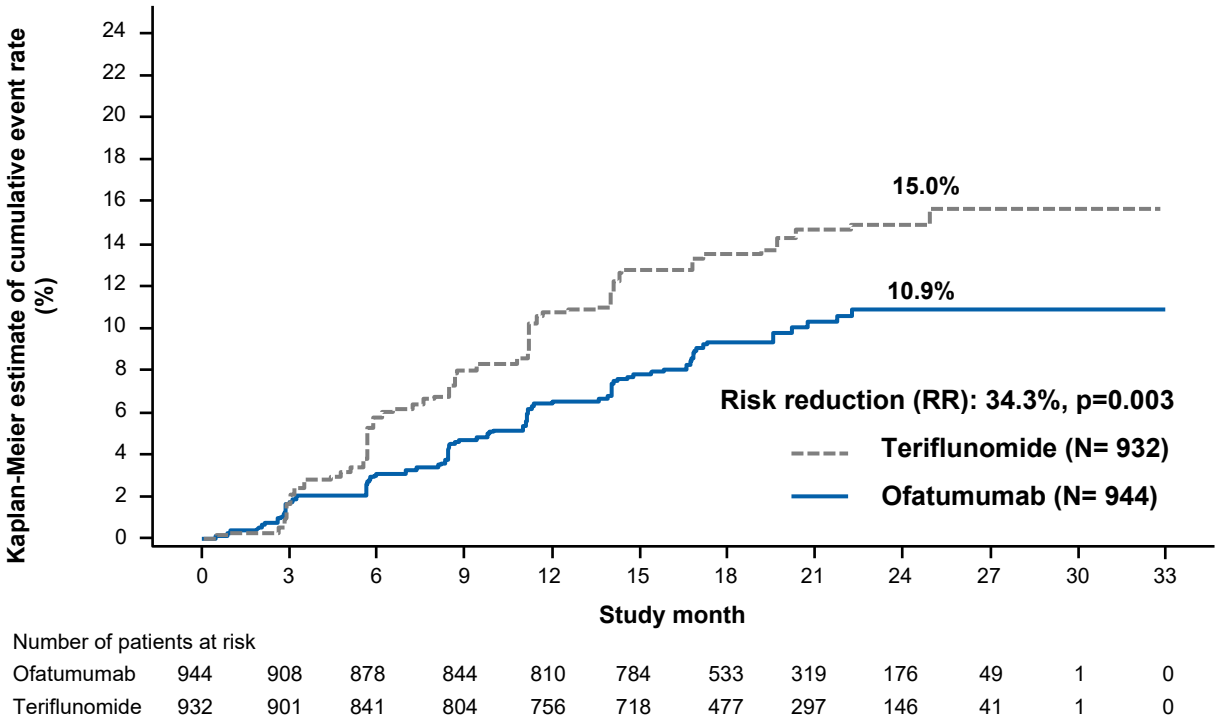
Endpoints	Study G2301 (ASCLEPIOS I)		Study G2302 (ASCLEPIOS II)	
	Ofatumumab 20 mg (n=465)	Teriflunomide 14 mg (n=462)	Ofatumumab 20 mg (n=481)	Teriflunomide 14 mg (n=474)

[5] Kaplan-Meier estimates at Month 24. Disability worsening was defined as an increase in EDSS of at least 1.5, 1, or 0.5 points in patients with a baseline EDSS of 0, 1 to 5, or 5.5 or greater, respectively.

[6] estimated from a Cox regression model adjusted for study as stratum, treatment, and region as factors and baseline EDSS as a continuous covariate.

The Type 1 error rate was controlled using a graphical procedure that included procedures at the trial-level and across the two trials.

Figure 1 Time to first 3-month confirmed disability worsening by treatment (G2301 and G2302 combined, full analysis set)



Number of patients at risk

Ofatumumab	944	908	878	844	810	784	533	319	176	49	1	0
Teriflunomide	932	901	841	804	756	718	477	297	146	41	1	0

15. Microbiology

No microbiological information is required for this drug product.

16. Non-Clinical Toxicology

General Toxicology: Repeated intravenous administration of ofatumumab to cynomolgus monkeys at doses of 20 and 100 mg/kg over 7 months (administered weekly in first 2 months and monthly thereafter) resulted in CD20+ B cell-depletion, attenuation of the humoral immune response to keyhole limpet hemocyanin (KLH), and atrophy of lymphoid organs,

which are consistent with the pharmacological effects of ofatumumab. Partial or complete recovery was observed within 6 months of dosing cessation. The following mortalities occurred in this study: two deaths were considered subsequent to gastrointestinal infection possibly exacerbated by immunosuppression; and three other deaths were considered related to the immunogenic response in monkeys (hemolytic anemia or immune-complex disease) The dose of 100 mg/kg was considered to be the no- observed- adverse -effect level (NOAEL) and is associated with an AUC-based safety margin of 118-fold when compared with the human exposure following subcutaneous administration at the therapeutic dose of 20 mg monthly.

In cynomolgus monkeys administered ofatumumab subcutaneously at 20 or 100 mg/kg or intravenously at 100 mg/kg on Days 1 and 15 of a 2-dose study, the expected pharmacological effect of B cell-depletion, as well as the rate of B cell recovery during the off-dose phase, were similar between the subcutaneous and intravenous routes of administration. There were no significant local effects at the intravenous and subcutaneous injection sites.

Carcinogenicity: No carcinogenicity studies have been performed to assess the carcinogenic potential of ofatumumab.

Genotoxicity: No genotoxicity studies have been performed to assess the genotoxic potential of ofatumumab. As an antibody, ofatumumab is not expected to interact directly with DNA.

Reproductive and Developmental Toxicology: Fertility, embryo-fetal development (EFD) and enhanced pre-/post-natal development (ePPND) studies were conducted in cynomolgus monkeys using the intravenous route of administration.
In the 13-week fertility study, the dosing regimen consisted of an initial dose of 10 or 100 mg/kg given weekly for the first 5 weeks followed by a dose of 3 or 20 mg/kg given every 2 weeks. Male and female fertility-related endpoints were unaffected by administration with ofatumumab. The NOAEL for fertility-related endpoints was therefore the 100/20 mg/kg dose, resulting in male and female AUC-based safety margins of 335-fold and 257-fold, respectively, when compared with the human exposure following subcutaneous administration at the therapeutic dose of 20 mg monthly.

In the EFD study, weekly administration of ofatumumab at 20 or 100 mg/kg to pregnant monkeys during organogenesis (gestation day [GD] 20 to 50; total of 5 doses) caused no maternal toxicity, no teratogenicity, and no adverse effects on embryofetal development. The pharmacologically expected depletion of CD20+ B cells was seen in maternal animals and their fetuses, which also had decreased spleen weights at 100 mg/kg without histological correlates. The dose of 100 mg/kg was considered to be the NOAEL, resulting in a maternal AUC-based safety margin of 1288-fold when compared with the human exposure following subcutaneous administration at the therapeutic dose of 20 mg monthly.

In the ePPND study, pregnant monkeys were administered ofatumumab starting from GD20 with an initial dose of 10 or 100 mg/kg given weekly for the first 5 weeks, followed by a maintenance dose of 3 or 20 mg/kg given every 2 weeks until parturition. Exposure to ofatumumab during gestation caused no maternal toxicity. The expected depletion of CD20+ B-cells was seen in maternal animals and their infants, along with a reduced humoral immune

response to KLH in infants at 100/20 mg/kg. All were reversible during the 6-month postnatal period. In infants, early postnatal mortality was observed at 100/20 mg/kg and was likely due to potential infections secondary to immunomodulation. No other adverse effects were observed in surviving infants. The dose of 10/3 mg/kg was considered to be the NOAEL for infants, resulting in a maternal AUC-based safety margin of 22-fold when compared with the human exposure following subcutaneous administration at the therapeutic dose of 20 mg monthly.

Ofatumumab was detected in cord blood (EFD study) and in infant blood (ePPND study), supporting that ofatumumab crosses the placental barrier.

Patient Medication Information

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

PrKESIMPTA®

ofatumumab injection

Pre-filled Syringe

This Patient Medication Information is written for the person who will be taking **KESIMPTA®**. This may be you or a person you are caring for. Read this information carefully. Keep it as you may need to read it again.

This Patient Medication Information is a summary. It will not tell you everything about this medication. If you have more questions about this medication or want more information about **KESIMPTA**, talk to a healthcare professional.

What KESIMPTA is used for:

- KESIMPTA is used for the treatment of adults with relapsing remitting multiple sclerosis.
- It is not known whether KESIMPTA is safe and effective in children.

How KESIMPTA works:

The active substance in KESIMPTA, ofatumumab is a type of protein called a monoclonal antibody designed to recognize and attach to a target called CD20 on the surface of certain types of white blood cells which are part of the immune system (so called B-cells).

Once an abnormal response by the body's immune system is triggered, these white blood cells play a role in multiple sclerosis by attacking the sheaths around the nerves in the brain and spinal cord, causing inflammation and damage. By targeting and removing the B-cells, KESIMPTA helps to reduce their activity and thereby reduces the chance of having a relapse, relieves symptoms and slows down the progression of the disease.

In controlled clinical studies in patients with relapsing forms of MS, KESIMPTA cut down significantly the number of attacks, significantly prolonged the time without relapses and slowed down the progression of the disease. The average number of relapses in patients treated with KESIMPTA was a little bit more than half in comparison to patients treated with another MS medicine teriflunomide.

If you have any questions about how KESIMPTA works or why this medicine has been prescribed for you, ask your healthcare professional.

The ingredients in KESIMPTA are:

Medicinal ingredient: ofatumumab

Non-medicinal ingredients: disodium edetate dihydrate; hydrochloric acid; L-arginine; polysorbate 80; sodium acetate trihydrate; sodium chloride and water for injection.

KESIMPTA comes in the following dosage form(s):

KESIMPTA is supplied as a 20 mg/0.4 mL pre-filled syringe* or a 20 mg/0.4 mL pre-filled Sensoready® pen.

*Pre-filled syringes are not available in Canada.

Do not use KESIMPTA if:

- you are allergic to ofatumumab or any of the other ingredients in KESIMPTA (listed above) or component of the container
- you have active Hepatitis B virus (HBV) infection
- you have severe, active infections
- you have or have had confirmed progressive multifocal leukoencephalopathy (PML)
- you have been told that you have severe problems with your immune system
- you have cancer

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take KESIMPTA. Talk about any health conditions or problems you may have, including if you:

- **have an infection** before initiation of treatment with KESIMPTA, your healthcare professional may decide that you cannot receive KESIMPTA or may delay your treatment with KESIMPTA until the infection is resolved.
- **have a weakened immune system**. KESIMPTA taken before or after other medicines that weaken the immune system could increase your risk of getting infections.
- **have a history of liver problems.**

After the initiation of treatment with KESIMPTA

Tell your healthcare professional during your treatment with KESIMPTA:

- **if you have injection-related reactions or injection site reactions.** Injection-related reactions (general) and injection site reactions (local) are the most common side effects of KESIMPTA treatment. They generally occur after the first subcutaneous injection of KESIMPTA and up to 24 hours after the injection. The first subcutaneous injection should take place under the guidance of a healthcare professional.
- **if you have an infection.** Any infection including hepatitis B virus infection that you already have may get worse or become active again. Infections including hepatitis B virus infection could be serious and sometimes life-threatening.
- **if you have a lowered immune response** (due to a disease or medicines that suppress the immune system, see “Taking other medicines”). You may get infections more easily

or an infection you already have may get worse. This is because the immune cells that KESIMPTA targets also help to fight infection.

Tell your healthcare professional immediately, if you get any of the following symptoms or diseases **during your treatment** with KESIMPTA, because it could be serious:

- if you believe your MS is getting worse (e.g. weakness or visual changes) or if you notice any new or unusual symptoms. These may also 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, because these may be the symptoms of a rare brain disorder caused by infection and called progressive multifocal leukoencephalopathy (PML).
- if you have rash, hives, trouble breathing, swelling of the face, eyelids, lips, mouth, tongue or throat, chest tightness, feeling faint. If any of these signs and symptoms become worse or you have new severe signs of reactions after subsequent injections, which could be a sign of allergic reaction.

Other warnings you should know about:

Before initiation of treatment with KESIMPTA

- **Your healthcare professional will check if you are at risk of hepatitis B infection.** Before initiation of treatment with KESIMPTA, your healthcare professional will check if you are at risk of hepatitis B infection. All patients will have a blood test and patients who have had hepatitis B or are carriers of the hepatitis B virus will be referred to a specialized healthcare professional. KESIMPTA may cause the hepatitis B virus to become active again.
- **Your healthcare professional will check your immunoglobulin levels.** KESIMPTA may cause a decrease in some types of antibodies. Your healthcare professional will do blood tests to check your blood immunoglobulin levels.
- **Your healthcare professional will do blood tests to check your liver** before you start KESIMPTA treatment and while you take KESIMPTA if needed.
- **If you plan to receive a vaccine,** tell your healthcare professional before initiation of treatment with KESIMPTA. You should receive your vaccines at least 4 weeks prior to starting KESIMPTA for live or live-attenuated vaccines and at least 2 weeks prior to starting KESIMPTA for the other vaccines. You should not receive certain types of vaccines (live or live-attenuated vaccines) during treatment with KESIMPTA. For the other vaccines, they can be less effective if administered during treatment with KESIMPTA.

Children and adolescents (below 18 years)

KESIMPTA has not been studied in patients below 18 years.

Older people

You can use KESIMPTA if you are aged 55 years or over at the same dose as younger adults.

Pregnancy and breast-feeding

If you are pregnant or breast-feeding, think you might be pregnant or are planning to have a baby, ask your healthcare professional for advice before using this medicine.

Your healthcare professional will discuss with you the potential risks of using KESIMPTA during pregnancy. This is because KESIMPTA can reduce immune cells (B-cells) in the mother and unborn baby.

Talk with your healthcare professional before breast-feeding while you use KESIMPTA. KESIMPTA can pass into breast milk. Ask and discuss with your healthcare professional about the benefits and the risks of breast-feeding your baby while you use KESIMPTA.

Talk with your healthcare professional before vaccinating your newborn.

Ask your healthcare professional for advice before vaccinating your newborn, if you have used KESIMPTA during your pregnancy.

Females of child-bearing potential

You should avoid becoming pregnant while using KESIMPTA and for 6 months after you stop using it. KESIMPTA may harm your unborn baby. Female patients who might become pregnant should use effective birth control methods during treatment and for 6 months after stopping KESIMPTA. Ask your healthcare professional about options of effective birth control.

If you become pregnant or think you are pregnant, tell your healthcare professional right away. You and your healthcare professional will decide what is best for you and your baby.

Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

Before you use KESIMPTA, tell your healthcare professional if you are taking any of the following medicines:

- **Medicines that suppress or modulate the immune system including other medicines used to treat MS** such as ocrelizumab, cladribine, fingolimod, natalizumab, teriflunomide, mitoxantrone, or dimethyl fumarate due to a possible added effect on the immune system.
- **Vaccines.** If you need to receive a vaccine, seek your healthcare professional's advice first. During treatment with KESIMPTA, administration of some vaccines containing live virus (live-attenuated vaccines for example BCG for tuberculosis or vaccines against yellow fever) may result in infection.

How to take KESIMPTA:

- Always use this medicine exactly as your healthcare professional has told you. Check with your healthcare professional if you are not sure.
- Do not exceed the recommended dose prescribed by your healthcare professional.
- Your healthcare professional will give you or your caregiver training in the right way to prepare and inject. Do not try to inject KESIMPTA until you or your caregiver have been shown the right way by your healthcare professional.

- If recommended by your healthcare professional, before you take KESIMPTA, you may receive other medicines to prevent or reduce possible side effects of the injection.

When to use KESIMPTA

You can use KESIMPTA at any time (morning, afternoon, evening) for the scheduled dose.

How to use KESIMPTA

KESIMPTA is given by subcutaneous injection (injection under the skin). See Instruction for Use at the end of this leaflet for the details.

How long to use KESIMPTA

Continue using KESIMPTA every month for as long as your healthcare professional tells you.

This is a long-term treatment, possibly lasting for months or years. Your healthcare professional will regularly monitor your condition to check that the treatment is having the desired effect.

If you have questions about how long to use KESIMPTA, talk to your healthcare professional.

If you stop using KESIMPTA

Do not stop using KESIMPTA or change your dose without talking with your healthcare professional.

Some side effects can be related to having low level of B-cells in your blood. After you stop KESIMPTA your blood B-cells count will gradually increase to normal levels. This can take several months. During this time some side effects described in this leaflet may still occur.

If you have any further questions on the use of this medicine, ask your healthcare professional.

Usual dose:

- The initial dosing is 20 mg KESIMPTA administered by subcutaneous injection at weeks 0, 1 and 2. There is no injection at week 3.
- Starting at week 4 and then every month, the recommended dose is 20 mg KESIMPTA administered by subcutaneous injection.

Dosage regimen with subcutaneous injection of KESIMPTA

Time	Dose
Week 0 (beginning of treatment)	20 mg
Week 1	20 mg
Week 2	20 mg
Week 4	20 mg
Every month (starting from week 4)	20 mg

Overdose:

If you have used too much KESIMPTA at one time, or if you have used a first dose of KESIMPTA by mistake, contact your healthcare professional right away.

If you think you, or a person you are caring for, have taken too much KESIMPTA, contact a healthcare professional, hospital emergency department, regional poison control centre or Health Canada's toll-free number, 1-844 POISON-X (1-844-764-7669) immediately, even if there are no signs or symptoms.

Missed dose:

If an injection of KESIMPTA is missed, it should be administered as soon as possible. Do not wait until the next scheduled dose. The treatment interval as recommended should be maintained for the following doses.

To get the full benefit of KESIMPTA, it is important that you receive each subcutaneous injection when it is due.

Possible side effects from using KESIMPTA:

As with all medicines, patients treated with KESIMPTA may experience side effects, although not everybody gets them.

Side effects include the following listed below. If these side effects become severe, please tell your healthcare professional.

Most of the side effects are mild to moderate and will generally disappear after a few days to a few weeks of treatment.

Liver Damage

- KESIMPTA may cause liver damage. Your healthcare provider will do blood tests to check your liver before you start KESIMPTA and while you take KESIMPTA if needed. Tell your healthcare provider right away if you have any symptoms of liver damage, such as:
    - yellowing of the skin and eyes (jaundice)
    - nausea
    - vomiting
    - unusual darkening of the urine
    - feeling tired or weak.

Very Common: *may affect more than 1 in 10 people*

- Upper respiratory tract infection with symptoms such as sore throat and runny nose
- Injection site reactions (local) such as redness, pain, itching and swelling at the injection site

- Injection-related reactions (general) such as fever, headache, muscle pain, chills and tiredness

Common: *may affect up to 1 in every 10 people*

- Decrease in specific proteins in the blood (immunoglobulins M) which help protect against infection

Not known: *frequency cannot be estimated from the available data*

- Allergic reactions
- Liver damage: Possible signs and symptoms of liver damage may include yellowing of the skin and eyes, nausea, vomiting, unusual darkening of the urine, feeling tired or weak.

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, talk to your healthcare professional.

Serious side effects and what to do about them

Frequency/Side Effect/Symptom	Talk to your healthcare professional		Stop taking this drug and get immediate medical help
	Only if severe	In all cases	
Common			
Infections: fever or chills, cough which does not go away, herpes (such as cold sore, shingles and genital sores).		✓	
Uncommon			
Injection-related Reactions/Severe Allergy (hypersensitivity): fever, headache, muscle aches and pain, chills, tiredness, itchy skin, rash, hives, redness of the skin, flushing, low blood pressure, dizziness, headache, throat irritation or pain, shortness of breath, swelling of the throat, feeling sick or nausea, fast/irregular heart beat, chest pain.		✓	
Liver damage: yellowing of the skin and eyes (jaundice), nausea, vomiting, unusual darkening of the urine, feeling tired or weak.		✓	

Frequency/Side Effect/Symptom	Talk to your healthcare professional		Stop taking this drug and get immediate medical help
	Only if severe	In all cases	
Progressive multifocal leukoencephalopathy (PML), a rare brain infection: progressive weakness on one side of the body, clumsiness of limbs, disturbance of vision, changes in thinking, memory and orientation, confusion, personality changes.		✓	
Hepatitis B: mild fever, feeling of sickness, fatigue, loss of appetite, joint and/or abdominal pain and yellowing of whites of the eyes, skin and tongue.		✓	

Reporting side effects

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (canada.ca/drug-device-reporting) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

NOTE: Contact your healthcare professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

Storage:

- Keep out of reach and sight of children.
- Do not use this medicine after the expiry date, which is stated on the carton.
- Store between 2 to 8°C. Keep in the original package.
- Protect from light. Do not freeze.
- If necessary, KESIMPTA can be left out of the refrigerator for a single period of up to 7 days at room temperature (not above 30°C). If not used during this period KESIMPTA can then be returned to the refrigerator for a maximum of 7 days.

Ask your healthcare professional how to dispose of medicines you no longer use.

If you want more information about KESIMPTA:

- Talk to your healthcare professional
- Find the full product monograph that is prepared for healthcare professionals and includes the Patient Medication Information by visiting the Health Canada Drug Product Database website (https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/drug-product-database.html); the manufacturer's website (www.novartis.ca); or by calling 1-800-363-8883.

This leaflet was prepared by Novartis Pharmaceuticals Canada Inc.

Date of Authorization: 2026-11-10

KESIMPTA and Sensoready are registered trademarks.

Instruction for Use

Instructions for Use of KESIMPTA pre-filled syringe

Be sure that you read, understand, and follow these "Instructions for Use" before injecting KESIMPTA. Talk to your healthcare professional if you have any questions before you use KESIMPTA for the first time.

Remember:

- **Do not use** the KESIMPTA pre-filled syringe if either the seal on the outer carton or the seal of the blister is broken. Keep the KESIMPTA pre-filled syringe in the sealed carton until you are ready to use it.
- **Do not shake** the KESIMPTA pre-filled syringe.
- The pre-filled syringe has a needle guard that will be activated to cover the needle after the injection is finished. The needle guard will help to prevent needle stick injuries to anyone who handles the pre-filled syringe after injection.
- Do not remove the needle cap until just before you give the injection.
- Avoid touching the syringe guard wings before use. Touching them may cause the needle guard to be activated too early.
- **Do not use** if the pre-filled syringe has been dropped onto a hard surface or dropped after removing the needle cap.
- Throw away (dispose of) the used KESIMPTA pre-filled syringe right away after use. **Do not re-use a KESIMPTA pre-filled syringe**. See "**How should I dispose of used KESIMPTA pre-filled syringe?**" at the end of these "Instructions for Use".

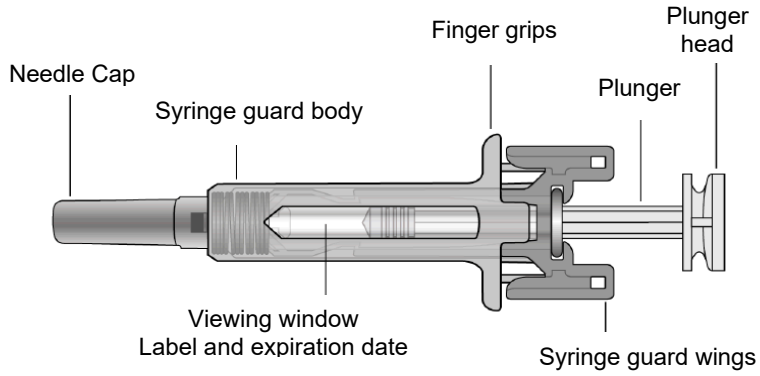
How should I store KESIMPTA?

- Store your carton of the KESIMPTA pre-filled syringe in a refrigerator, 2°C to 8°C.
- Keep the KESIMPTA pre-filled syringe in the original carton until ready to use to protect from light.
- **Do not freeze** the KESIMPTA pre-filled syringe.
- **If necessary,** KESIMPTA can be left out of the refrigerator for a single period of up to 7 days at room temperature (not above 30°C). If not used during this period KESIMPTA can then be returned to the refrigerator for a maximum of 7 days.

Keep KESIMPTA and all medicines out of the reach of children.

KESIMPTA pre-filled syringe parts (see Figure A):

Figure A



What you need for your injection:

Included in the carton:

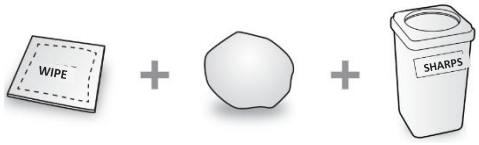
A new KESIMPTA pre-filled syringe.

Not included in the carton (**see Figure B**):

- 1 alcohol wipe
- 1 cotton ball or gauze
- Sharps disposal container

See "**How should I dispose of used KESIMPTA pre-filled syringes?**" at the end of these "Instructions for Use".

Figure B



Prepare the KESIMPTA pre-filled syringe

Step 1. Find a clean, well-lit, flat work surface.

Step 2. Take the carton containing the KESIMPTA pre-filled syringe out of the refrigerator and leave it **unopened** on your work surface for about 15 to 30 minutes so that it reaches room temperature.

Step 3. Wash your hands well with soap and water.

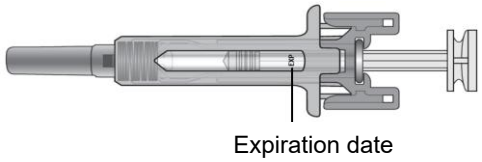
Step 4. Remove the pre-filled syringe from the outer carton and take it out of the blister by holding the syringe guard body.

Step 5. Look through the viewing window on the pre-filled syringe. The liquid inside should be clear to slightly cloudy. You may see a small air bubble in the liquid, which is normal. **Do not use** the pre-filled syringe if the liquid contains visible particles or is cloudy.

Step 6. **Do not use** the pre-filled syringe if it is broken. Return the pre-filled syringe and the package it came in to the pharmacy.

Figure C

Step 7. **Do not use** the pre-filled syringe if the expiration date has passed (**see Figure C**). Return the expired pre-filled syringe and the package it came in to the pharmacy.



Choose and clean the injection site

- Areas of your body that you may use as injection sites include:
  - the front of your thighs (**see Figure D**)
  - the lower stomach-area (abdomen), but not the area five cm (2 inches) around your navel (belly button) (**see Figure D**)
  - your upper outer arms, if a healthcare professional or caregiver is giving you the injection (**see Figure E**).
- Choose a different site each time you inject KESIMPTA.
- **Do not inject** into areas where the skin is tender, bruised, red, scaly, or hard. Avoid areas with scars or stretch marks.

Step 8. Using a circular motion, clean the injection site with the alcohol wipe. Leave it to dry before injecting. Do not touch the cleaned area again before injecting.

Figure D

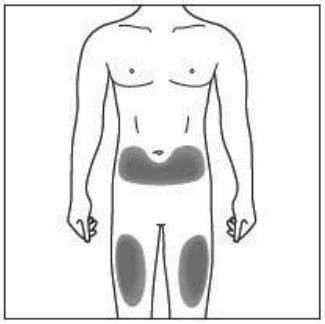
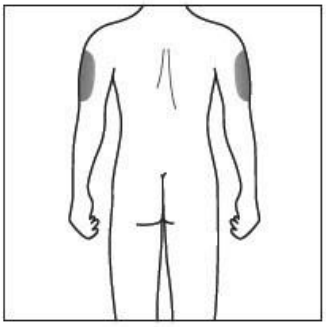


Figure E
(Caregiver and healthcare professional only)



Giving your injection

Step 9. Carefully remove the needle cap from the pre-filled syringe (**see Figure F**). Throw away the needle cap. You may see a drop of liquid at the end of the needle. This is normal.

Figure F

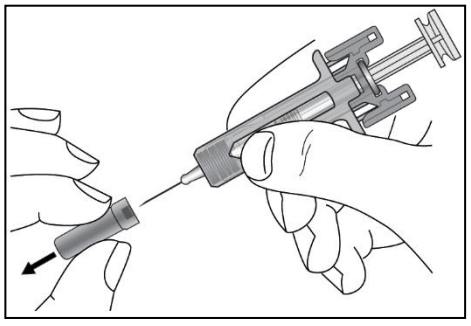


Figure G

Step 10. With one hand, gently pinch the skin at the injection site. With your other hand insert the needle into your skin as shown (**see Figure G**). Push the needle all the way in to make sure that you inject your full dose.

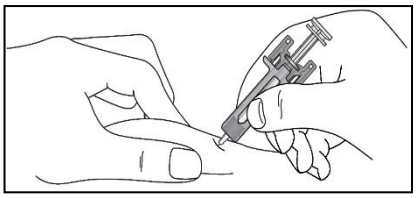


Figure H

Step 11. Hold the pre-filled syringe finger grips as shown (**see Figure H**). Slowly press down on the plunger as far as it will go, so that the plunger head is completely between the syringe guard wings.

Step 12. Continue to press fully on the plunger for an additional 5 seconds. Hold the syringe in place for the full 5 seconds.

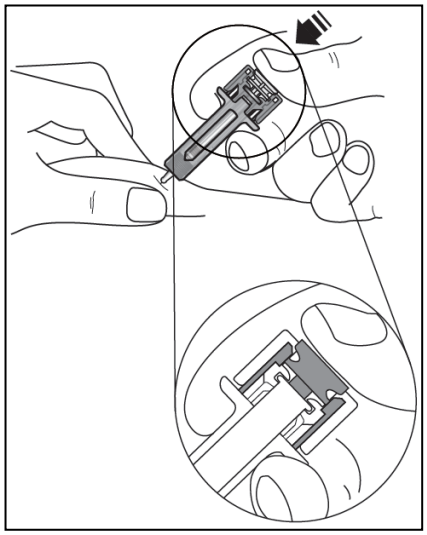
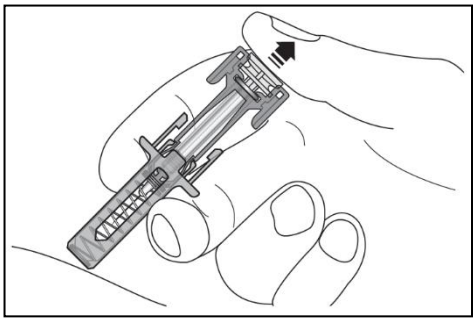


Figure I

Step 13. **Slowly** release the plunger until the needle is covered (**see Figure I**), and then remove the syringe from the injection site.

Step 14. There may be a small amount of blood at the injection site. You can press a cotton ball or gauze over the injection site and hold it for 10 seconds. Do not rub the injection site. You may cover the injection site with a small adhesive bandage, if needed.



How should I dispose of used KESIMPTA pre-filled syringe?

Step 15. Dispose of your used pre-filled syringe:

- Dispose of the used pre-filled syringe in a sharps disposal container (i.e. a puncture-resistant closable container, or similar) (**see Figure J**).
- **Do not throw away (dispose of)** your used pre-filled syringe in your household trash.
- Never try to reuse your pre-filled syringe.

Keep the sharps container out of the reach of children.

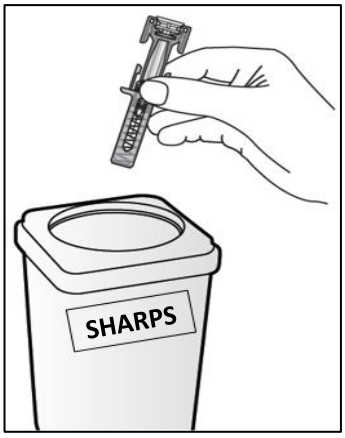


Figure J

Patient Medication Information

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

PrKESIMPTA®

ofatumumab injection

Pre-filled Sensoready® pen

This Patient Medication Information is written for the person who will be taking **KESIMPTA®**. This may be you or a person you are caring for. Read this information carefully. Keep it as you may need to read it again.

This Patient Medication Information is a summary. It will not tell you everything about this medication. If you have more questions about this medication or want more information about **KESIMPTA**, talk to a healthcare professional.

What KESIMPTA is used for:

- KESIMPTA is used for the treatment of adults with relapsing remitting multiple sclerosis.
- It is not known whether KESIMPTA is safe and effective in children.

How KESIMPTA works:

The active substance in KESIMPTA, ofatumumab is a type of protein called a monoclonal antibody designed to recognize and attach to a target called CD20 on the surface of certain types of white blood cells which are part of the immune system (so called B-cells).

Once an abnormal response by the body's immune system is triggered, these white blood cells play a role in multiple sclerosis by attacking the sheaths around the nerves in the brain and spinal cord, causing inflammation and damage. By targeting and removing the B-cells, KESIMPTA helps to reduce their activity and thereby reduces the chance of having a relapse, relieves symptoms and slows down the progression of the disease.

In controlled clinical studies in patients with relapsing forms of MS, KESIMPTA cut down significantly the number of attacks, significantly prolonged the time without relapses and slowed down the progression of the disease. The average number of relapses in patients treated with KESIMPTA was a little bit more than half in comparison to patients treated with another MS medicine teriflunomide.

If you have any questions about how KESIMPTA works or why this medicine has been prescribed for you, ask your healthcare professional.

The ingredients in KESIMPTA are:

Medicinal ingredient: ofatumumab

Non-medicinal ingredients: disodium edetate dihydrate; hydrochloric acid; L-arginine; polysorbate 80; sodium acetate trihydrate; sodium chloride and water for injection.

KESIMPTA comes in the following dosage form(s):

KESIMPTA is supplied as a 20 mg/0.4 mL pre-filled syringe* or a 20 mg/0.4 mL pre-filled Sensoready® pen.

*Pre-filled syringes are not available in Canada.

Do not use KESIMPTA if:

- you are allergic to ofatumumab or any of the other ingredients in KESIMPTA (listed above) or component of the container
- you have active Hepatitis B virus (HBV) infection
- you have severe, active infections
- you have or have had confirmed progressive multifocal leukoencephalopathy (PML)
- you have been told that you have severe problems with your immune system
- you have cancer

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take KESIMPTA. Talk about any health conditions or problems you may have, including if you:

- **have an infection** before initiation of treatment with KESIMPTA, your healthcare professional may decide that you cannot receive KESIMPTA or may delay your treatment with KESIMPTA until the infection is resolved.
- **have a weakened immune system**. KESIMPTA taken before or after other medicines that weaken the immune system could increase your risk of getting infections.
- **have a history of liver problems.**

After the initiation of treatment with KESIMPTA

Tell your healthcare professional during your treatment with KESIMPTA:

- **if you have injection-related reactions or injection site reactions.** Injection-related reactions (general) and injection site reactions (local) are the most common side effects of KESIMPTA treatment. They generally occur after the first subcutaneous injection of KESIMPTA and up to 24 hours after the injection. The first subcutaneous injection should take place under the guidance of a healthcare professional.
- **if you have an infection.** Any infection including hepatitis B virus infection that you already have may get worse or become active again. Infections including hepatitis B virus infection could be serious and sometimes life-threatening.
- **if you have a lowered immune response** (due to a disease or medicines that suppress the immune system, see “Taking other medicines”). You may get infections more easily

or an infection you already have may get worse. This is because the immune cells that KESIMPTA targets also help to fight infection.

Tell your healthcare professional immediately, if you get any of the following symptoms or diseases **during your treatment** with KESIMPTA, because it could be serious:

- if you believe your MS is getting worse (e.g. weakness or visual changes) or if you notice any new or unusual symptoms. These may also 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, because these may be the symptoms of a rare brain disorder caused by infection and called progressive multifocal leukoencephalopathy (PML).
- if you have rash, hives, trouble breathing, swelling of the face, eyelids, lips, mouth, tongue or throat, chest tightness, feeling faint. If any of these signs and symptoms become worse or you have new severe signs of reactions after subsequent injections, which could be a sign of allergic reaction.

Other warnings you should know about:

Before initiation of treatment with KESIMPTA

- **Your healthcare professional will check if you are at risk of hepatitis B infection.** Before initiation of treatment with KESIMPTA, your healthcare professional will check if you are at risk of hepatitis B infection. All patients will have a blood test and patients who have had hepatitis B or are carriers of the hepatitis B virus will be referred to a specialized healthcare professional. KESIMPTA may cause the hepatitis B virus to become active again.
- **Your healthcare professional will check your immunoglobulin levels.** KESIMPTA may cause a decrease in some types of antibodies. Your healthcare professional will do blood tests to check your blood immunoglobulin levels.
- **Your healthcare professional will do blood tests to check your liver** before you start KESIMPTA treatment and while you take KESIMPTA if needed.
- **If you plan to receive a vaccine,** tell your healthcare professional before initiation of treatment with KESIMPTA. You should receive your vaccines at least 4 weeks prior to starting KESIMPTA for live or live-attenuated vaccines and at least 2 weeks prior to starting KESIMPTA for the other vaccines. You should not receive certain types of vaccines (live or live-attenuated vaccines) during treatment with KESIMPTA. For the other vaccines, they can be less effective if administered during treatment with KESIMPTA.

Children and adolescents (below 18 years)

KESIMPTA has not been studied in patients below 18 years.

Older people

You can use KESIMPTA if you are aged 55 years or over at the same dose as younger adults.

Pregnancy and breast-feeding

If you are pregnant or breast-feeding, think you might be pregnant or are planning to have a baby, ask your healthcare professional for advice before using this medicine.

Your healthcare professional will discuss with you the potential risks of using KESIMPTA during pregnancy. This is because KESIMPTA can reduce immune cells (B-cells) in the mother and unborn baby.

Talk with your healthcare professional before breast-feeding while you use KESIMPTA. KESIMPTA can pass into breast milk. Ask and discuss with your healthcare professional about the benefits and the risks of breast-feeding your baby while you use KESIMPTA.

Talk with your healthcare professional before vaccinating your newborn.

Ask your healthcare professional for advice before vaccinating your newborn, if you have used KESIMPTA during your pregnancy.

Females of child-bearing potential

You should avoid becoming pregnant while using KESIMPTA and for 6 months after you stop using it. KESIMPTA may harm your unborn baby. Female patients who might become pregnant should use effective birth control methods during treatment and for 6 months after stopping KESIMPTA. Ask your healthcare professional about options of effective birth control.

If you become pregnant or think you are pregnant, tell your healthcare professional right away. You and your healthcare professional will decide what is best for you and your baby.

Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

Before you use KESIMPTA, tell your healthcare professional if you are taking any of the following medicines:

- **Medicines that suppress or modulate the immune system including other medicines used to treat MS** such as ocrelizumab, cladribine, fingolimod, natalizumab, teriflunomide, mitoxantrone, or dimethyl fumarate due to a possible added effect on the immune system.
- **Vaccines.** If you need to receive a vaccine, seek your healthcare professional's advice first. During treatment with KESIMPTA, administration of some vaccines containing live virus (live-attenuated vaccines for example BCG for tuberculosis or vaccines against yellow fever) may result in infection.

How to take KESIMPTA:

- Always use this medicine exactly as your healthcare professional has told you. Check with your healthcare professional if you are not sure.
- Do not exceed the recommended dose prescribed by your healthcare professional.
- Your healthcare professional will give you or your caregiver training in the right way to prepare and inject. Do not try to inject KESIMPTA until you or your caregiver have been shown the right way by your healthcare professional.

- If recommended by your healthcare professional, before you take KESIMPTA, you may receive other medicines to prevent or reduce possible side effects of the injection.

When to use KESIMPTA

You can use KESIMPTA at any time (morning, afternoon, evening) for the scheduled dose.

How to use KESIMPTA

KESIMPTA is given by subcutaneous injection (injection under the skin). See Instruction for Use at the end of this leaflet for the details.

How long to use KESIMPTA

Continue using KESIMPTA every month for as long as your healthcare professional tells you.

This is a long-term treatment, possibly lasting for months or years. Your healthcare professional will regularly monitor your condition to check that the treatment is having the desired effect.

If you have questions about how long to use KESIMPTA, talk to your healthcare professional.

If you stop using KESIMPTA

Do not stop using KESIMPTA or change your dose without talking with your healthcare professional.

Some side effects can be related to having low level of B-cells in your blood. After you stop KESIMPTA your blood B-cells count will gradually increase to normal levels. This can take several months. During this time some side effects described in this leaflet may still occur.

If you have any further questions on the use of this medicine, ask your healthcare professional.

Usual dose:

- The initial dosing is 20 mg KESIMPTA administered by subcutaneous injection at weeks 0, 1 and 2. There is no injection at week 3.
- Starting at week 4 and then every month, the recommended dose is 20 mg KESIMPTA administered by subcutaneous injection.

Dosage regimen with subcutaneous injection of KESIMPTA

Time	Dose
Week 0 (beginning of treatment)	20 mg
Week 1	20 mg
Week 2	20 mg
Week 4	20 mg
Every month (starting from week 4)	20 mg

Overdose:

If you have used too much KESIMPTA at one time, or if you have used a first dose of KESIMPTA by mistake, contact your healthcare professional right away.

If you think you, or a person you are caring for, have taken too much KESIMPTA, contact a healthcare professional, hospital emergency department, regional poison control centre or Health Canada's toll-free number, 1-844 POISON-X (1-844-764-7669) immediately, even if there are no signs or symptoms.

Missed dose:

If an injection of KESIMPTA is missed, it should be administered as soon as possible. Do not wait until the next scheduled dose. The treatment interval as recommended should be maintained for the following doses.

To get the full benefit of KESIMPTA, it is important that you receive each subcutaneous injection when it is due.

Possible side effects from using KESIMPTA:

As with all medicines, patients treated with KESIMPTA may experience side effects, although not everybody gets them.

Side effects include the following listed below. If these side effects become severe, please tell your healthcare professional.

Most of the side effects are mild to moderate and will generally disappear after a few days to a few weeks of treatment.

Liver Damage

- KESIMPTA may cause liver damage. Your healthcare provider will do blood tests to check your liver before you start KESIMPTA and while you take KESIMPTA if needed. Tell your healthcare provider right away if you have any symptoms of liver damage, such as:
    - yellowing of the skin and eyes (jaundice)
    - nausea
    - vomiting
    - unusual darkening of the urine
    - feeling tired or weak

Very Common: *may affect more than 1 in 10 people*

- Upper respiratory tract infection with symptoms such as sore throat and runny nose
- Injection site reactions (local) such as redness, pain, itching and swelling at the injection site
- Injection-related reactions (general) such as fever, headache, muscle pain, chills and tiredness

Common: *may affect up to 1 in every 10 people*

- Decrease in specific proteins in the blood (immunoglobulins M) which help protect against infection

Not known: *frequency cannot be estimated from the available data*

- Allergic reactions
- Liver damage: Possible signs and symptoms of liver damage may include yellowing of the skin and eyes, nausea, vomiting, unusual darkening of the urine, feeling tired or weak.

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, talk to your healthcare professional.

Serious side effects and what to do about them

Frequency/Side Effect/Symptom	Talk to your healthcare professional		Stop taking this drug and get immediate medical help
	Only if severe	In all cases	
Common			
Infections: fever or chills, cough which does not go away, herpes (such as cold sore, shingles and genital sores).		✓	
Uncommon			
Injection-related Reactions/Severe Allergy (hypersensitivity): fever, headache, muscle aches and pain, chills, tiredness, itchy skin, rash, hives, redness of the skin, flushing, low blood pressure, dizziness, headache, throat irritation or pain, shortness of breath, swelling of the throat, feeling sick or nausea, fast/irregular heart beat, chest pain.		✓	
Liver damage: yellowing of the skin and eyes (jaundice), nausea, vomiting, unusual darkening of the urine, feeling tired or weak.		✓	
Progressive multifocal leukoencephalopathy (PML), a		✓	

Frequency/Side Effect/Symptom	Talk to your healthcare professional		Stop taking this drug and get immediate medical help
	Only if severe	In all cases	
rare brain infection: progressive weakness on one side of the body, clumsiness of limbs, disturbance of vision, changes in thinking, memory and orientation, confusion, personality changes.			
Hepatitis B: mild fever, feeling of sickness, fatigue, loss of appetite, joint and/or abdominal pain and yellowing of whites of the eyes, skin and tongue.		✓	

Reporting side effects

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (canada.ca/drug-device-reporting) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

NOTE: Contact your healthcare professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

Storage:

- Keep out of reach and sight of children.
- Do not use this medicine after the expiry date, which is stated on the carton.
- Store between 2 to 8°C. Keep in the original package.
- Protect from light. Do not freeze.
- If necessary, KESIMPTA can be left out of the refrigerator for a single period of up to 7 days at room temperature (not above 30°C). If not used during this period KESIMPTA can then be returned to the refrigerator for a maximum of 7 days.

Ask your healthcare professional how to dispose of medicines you no longer use.

If you want more information about KESIMPTA:

- Talk to your healthcare professional
- Find the full product monograph that is prepared for healthcare professionals and includes the Patient Medication Information by visiting the Health Canada Drug Product Database website (https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/drug-product-database.html); the manufacturer's website (www.novartis.ca); or by calling 1-800-363-8883.

This leaflet was prepared by Novartis Pharmaceuticals Canada Inc.

Date of Authorization: 2026-11-10

KESIMPTA and Sensoready are registered trademarks.

Instruction for Use

Instructions for Use of KESIMPTA pre-filled Sensoready pen

Be sure that you read, understand, and follow this "Instructions for Use" before injecting KESIMPTA. Talk to your healthcare professional if you have any questions before you use KESIMPTA Sensoready pen for the first time.

Remember:

- **Do not use** the KESIMPTA Sensoready pen if either the seal on the outer carton or the seal on the Sensoready pen is broken. Keep the KESIMPTA Sensoready pen in the sealed outer carton until you are ready to use it.
- **Do not shake** the KESIMPTA Sensoready pen.
- If you drop your KESIMPTA Sensoready pen, **do not use** it if the Sensoready pen looks damaged, or if you dropped it with the cap removed.

Throw away (dispose of) the used KESIMPTA Sensoready pen right away after use. **Do not re-use a KESIMPTA Sensoready pen**. See "How should I dispose of used KESIMPTA Sensoready pen?" at the end of this "Instructions for Use".

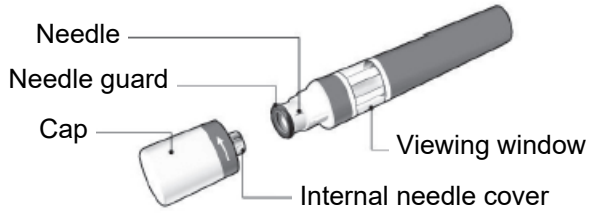
How should I store KESIMPTA?

- Store your carton of KESIMPTA Sensoready pen in a refrigerator, 2°C to 8°C.
- Keep KESIMPTA Sensoready pen in the original carton until ready to use to protect from light.
- **Do not freeze** KESIMPTA Sensoready pen.
- **If necessary**, KESIMPTA can be left out of the refrigerator for a single period of up to 7 days at room temperature (not above 30°C). If not used during this period KESIMPTA can then be returned to the refrigerator for a maximum of 7 days.

Keep KESIMPTA and all medicines out of the reach of children.

KESIMPTA Sensoready pen parts (see Figure A):

Figure A



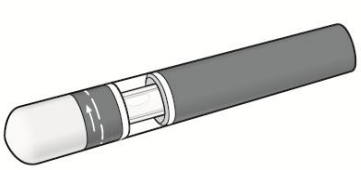
The KESIMPTA Sensoready pen is shown with the cap removed. **Do not** remove the cap until you are ready to inject.

What you need for your injection:

Included in the carton:

A new KESIMPTA Sensoready pen (**see Figure B**).

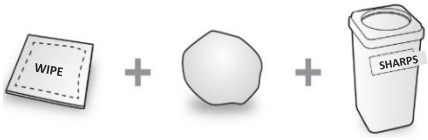
Figure B



Not included in the carton (**see Figure C**):

Figure C

- 1 alcohol wipe
- 1 cotton ball or gauze
- Sharps disposal container



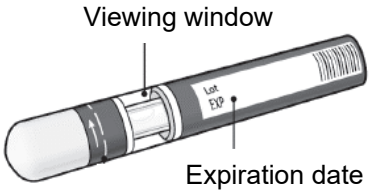
See "**How should I dispose of used KESIMPTA Sensoready pen?**" at the end of this "Instructions for Use"

Before your injection:

Take the KESIMPTA Sensoready pen out of the refrigerator **15 to 30 minutes before injecting** to allow it to reach room temperature.

Step 1. Important safety checks before you inject (see Figure D):

Figure D



- Look through the viewing window. The liquid should be clear to slightly cloudy.
  Do not use if the liquid contains visible particles or is cloudy.

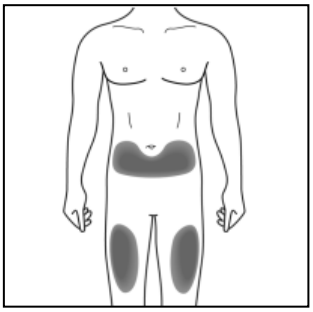
  You may see a small air bubble, which is normal.
- Look at the **expiration date (EXP)** on your KESIMPTA Sensoready pen. **Do not use** your Sensoready pen if the expiration date has passed.

Contact your healthcare professional if your Sensoready pen fails any of these checks.

Step 2. Choose your injection site:

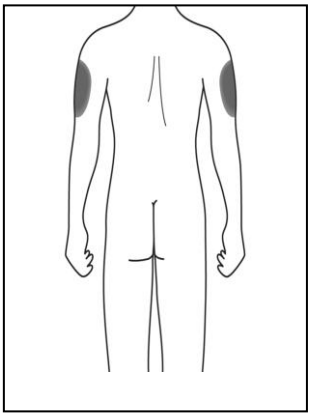
- The recommended site is the front of the thighs. You may also use the lower stomach area (lower abdomen), but **not** the area five cm (2 inches) around the navel (belly button) (**see Figure E**).
- Choose a different site each time you inject KESIMPTA.
- Do not inject into areas where the skin is tender, bruised, red, scaly or hard. Avoid areas with scars or stretch marks.

Figure E



If a **caregiver** or **healthcare professional** is giving you your injection, they may also inject into your upper outer arm (**see Figure F**).

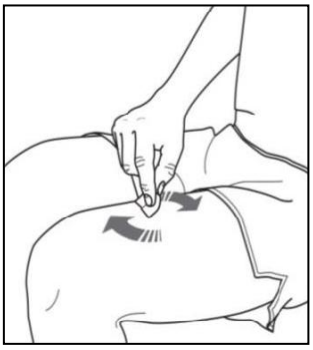
Figure F
(Caregiver and healthcare professional only)



Step 3. Clean your injection site:

- Wash your hands with soap and water.
- Using a circular motion, clean the injection site with the alcohol wipe. Leave it to dry before injecting (**see Figure G**).
- Do not touch the cleaned area again before injecting.

Figure G



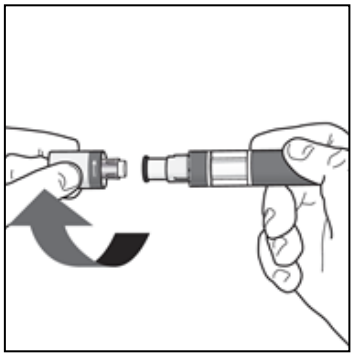
Your injection:

Step 4. Remove the cap:

- Only remove the cap when you are ready to use the Sensoready pen.
- Twist off the cap in the direction of the arrow (**see Figure H**).
- Throw away the cap. **Do not try to re-attach the cap.**
- Use the Sensoready pen within 5 minutes of removing the cap.

You may see a few drops of medicine come out of the needle. This is normal.

Figure H



Step 5. Hold your KESIMPTA Sensoready pen:

- Hold the Sensoready pen at 90 degrees to the cleaned injection site (**see Figure I**).

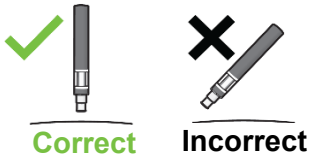
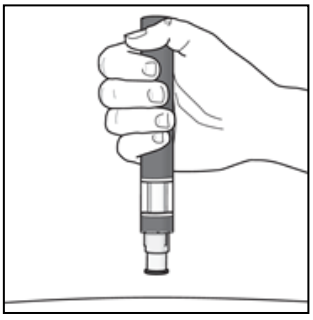


Figure I



Important: **During the injection** you will hear **2 loud clicks**:

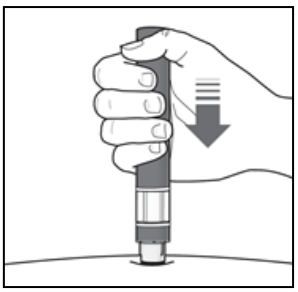
- The **1st click** indicates that **the injection has started**.
- A **2nd click** will indicate that **the injection is almost complete**.

You must keep holding the KESIMPTA Sensoready pen firmly against your skin until the **green indicator** fills the window and stops moving.

Step 6. Start your injection:

- Press the Sensoready pen firmly against the skin to start the injection (**see Figure J**).
- The **1st click** indicates the injection has started.
- **Keep holding** the Sensoready pen firmly against your skin.
- The **green indicator** shows the progress of the injection.

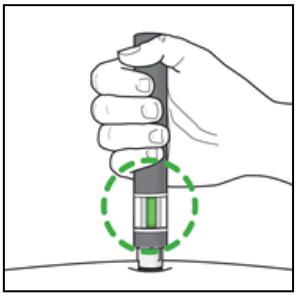
Figure J



Step 7. Complete your injection:

- Listen for the **2nd click**. This indicates that the injection is **almost** complete.
- Check to see if the **green indicator** fills the window and has stopped moving (**see Figure K**).
- The Sensoready pen can now be removed (**see Figure L**).

Figure K



After your injection:

- In case the green indicator does not fill the window, it means the medicine has not been delivered. Contact your healthcare professional if the green indicator is not visible.
- There may be a small amount of blood at the injection site. You can press a cotton ball or gauze over the injection site and hold it for 10 seconds. Do not rub the injection site. You may cover the injection site with a small adhesive bandage, if needed.

Figure L



How should I dispose of used KESIMPTA Sensoready pens?

Step 8. Dispose of your KESIMPTA Sensoready pen:

- Dispose of the used Sensoready pen in a sharps disposal container (i.e. a puncture-resistant closable container, or similar) (**see Figure M**).
- Never try to reuse your Sensoready pen.

Keep the sharps container out of the reach of children.

Figure M

