ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

▼This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions. See section 4.8 for how to report adverse reactions.

1. NAME OF THE MEDICINAL PRODUCT

Kesimpta 20 mg solution for injection in pre-filled syringe
Kesimpta 20 mg solution for injection in pre-filled pen

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Kesimpta 20 mg solution for injection in pre-filled syringe

Each pre-filled syringe contains 20 mg ofatumumab in 0.4 ml solution (50 mg/ml).

Kesimpta 20 mg solution for injection in pre-filled pen

Each pre-filled pen contains 20 mg ofatumumab in 0.4 ml solution (50 mg/ml).

Ofatumumab is a fully human monoclonal antibody produced in a murine cell line (NS0) by recombinant DNA technology.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection (injection)
Solution for injection (injection) in pre-filled pen (Sensoready Pen)

The solution is clear to slightly opalescent, and colourless to slightly brownish-yellow.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Kesimpta is indicated for the treatment of adult patients with relapsing forms of multiple sclerosis (RMS) with active disease defined by clinical or imaging features (see section 5.1).

4.2 Posology and method of administration

Treatment should be initiated by a physician experienced in the management of neurological conditions.

Posology

The recommended dose is 20 mg ofatumumab administered by subcutaneous injection with:
- initial dosing at weeks 0, 1 and 2, followed by
- subsequent monthly dosing, starting at week 4.

Missed doses
If an injection is missed, it should be administered as soon as possible without waiting until the next scheduled dose. Subsequent doses should be administered at the recommended intervals.

Special populations
Adults over 55 years old
No studies have been performed in MS patients over 55 years old. Based on the limited data available, no dose adjustment is considered necessary in patients over 55 years old (see section 5.2).

Renal impairment
Patients with renal impairment are not expected to require dose modification (see section 5.2).

Hepatic impairment
Patients with hepatic impairment are not expected to require dose modification (see section 5.2).

Paediatric population
The safety and efficacy of Kesimpta in children aged 0 to 18 years have not yet been established. No data are available.

Method of administration

This medicinal product is intended for patient self-administration by subcutaneous injection.

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

The first injection should be performed under the guidance of a healthcare professional (see section 4.4).

Comprehensive instructions for administration are provided in the package leaflet.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.
Patients in a severely immunocompromised state (see section 4.4).
Severe active infection until resolution (see section 4.4).
Known active malignancy.

4.4 Special warnings and precautions for use

Traceability

In order to improve the traceability of biological medicinal products, the name and the batch number of the administered product should be clearly recorded.

Injection-related reactions

Patients should be informed that systemic injection-related reactions (SIRRs) could occur, generally within 24 hours and predominantly following the first injection (see section 4.8). Symptoms most frequently observed in RMS clinical studies include fever, headache, myalgia, chills, fatigue, nausea and vomiting and were predominantly (99.8%) mild to moderate in severity. There were no life-threatening SIRRs reported in RMS clinical studies (see section 4.8).

Additional SIRRs reported in the post-marketing setting include rash, urticaria, dyspnoea and angioedema (e.g. tongue, pharyngeal or laryngeal swelling), and rare cases which were reported as anaphylaxis. While there were some cases which were serious and resulted in discontinuation of ofatumumab treatment, there were also serious cases where patients were able to continue ofatumumab treatment without further incidents.

Some SIRR symptoms may be clinically indistinguishable from Type 1 acute hypersensitivity reactions (IgE-mediated). A hypersensitivity reaction may present during 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 ofatumumab must not be treated with ofatumumab (see section 4.3).

Only limited benefit of premedication with steroids was seen in RMS clinical studies. Injection-related reactions can be managed with symptomatic treatment, should they occur. Therefore, use of premedication is not required.

Injection site reaction (local) symptoms observed in clinical studies included erythema, swelling, itching and pain (see section 4.8).

The first injection should be performed under the guidance of an appropriately trained healthcare professional (see section 4.2).

Infections

It is recommended to evaluate the patient's immune status prior to initiating therapy.

Based on its mode of action and available clinical experience, ofatumumab has the potential for an increased risk of infections (see section 4.8).

Administration should be delayed in patients with an active infection until the infection is resolved.

Ofatumumab must not be given to patients in a severely immunocompromised state (e.g. significant neutropenia or lymphopenia).

Progressive multifocal leukoencephalopathy
Since John Cunningham (JC) virus infection resulting in progressive multifocal leukoencephalopathy (PML) has been observed in patients treated with anti-CD20 antibodies, other MS therapies, and ofatumumab at substantially higher doses in oncology indications, physicians should be vigilant for medical history of PML and for any clinical symptoms or MRI findings that may be suggestive of PML. If PML is suspected, treatment with ofatumumab should be suspended until PML has been excluded.

Hepatitis B virus reactivation
Hepatitis B 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 ofatumumab. HBV screening should be performed in all patients before initiation of treatment. As a 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. Patients with positive hepatitis B serology (either HBsAg or HBcAb) should consult a liver disease expert before the start of treatment and should be monitored and managed following local medical standards to prevent hepatitis B reactivation.

Treatment of severely immunocompromised patients

Patients in a severely immunocompromised state must not be treated until the condition resolves (see section 4.3).

It is not recommended to use other immunosuppressants concomitantly with ofatumumab except corticosteroids for symptomatic treatment of relapses.

Vaccinations

All immunisations should be administered according to immunisation guidelines at least 4 weeks prior to initiation of ofatumumab for live or live-attenuated vaccines and, whenever possible, at least 2 weeks prior to initiation of ofatumumab for inactivated vaccines.

Ofatumumab may interfere with the effectiveness of inactivated vaccines.

The safety of immunisation with live or live-attenuated vaccines following ofatumumab 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 section 4.5). The median time to B-cell recovery to the lower limit of normal (LLN, defined as 40 cells/µl) or baseline value is 24.6 weeks post treatment discontinuation based on data from phase III studies (see section 5.1).

Vaccination of infants born to mothers treated with ofatumumab during pregnancy
In infants of mothers treated with ofatumumab during pregnancy live or live-attenuated vaccines should not be administered before the recovery of B-cell counts has been confirmed. Depletion of B cells in these infants may increase the risks from live or live-attenuated vaccines.

Inactivated vaccines may be administered as indicated prior to recovery from B-cell depletion, however assessment of vaccine immune responses, including consultation with a qualified specialist, should be considered to determine whether a protective immune response was mounted (see section 4.6).

Sodium content

This medicinal product contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially 'sodium-free'.

4.5 Interaction with other medicinal products and other forms of interaction

No interaction studies have been performed, as no interactions are expected via cytochrome P450 enzymes, other metabolising enzymes or transporters.

Vaccinations

The safety of and the ability to generate a primary or anamnestic (recall) response to immunisation 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 immunisations prior to the start of ofatumumab therapy (see section 4.4).

Other immunosuppressive or immune-modulating therapies

The risk of additive immune system effects should be considered when co-administering immunosuppressive therapies with ofatumumab.

When initiating ofatumumab after other immunosuppressive therapies with prolonged immune effects or initiating other immunosuppressive therapies with prolonged immune effects after ofatumumab, the duration and mode of action of these medicinal products should be taken into account because of potential additive immunosuppressive effects (see section 5.1).

4.6 Fertility, pregnancy and lactation

Women of childbearing potential

Women 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 administration of Kesimpta.

Pregnancy

There is a limited amount of data from the use of ofatumumab in pregnant women. Ofatumumab may cross the placenta and cause foetal B-cell depletion based on findings from animal studies (see section 5.3). No teratogenicity was observed after intravenous administration of ofatumumab to pregnant monkeys during organogenesis.

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 sections 4.4 and 5.1).

Treatment with ofatumumab should be avoided during pregnancy unless the potential benefit to the mother outweighs the potential risk to the foetus.

To help determine the effects of ofatumumab in pregnant women, healthcare professionals are encouraged to report all pregnancy cases and complications that happen during treatment or within 6 months after the last dose of ofatumumab to the local representative of the marketing authorisation holder, in order to allow monitoring of these patients through the PRegnancy outcomes Intensive Monitoring programme (PRIM). In addition, all adverse pregnancy events should be reported via the national reporting system listed in Appendix V.

Lactation

The use of ofatumumab in women during lactation has not been studied. It is unknown whether ofatumumab is excreted in human milk. In humans, excretion of IgG antibodies in milk occurs during the first few days after birth, which is decreasing to low concentrations soon afterwards. Consequently, a risk to the breast-fed child cannot be excluded during this short period. Afterwards, ofatumumab could be used during breast-feeding if clinically needed. However, if the patient was treated with ofatumumab up to the last few months of pregnancy, breast-feeding can be started immediately after birth.

Fertility

There are no data on the effect of ofatumumab on human fertility.

Non-clinical data did not indicate potential hazards for humans based on male and female fertility parameters assessed in monkeys.

4.7 Effects on ability to drive and use machines

Kesimpta has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

Summary of the safety profile

The most important and frequently reported adverse reactions are upper respiratory tract infections (39.4%), systemic injection-related reactions (20.6%), injection-site reactions (10.9%) and urinary

tract infections (11.9%) (see section 4.4 and below subsection "Description of selected adverse reactions" for further details).

Tabulated list of adverse reactions

Adverse reactions that have been reported in association with the use of ofatumumab in pivotal RMS clinical studies and from post-marketing experience are listed by MedDRA system organ class in Table 1. Within each system organ class, the adverse reactions are ranked by frequency, with the most frequent reactions first. Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness. In addition, the corresponding frequency category for each adverse reaction is based on the following convention: very common (≥1/10); common (≥1/100 to <1/10); uncommon (≥1/1 000 to <1/100); rare (≥1/10 000 to <1/1 000); very rare (<1/10 000) and not known (cannot be estimated from the available data).

Table 1 Tabulated list of adverse reactions

Infections and infestations	
Very common	Upper respiratory tract infections[1] Urinary tract infections[2]
Common	Oral herpes
Immune system disorders	
Not known	Hypersensitivity reactions[3]
General disorders and administration site conditions	
Very common	Injection-site reactions (local)
Injury, poisoning and procedural complications	
Very common	Injection-related reactions (systemic)
Gastrointestinal disorders	
Common	Nausea, vomiting[4]
Investigations	
Common	Blood immunoglobulin M decreased

[1] Grouping of preferred terms (PTs) was considered for ADR 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.
[2] Grouping of preferred terms (PTs) was considered for ADR frequency determination and includes the following: urinary tract infection, cystitis, escherichia urinary tract infection, asymptomatic bacteriuria, bacteriuria.
[3] Reported during post-marketing experience (see section 4.4).
[4] Nausea and vomiting have been reported in association with systemic injection-related reactions (see below and section 4.4)

Description of selected adverse reactions

Infections
In the RMS phase III clinical studies, the overall rate of infections and serious infections in patients treated with ofatumumab was similar to patients who were treated with teriflunomide (51.6% vs 52.7%, and 2.5% vs 1.8%, respectively). Two patients (0.2%) discontinued and 11 patients (1.2%) temporarily interrupted study treatment due to a serious infection.

Upper respiratory tract infections
In these 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.

Injection-related reactions
In the RMS phase III clinical studies, injection-related reactions (systemic) were reported in 20.6% of patients treated with ofatumumab.

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. Two (0.2%) ofatumumab-treated MS patients reported serious injection-related reactions but not life-threatening. The most frequently reported symptoms (≥2%) included fever, headache, myalgia, chills and fatigue. Additional reported symptoms included nausea (1.7%) and vomiting (0.6%).

Injection-site reactions
In the RMS phase III clinical studies, injection-site reactions (local) were reported in 10.9% of patients treated with ofatumumab.

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.

Laboratory abnormalities
Immunoglobulins
During the course of the RMS phase III clinical studies, decrease in mean value of immunoglobulin M (IgM) (30.9% decrease after 48 weeks and 38.8% decrease after 96 weeks) was observed and no association with risk of infections, including serious infections, was shown.

In 14.3% of patients, treatment with ofatumumab resulted in a decrease in IgM that reached a value below 0.34 g/l.

Ofatumumab was associated with a transient decrease of 4.3% in mean immunoglobulin G (IgG) levels after 48 weeks of treatment but an increase of 2.2% after 96 weeks.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system listed in Appendix V.

4.9 Overdose

Doses up to 700 mg have been administered 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.

Ofatumumab has been previously used in chronic lymphocytic leukaemia (CLL) indications, at doses up to 2 000 mg administered intravenously via infusion. Ofatumumab administered via subcutaneous injection has not been assessed and is not approved for these indications, and must not be used for the treatment of oncology indications.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: immunosuppressants, monoclonal antibodies, ATC code: L04AG12

Mechanism of action

Ofatumumab is a fully human anti-CD20 monoclonal immunoglobulin G1 (IgG1) antibody with a theoretical average molecular weight of 145kDa. 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. A subcutaneous route of administration of ofatumumab and subsequent release/absorption from the tissue allows a gradual interaction with B 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.

Pharmacodynamic effects

B-cell depletion
In the RMS clinical studies using ofatumumab 20 mg every 4 weeks, after an initial dose regimen of 20 mg on days 1, 7, and 14, administration resulted in a rapid and sustained reduction of B cells to below LLN (defined as 40 cells/µl) as early as two weeks after treatment initiation. Before initiation of the maintenance phase starting at week 4, total B-cell levels of <10 cells/µl were reached in 94% of patients, increasing to 98% of patients at week 12, and were sustained for as long as 120 weeks (i.e. while on study treatment).

B-cell repletion
Data from RMS phase III clinical studies indicate a median time to B-cell recovery to LLN or baseline value of 24.6 weeks post treatment discontinuation. PK-B cell modelling and simulation for B-cell repletion corroborate this data, predicting median time to B-cell recovery to LLN of 23 weeks post treatment discontinuation.

Immunogenicity
In RMS phase III studies, the overall incidence of treatment-induced anti-drug antibodies (ADAs) was 0.2% (2 of 914) in ofatumumab-treated patients and no patients with treatment enhancing or neutralising ADA were identified. The impact of positive ADA titers on PK, safety profile or B-cell kinetics cannot be assessed given the low incidence of ADA associated with ofatumumab.

Clinical efficacy and safety

The efficacy and safety of ofatumumab were evaluated in two randomised, double-blind, active-controlled phase III pivotal studies of identical design (Study 1 [ASCLEPIOS I] and Study 2 [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 positive gadolinium (Gd)-enhancing MRI scan during the previous year. Both newly diagnosed patients and patients switching from their current treatment were enrolled.

In the two studies, 927 and 955 patients with RMS, respectively, were randomised 1:1 to receive either ofatumumab 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. Across both studies, the median treatment duration was 85 weeks, 33.0% of patients in the ofatumumab group vs 23.2% of patients in the teriflunomide group were treated more than 96 weeks.

Demographics and baseline characteristics were well-balanced across treatment arms and both studies (see Table 2). Mean age was 38 years, mean disease duration was 8.2 years since onset of first symptom, and mean EDSS score was 2.9; 40% of patients had not been previously treated with a disease-modifying therapy (DMT) and 40% had gadolinium (Gd)-enhancing T1 lesions on their baseline MRI scan.

The primary efficacy endpoint of both studies was the annualised 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 included the number of Gd-enhancing T1 lesions per MRI scan, the annualised rate of new or enlarging T2 lesions and the neurofilament light chain (NfL) concentration in serum. Disability-related key secondary endpoints were evaluated in a meta-analysis of combined data from ASCLEPIOS Study 1 and Study 2, as defined in the study protocols.

Table 2 Demographics and baseline characteristics

Characteristics	**Study 1 (ASCLEPIOS I)**		**Study 2 (ASCLEPIOS II)**	
	Ofatumumab (N=465)	Teriflunomide (N=462)	Ofatumumab (N=481)	Teriflunomide (N=474)
Age (mean ± standard deviation; years)	39±9	38±9	38±9	38±9
Sex (female; %)	68.4	68.6	66.3	67.3
Duration of MS since diagnosis (mean/median; 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	1.2	1.3	1.3	1.3
EDSS score (mean/median)	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 with Gd+ T1 lesions (%)	37.4	36.6	43.9	38.6
Number of Gd+ T1 lesions (mean)	1.7	1.2	1.6	1.5

The efficacy results for both studies are summarised in Table 3, Figure 1 and Figure 2.

In both phase III studies, ofatumumab compared to teriflunomide demonstrated a significant reduction in the annualised relapse rate of 50.5% and 58.4%, respectively.

The pre-specified meta-analysis of combined data showed that ofatumumab compared to teriflunomide significantly reduced the risk of 3-month confirmed disability progression (CDP) by 34.3% and the risk of 6-month CDP by 32.4% (see Figure 1).

Ofatumumab compared to teriflunomide significantly reduced the number of Gd-enhancing T1 lesions by 95.9% and the rate of new or enlarging T2 lesions by 83.5% (values represent mean reductions for the combined studies).

Ofatumumab compared to teriflunomide significantly reduced NfL concentrations from the first assessment at 3 months (see Table 3 and Figure 2).

A similar effect of ofatumumab on the key efficacy results compared to teriflunomide was observed across the two phase III studies in exploratory subgroups defined by sex, age, body weight, prior non-steroid MS therapy, and baseline disability and disease activity.

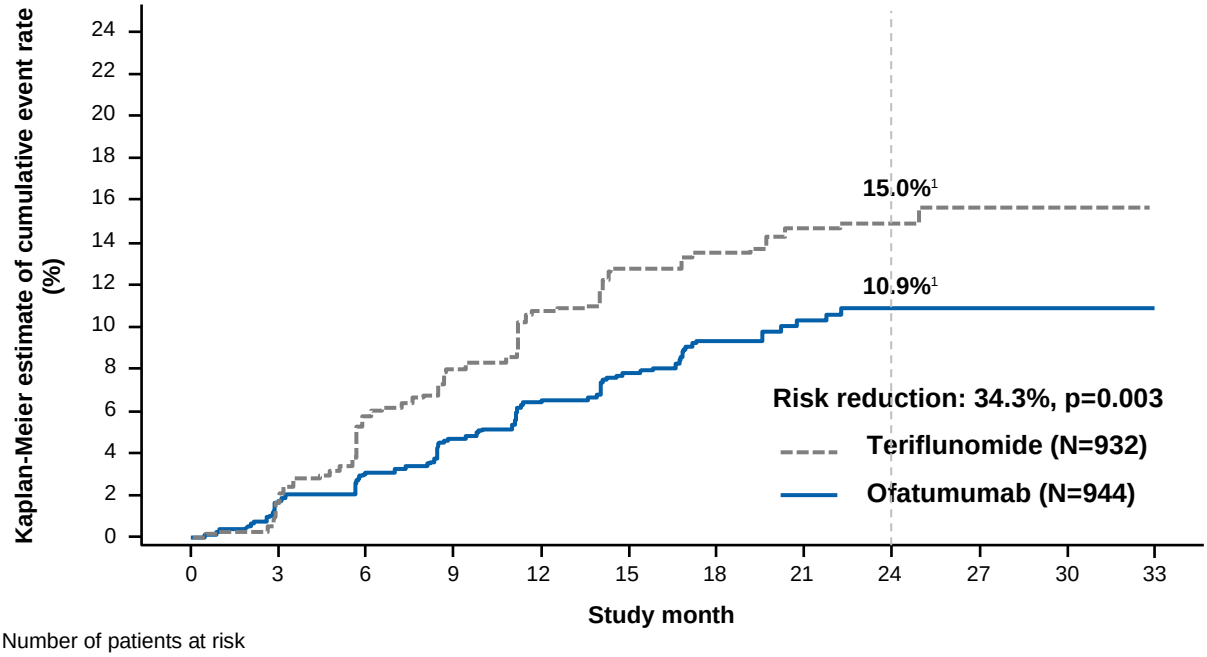
Table 3 Overview of key results from phase III studies in RMS

Endpoints	**Study 1 (ASCLEPIOS I)**		**Study 2 (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				
Annualised relapse rate (ARR) (primary endpoint)[1]	0.11	0.22	0.10	0.25
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
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
Relative reduction	81.9% (p<0.001)		84.6% (p<0.001)	
NfL at 3 months (pg/ml)	8.80	9.41	8.92	10.02
Relative reduction	7% (p=0.011)		11% (p<0.001)	
Endpoints based on pre-specified meta-analyses				
Proportion of patients with 3-month confirmed disability progression[2] Risk reduction	10.9% ofatumumab vs. 15.0% teriflunomide 34.3% (p=0.003)			
Proportion of patients with 6-month confirmed disability progression[2] Risk reduction	8.1% ofatumumab vs. 12.0% teriflunomide 32.4% (p=0.012)			

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

[2] Kaplan-Meier estimates at 24 months. 3- and 6-month CDP were assessed based on prospectively planned analysis of the combined data from the two phase III studies and defined as a clinically meaningful increase in the EDSS sustained for at least 3 or 6 months, respectively. A clinically meaningful increase in EDSS is defined as an increase of at least 1.5 points if the baseline EDSS score was 0, an increase of at least 1.0 point if the baseline EDSS score was 1.0–5.0, and an increase of at least 0.5 points if the baseline EDSS score was 5.5 or greater.

Figure 1 **Time to first 3-month CDP by treatment (ASCLEPIOS Study 1 and Study 2 combined, full analysis set)**

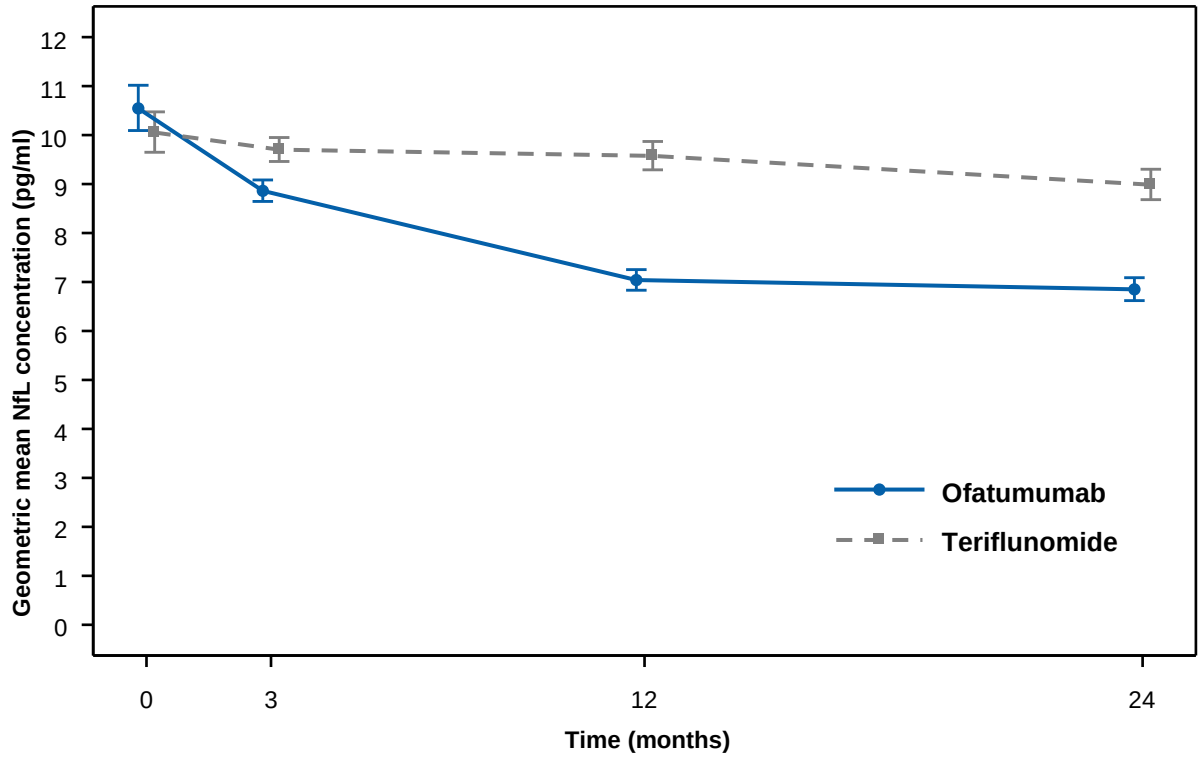


Number of patients at risk

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

[1] The numbers shown on the curves represent Kaplan-Meier estimates of the risk of the event at 24 months (marked by the vertical dashed line).

Figure 2 **NfL concentrations in serum by treatment (ASCLEPIOS Study 1 and Study 2 combined, full analysis set)**



The line plots represent the adjusted geometric means with 95% CI at each time point which are from Repeated measures model. Geometric means at baseline are derived as exponentiated arithmetic mean of natural logarithmic of raw values of NfL concentrations in serum.

In the phase III studies, the proportion of patients with adverse events (AEs) (83.6% vs 84.2%) and the AEs leading to discontinuation (5.7% vs 5.2%) were similar in the ofatumumab and teriflunomide groups.

Paediatric population

The European Medicines Agency has deferred the obligation to submit the results of studies with Kesimpta in one or more subsets of the paediatric population in the treatment of multiple sclerosis (see section 4.2 for information on paediatric use).

5.2 Pharmacokinetic properties

Absorption

After subcutaneous administration, ofatumumab has a prolonged release/absorption profile (T_{max} of 4.3 days) and is predominantly absorbed via the lymphatic system.

A monthly subcutaneous dose of 20 mg leads to a mean AUC_{tau} of 483 µg*h/ml and a mean C_{max} of 1.43 µg/ml at steady state.

Distribution

The volume of distribution at steady state was estimated to be 5.42 litres following repeated subcutaneous administration of ofatumumab at a dose of 20 mg.

Biotransformation

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 in two ways: a target-mediated route that is related to binding to B cells and a target-independent route mediated by non-specific endocytosis followed by intracellular catabolism, as with other IgG molecules. B cells present at baseline result in a greater component of target-mediated clearance of ofatumumab at the start of therapy. Ofatumumab dosing leads to potent depletion of B cells resulting in reduced overall clearance.

The half-life at steady state was estimated to be approximately 16 days following repeated subcutaneous administration of ofatumumab at a dose of 20 mg.

Linearity/non-linearity

Ofatumumab had non-linear pharmacokinetics related to its decreasing clearance over time.

Special populations

Adults over 55 years old
There are no dedicated pharmacokinetic studies of ofatumumab in patients over 55 years old due to limited clinical experience (see section 4.2).

Paediatric population
No studies have been conducted to investigate the pharmacokinetics of ofatumumab in paediatric patients below the age of 18 years.

Gender
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 clinically relevant, and no dose adjustment is recommended.

Body weight
Based on the results of a cross-study population analysis, body weight was identified as a covariate of exposure (C_{max} and AUC) to ofatumumab in RMS subjects. However, body weight did not affect safety and efficacy measures evaluated in the clinical studies; therefore, dose adjustment is not required.

Renal impairment
No specific studies of ofatumumab in patients with renal impairment have been performed.

Patients with mild renal impairment were included in clinical studies. There is no experience in patients with moderate and severe renal impairment. However, as ofatumumab is not excreted via urine, it is not expected that patients with renal impairment require dose modification.

Hepatic impairment
No studies of ofatumumab in patients with hepatic impairment have been performed.

Since hepatic metabolism of monoclonal antibodies such as ofatumumab is negligible, hepatic impairment is not expected to impact its pharmacokinetics. Therefore, it is not expected that patients with hepatic impairment require dose modification.

5.3 Preclinical safety data

Non-clinical data revealed no special hazard for humans based on conventional studies of repeated dose toxicity including safety pharmacology endpoints.

Neither carcinogenicity nor mutagenicity studies have been conducted with ofatumumab. As an antibody, ofatumumab is not expected to interact directly with DNA.

The embryo-foetal development (EFD) and the enhanced pre/post-natal development (ePPND) studies in monkeys showed that exposure to ofatumumab given intravenously during gestation caused no maternal toxicity, no teratogenicity, and no adverse effects on embryo-foetal and pre/post-natal development.

In these studies, ofatumumab was detected in the blood of the foetuses and infants, confirming placental transfer and foetal exposure to ofatumumab persisting post-natally (long half-life of the monoclonal antibody). Exposure to ofatumumab during gestation led to the expected depletion of CD20+ B cells in maternal animals and their foetuses and infants, along with a reduced spleen weight (without histological correlate) in foetuses and a reduced humoral immune response to keyhole limpet haemocyanin (KLH) in infants at high doses. All these changes were reversible during the 6-month post-natal period. In infants, early post-natal mortality was observed at a dose 160 times higher than the therapeutic dose (on AUC basis) and was likely due to potential infections secondary to immunomodulation. The NOAEL related to the pharmacological activity of ofatumumab in infants of the ePPND study leads to an AUC-based safety margin of at least 22-fold when maternal exposure at the NOAEL is compared with human exposure at the therapeutic dose of 20 mg monthly.

In a dedicated monkey fertility study, male and female fertility endpoints were unaffected.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

L-arginine
Sodium acetate trihydrate
Sodium chloride
Polysorbate 80 (E 433)
Disodium edetate dihydrate
Hydrochloric acid (for pH adjustment)
Water for injections

6.2 Incompatibilities

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

6.3 Shelf life

3 years

6.4 Special precautions for storage

Kesimpta 20 mg solution for injection in pre-filled syringe

Store in a refrigerator (2°C - 8°C). Do not freeze.
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.
Keep the pre-filled syringe in the outer carton in order to protect from light.

Kesimpta 20 mg solution for injection in pre-filled pen

Store in a refrigerator (2°C - 8°C). Do not freeze.
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.
Keep the pre-filled pen in the outer carton in order to protect from light.

6.5 Nature and contents of container

Kesimpta 20 mg solution for injection in pre-filled syringe

Kesimpta is supplied in a single-use glass syringe, equipped with a stainless steel needle, a plunger stopper and a rigid needle shield. The syringe is assembled with a plunger rod and a needle safety device.

Kesimpta is available in unit packs containing 1 pre-filled syringe and in multipacks containing 3 (3 packs of 1) pre-filled syringes.

Not all pack sizes may be marketed.

Kesimpta 20 mg solution for injection in pre-filled pen

Kesimpta is supplied in a single-use glass syringe, equipped with a stainless steel needle, a plunger stopper and a rigid needle shield. The syringe is assembled into an auto-injector.

Kesimpta is available in unit packs containing 1 pre-filled pen and in multipacks containing 3 (3 packs of 1) pre-filled pens.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

Instructions for handling of the pre-filled syringe

Before injection, the pre-filled syringe should be taken out of the refrigerator for about 15 to 30 minutes to allow it to reach room temperature. The pre-filled syringe should be kept in the original carton until ready to use, and the needle cap should not be removed until just before the injection is performed. Prior to use, the solution should be inspected visually by looking through the viewing window. The pre-filled syringe should not be used if the liquid contains visible particles or is cloudy.

Comprehensive instructions for administration are given in the package leaflet.

Instructions for handling of the pre-filled pen

Before injection, the pre-filled pen should be taken out of the refrigerator for about 15 to 30 minutes to allow it to reach room temperature. The pre-filled pen should be kept in the original carton until ready to use, and the cap should not be removed until just before the injection is performed. Prior to use, the solution should be inspected visually by looking through the viewing window. The pre-filled pen should not be used if the liquid contains visible particles or is cloudy.

Comprehensive instructions for administration are given in the package leaflet.

Disposal

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

7. MARKETING AUTHORISATION HOLDER

Novartis Europharm Limited
Vista Building
Elm Park, Merrion Road
Dublin 4
Ireland

8. MARKETING AUTHORISATION NUMBER(S)

EU/1/21/1532/001-004

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

26 March 2021

10. DATE OF REVISION OF THE TEXT

Detailed information on this medicinal product is available on the website of the European Medicines Agency https://www.ema.europa.eu.

ANNEX II

A. MANUFACTURER(S) OF THE BIOLOGICAL ACTIVE SUBSTANCE(S) AND MANUFACTURER(S) RESPONSIBLE FOR BATCH RELEASE

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

A. MANUFACTURER(S) OF THE BIOLOGICAL ACTIVE SUBSTANCE(S) AND MANUFACTURER(S) RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturer of the biological active substance

Lonza Biologics, Inc.
101 International Drive
Portsmouth, NH 03801
United States

Name and address of the manufacturers responsible for batch release

Novartis Pharma GmbH
Roonstrasse 25
90429 Nuremberg
Germany

Novartis Farmacéutica, S.A.
Gran Via de les Corts Catalanes, 764
08013 Barcelona
Spain

Novartis Pharma GmbH
Sophie-Germain-Strasse 10
90443 Nuremberg
Germany

The printed package leaflet of the medicinal product must state the name and address of the manufacturer responsible for the release of the concerned batch.

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

Medicinal product subject to restricted medical prescription (see Annex I: Summary of Product Characteristics, section 4.2).

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

- **Periodic safety update reports (PSURs)**

The requirements for submission of PSURs for this medicinal product are set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC and any subsequent updates published on the European medicines web-portal.

The marketing authorisation holder (MAH) shall submit the first PSUR for this product within 6 months following authorisation.

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

- **Risk management plan (RMP)**

The marketing authorisation holder (MAH) shall perform the required pharmacovigilance activities and interventions detailed in the agreed RMP presented in Module 1.8.2 of the marketing authorisation and any agreed subsequent updates of the RMP.

An updated RMP should be submitted:

- At the request of the European Medicines Agency;
- Whenever the risk management system is modified, especially as the result of new information being received that may lead to a significant change to the benefit/risk profile or as the result of an important (pharmacovigilance or risk minimisation) milestone being reached.

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

CARTON OF UNIT PACK – pre-filled syringe

1. NAME OF THE MEDICINAL PRODUCT

Kesimpta 20 mg solution for injection in pre-filled syringe
ofatumumab

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One pre-filled syringe contains 20 mg ofatumumab in 0.4 ml solution.

3. LIST OF EXCIPIENTS

Also contains: L-arginine, sodium acetate trihydrate, sodium chloride, polysorbate 80 (E 433), disodium edetate dihydrate, hydrochloric acid, water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection

1 pre-filled syringe

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Subcutaneous use
Read the package leaflet before use.
Single use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator. Do not freeze.
Keep the pre-filled syringe in the outer carton in order to protect from light.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Novartis Europharm Limited
Vista Building
Elm Park, Merrion Road
Dublin 4
Ireland

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/21/1532/001 Pack containing 1 pre-filled syringe

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Kesimpta 20 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON OF MULTIPACK (INCLUDING BLUE BOX) – pre-filled syringe

1. NAME OF THE MEDICINAL PRODUCT

Kesimpta 20 mg solution for injection in pre-filled syringe
ofatumumab

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One pre-filled syringe contains 20 mg ofatumumab in 0.4 ml solution.

3. LIST OF EXCIPIENTS

Also contains: L-arginine, sodium acetate trihydrate, sodium chloride, polysorbate 80 (E 433), disodium edetate dihydrate, hydrochloric acid, water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection

Multipack: 3 (3 packs of 1) pre-filled syringes

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Subcutaneous use
Read the package leaflet before use.
Single use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator. Do not freeze.
Keep the pre-filled syringes in the outer carton in order to protect from light.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Novartis Europharm Limited
Vista Building
Elm Park, Merrion Road
Dublin 4
Ireland

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/21/1532/002 Multipack containing 3 (3 packs of 1) pre-filled syringes

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Kesimpta 20 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

INTERMEDIATE CARTON OF MULTIPACK (WITHOUT BLUE BOX) – pre-filled syringe

1. NAME OF THE MEDICINAL PRODUCT

Kesimpta 20 mg solution for injection in pre-filled syringe
ofatumumab

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One pre-filled syringe contains 20 mg ofatumumab in 0.4 ml solution.

3. LIST OF EXCIPIENTS

Also contains: L-arginine, sodium acetate trihydrate, sodium chloride, polysorbate 80 (E 433), disodium edetate dihydrate, hydrochloric acid, water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection

1 pre-filled syringe. Component of a multipack. Not to be sold separately.

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Subcutaneous use
Read the package leaflet before use.
Single use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator. Do not freeze.
Keep the pre-filled syringe in the outer carton in order to protect from light.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Novartis Europharm Limited
Vista Building
Elm Park, Merrion Road
Dublin 4
Ireland

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/21/1532/002 Multipack containing 3 (3 packs of 1) pre-filled syringes

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Kesimpta 20 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

BLISTER OF PRE-FILLED SYRINGE

1. NAME OF THE MEDICINAL PRODUCT

Kesimpta 20 mg solution for injection in pre-filled syringe
ofatumumab

2. NAME OF THE MARKETING AUTHORISATION HOLDER

Novartis Europharm Limited

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. OTHER

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

SYRINGE LABEL

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Kesimpta 20 mg injection
ofatumumab
SC

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

6. OTHER

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

CARTON OF UNIT PACK – pre-filled pen

1. NAME OF THE MEDICINAL PRODUCT

Kesimpta 20 mg solution for injection in pre-filled pen
ofatumumab

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One pre-filled pen contains 20 mg ofatumumab in 0.4 ml solution.

3. LIST OF EXCIPIENTS

Also contains: L-arginine, sodium acetate trihydrate, sodium chloride, polysorbate 80 (E 433), disodium edetate dihydrate, hydrochloric acid, water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection

1 pre-filled Sensoready Pen

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Subcutaneous use
Read the package leaflet before use.
Single use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator. Do not freeze.
Keep the pre-filled pen in the outer carton in order to protect from light.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Novartis Europharm Limited
Vista Building
Elm Park, Merrion Road
Dublin 4
Ireland

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/21/1532/003 Pack containing 1 pre-filled pen

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Kesimpta 20 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON OF MULTIPACK (INCLUDING BLUE BOX) – pre-filled pen

1. NAME OF THE MEDICINAL PRODUCT

Kesimpta 20 mg solution for injection in pre-filled pen
ofatumumab

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One pre-filled pen contains 20 mg ofatumumab in 0.4 ml solution.

3. LIST OF EXCIPIENTS

Also contains: L-arginine, sodium acetate trihydrate, sodium chloride, polysorbate 80 (E 433), disodium edetate dihydrate, hydrochloric acid, water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection

Multipack: 3 (3 packs of 1) pre-filled Sensoready Pens

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Subcutaneous use
Read the package leaflet before use.
Single use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator. Do not freeze.
Keep the pre-filled pens in the outer carton in order to protect from light.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Novartis Europharm Limited
Vista Building
Elm Park, Merrion Road
Dublin 4
Ireland

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/21/1532/004 Multipack containing 3 (3 packs of 1) pre-filled pens

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Kesimpta 20 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

INTERMEDIATE CARTON OF MULTIPACK (WITHOUT BLUE BOX) – pre-filled pen

1. NAME OF THE MEDICINAL PRODUCT

Kesimpta 20 mg solution for injection in pre-filled pen
ofatumumab

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One pre-filled pen contains 20 mg ofatumumab in 0.4 ml solution.

3. LIST OF EXCIPIENTS

Also contains: L-arginine, sodium acetate trihydrate, sodium chloride, polysorbate 80 (E 433), disodium edetate dihydrate, hydrochloric acid, water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection

1 pre-filled Sensoready Pen. Component of a multipack. Not to be sold separately.

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Subcutaneous use
Read the package leaflet before use.
Single use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator. Do not freeze.
Keep the pre-filled pen in the outer carton in order to protect from light.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Novartis Europharm Limited
Vista Building
Elm Park, Merrion Road
Dublin 4
Ireland

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/21/1532/004 Multipack containing 3 (3 packs of 1) pre-filled pens

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Kesimpta 20 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

PEN LABEL

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Kesimpta 20 mg injection
ofatumumab
Subcutaneous use

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

6. OTHER

Sensoready Pen

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

INNER LID OF OUTER CARTON OF UNIT PACK AND OF INTERMEDIATE CARTON OF MULTIPACK (pre-filled syringe and pre-filled pen)

1. OTHER

Scan code for more information.

QR code to be included + pictogram

www.kesimpta.eu

B. PACKAGE LEAFLET

Package leaflet: Information for the patient

Kesimpta 20 mg solution for injection in pre-filled syringe
ofatumumab

▼This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See the end of section 4 for how to report side effects.

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Kesimpta is and what it is used for

What Kesimpta is
Kesimpta contains the active substance ofatumumab. Ofatumumab belongs to a group of medicines called monoclonal antibodies.

What Kesimpta is used for
Kesimpta is used to treat adults with relapsing forms of multiple sclerosis (RMS).

How Kesimpta works
Kesimpta works by attaching to a target called CD20 on the surface of B cells. B cells are a type of white blood cell which are part of the immune system (the body's defences). In multiple sclerosis, the immune system attacks the protective layer around nerve cells. B cells are involved in this process. Kesimpta targets and removes the B cells and thereby reduces the chance of a relapse, relieves symptoms and slows down the progression of the disease.

2. What you need to know before you use Kesimpta

Do not use Kesimpta
- if you are allergic to ofatumumab or any of the other ingredients of this medicine (listed in section 6).
- if you have been told that you have severe problems with your immune system.
- if you are suffering from a severe infection.
- if you have cancer.

Warnings and precautions
Talk to your doctor before using Kesimpta
- Kesimpta may cause the hepatitis B virus to become active again. Your doctor will perform a blood test to check if you are at risk of hepatitis B infection. If this shows that you have had hepatitis B or are a carrier of the hepatitis B virus, your doctor will ask you to see a specialist.
- Before you start treatment with Kesimpta, your doctor may check your immune system.
- If you have an infection, your doctor may decide that you cannot be given Kesimpta or may delay your treatment with Kesimpta until the infection is resolved.
- Your doctor will check if you need any vaccinations before you start your treatment with Kesimpta. If you need a type of vaccine called a live or live-attenuated vaccine, it should be given at least 4 weeks before you start Kesimpta treatment. Other types of vaccines should be given at least 2 weeks before you start Kesimpta treatment.

While using Kesimpta
Tell your doctor:
- if you have a general injection-related reaction or a local injection-site reaction. These are the most common side effects of Kesimpta treatment and are described in section 4. They usually occur in the 24 hours after Kesimpta is injected, in particular after the first injection. The first injection should take place under the guidance of a healthcare professional.
- if you have an infection. 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. Infections could be serious and sometimes even life-threatening.
- if you plan to have any vaccinations. Your doctor will tell you whether the vaccination you need is a live vaccine, a live-attenuated vaccine, or another type of vaccine. You should not be given live or live-attenuated vaccines during treatment with Kesimpta as this may result in infection. Other types of vaccines may work less well if they are given during treatment with Kesimpta.

Tell your doctor straight away if you get any of the following during your treatment with Kesimpta, because they could be signs of a serious condition:
- if you have rash, hives, trouble breathing, swelling of the face, eyelids, lips, mouth, tongue or throat, chest tightness, or feel faint. These could be signs or symptoms of an allergic reaction.
- if you think your multiple sclerosis is getting worse (e.g. weakness or visual changes) or if you notice any new or unusual symptoms. These effects may indicate a rare brain disorder called progressive multifocal leukoencephalopathy (PML), which is caused by a virus infection.

Children and adolescents
Do not give this medicine to children and adolescents below 18 years of age because Kesimpta has not yet been studied in this age group.

Other medicines and Kesimpta
Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines.

In particular, tell your doctor or pharmacist:
- if you are taking, have recently taken or might take medicines that affect the immune system. This is because these may have an added effect on the immune system.
- if you plan to have any vaccinations (see “Warnings and Precautions” above).

Pregnancy and breast-feeding
If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor for advice before using this medicine.

Pregnancy
You should avoid becoming pregnant while using Kesimpta and for 6 months after you stop using it.

If there is a possibility that you could become pregnant you should use an effective birth control method during treatment and for 6 months after stopping Kesimpta. Ask your doctor about the available options.

If you do become pregnant or think you may be pregnant during treatment or within 6 months after the last dose, tell your doctor straight away. Your doctor will discuss with you the potential risks of Kesimpta on pregnancy. This is because Kesimpta can reduce the number of immune cells (B cells) in both the mother and the unborn baby. Your doctor should report your pregnancy to Novartis. You can also report your pregnancy by contacting the local representative of Novartis (see section 6), in addition to contacting your doctor.

Breast-feeding
Kesimpta can pass into breast milk. Talk to your doctor about the benefits and risks before breast-feeding your baby while using Kesimpta.

Vaccination of newborn babies
Ask your doctor or pharmacist for advice before vaccinating your newborn baby if you have used Kesimpta during your pregnancy (see "Warnings and precautions" above).

Driving and using machines
Kesimpta is unlikely to affect your ability to drive and use machines.

Kesimpta contains sodium
This medicine contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially 'sodium-free'.

Kesimpta contains polysorbate 80
This medicine contains 0.08 mg of polysorbate 80 per dose. Polysorbates may cause allergic reactions. Tell your doctor if you have any known allergies.

3. How to use Kesimpta

Always use this medicine exactly as your doctor has told you. Check with your doctor or pharmacist if you are not sure.

Kesimpta is given by subcutaneous injection (injection under your skin).

The first injection should take place under the guidance of a healthcare professional.

Kesimpta pre-filled syringes are for single use only.

For detailed instructions on how to inject Kesimpta, see "Instructions for use of Kesimpta pre-filled syringe" at the end of this leaflet.

'QR code to be included' + www.kesimpta.eu

You can use Kesimpta at any time of day (morning, afternoon or evening).

How much Kesimpta to use and how often to use it

Do not exceed the dose prescribed by your doctor.

- The initial dosing is 20 mg Kesimpta administered on the first day of treatment (Week 0) and after 1 and 2 weeks (Week 1 and Week 2). After these first 3 injections, there is no injection in the following week (Week 3).
- Starting at Week 4 and then every month, the recommended dose is 20 mg Kesimpta.

Time	**Dose**
Week 0 (first day of treatment)	20 mg
Week 1	20 mg
Week 2	20 mg
Week 3	No injection
Week 4	20 mg
Every month afterwards	20 mg

How long to use Kesimpta
Continue using Kesimpta every month for as long as your doctor tells you to.

Your doctor will regularly check your condition to determine whether the treatment is having the desired effect.

If you have questions about how long to use Kesimpta, talk to your doctor, pharmacist or nurse.

If you use more Kesimpta than you should
If you have injected too much Kesimpta, contact your doctor right away.

If you forget to use Kesimpta
To get the full benefit of Kesimpta, it is important that you have every injection on time.

If you have forgotten an injection of Kesimpta, inject yourself as soon as possible. Do not wait until the next scheduled dose. The timing of future injections should then be calculated from the day you injected this dose and not based on the original schedule (see also “How much Kesimpta to use and how often to use it” above).

If you stop using Kesimpta
Do not stop using Kesimpta or change your dose without talking with your doctor.

Some side effects can be related to a low level of B cells in your blood. After you stop treatment with Kesimpta your blood level of B cells will gradually increase to normal. 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 doctor or pharmacist.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

The side effects of Kesimpta are listed below. If any of these side effects becomes severe, tell your doctor, pharmacist or nurse.

Very common (may affect more than 1 in 10 people)
- upper respiratory tract infections, with symptoms such as sore throat and runny nose
- injection-related reactions, such as fever, headache, muscle pain, chills and tiredness - these usually occur in the 24 hours after an injection of Kesimpta, in particular after the first injection
- urinary tract infections
- injection-site reactions, such as redness, pain, itching and swelling at the injection site

Common (may affect up to 1 in 10 people)
- decrease in the blood level of a protein called immunoglobulin M, which helps protect against infection
- oral herpes
- nausea, vomiting (have been reported in association with injection-related reactions)

Not known (frequency cannot be estimated from the available data)
- allergic reactions, with symptoms such as rash, hives, trouble breathing, swelling of the face, eyelids, lips, mouth, tongue or throat, chest tightness, or feeling faint

Reporting of side effects
If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Kesimpta

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the carton and label after EXP. The expiry date refers to the last day of that month.

Keep the pre-filled syringe(s) in the outer carton in order to protect from light. Store in a refrigerator (2°C – 8°C). 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.

Do not use this medicine if you notice that the solution contains visible particules or is cloudy.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Kesimpta contains
- The active substance is ofatumumab. Each pre-filled syringe contains 20 mg ofatumumab.
- The other ingredients are L-arginine, sodium acetate trihydrate, sodium chloride, polysorbate 80 (E 433), disodium edetate dihydrate, hydrochloric acid (for pH adjustment) and water for injections.

What Kesimpta looks like and contents of the pack
Kesimpta solution for injection is clear to slightly opalescent, and colourless to slightly brownish-yellow.

Kesimpta is available in unit packs containing 1 pre-filled syringe and in multipacks comprising 3 cartons, each containing 1 pre-filled syringe.

Not all pack sizes may be marketed.

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This leaflet was last revised in

Other sources of information

Detailed information on this medicine is available on the European Medicines Agency web site: https://www.ema.europa.eu.

Instructions for use of Kesimpta pre-filled syringe

It is important that you understand and follow these instructions for use before injecting Kesimpta. Talk to your doctor, pharmacist or nurse 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 automatically cover the needle after the injection is finished. The needle guard helps to prevent needlestick 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 cover the needle too early.
- Do not use if the pre-filled syringe has been dropped onto a hard surface or dropped after removing the needle cap.
- Dispose of the used Kesimpta pre-filled syringe immediately after use. **Do not re-use a Kesimpta pre-filled syringe**. See "How should I dispose of the used Kesimpta pre-filled syringe?" at the end of these Instructions for Use.

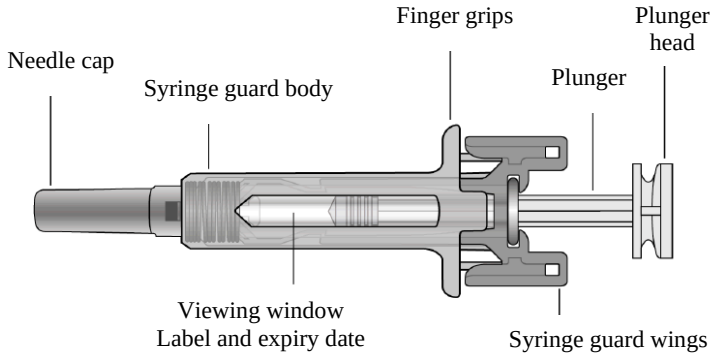
How should I store Kesimpta?

- Store the Kesimpta pre-filled syringe carton in a refrigerator between 2°C and 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.

Keep Kesimpta out of the sight and reach of children.

Kesimpta pre-filled syringe parts (see Picture A):

Picture A



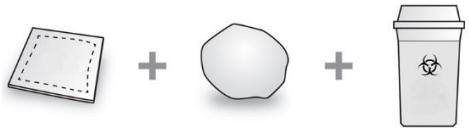
What you need for your injection:
Included in the carton:

- A new Kesimpta pre-filled syringe

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

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

Picture B



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

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.

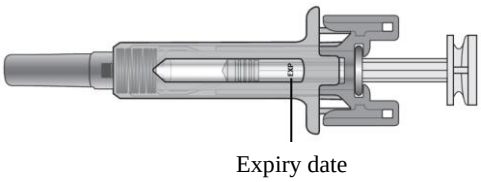
Step 4. Remove the pre-filled syringe from the outer carton and take it out of the blister by holding the syringe guard body.

Step 5. Look through the viewing window on the pre-filled syringe. The liquid inside should be clear to slightly opalescent. 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 damaged. Return the pre-filled syringe and the package it came in to the pharmacy.

Step 7. **Do not use** the pre-filled syringe if the expiry date has passed (**see Picture C**). Return the expired pre-filled syringe and its packaging to the pharmacy.

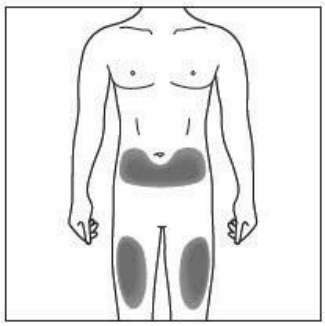
Picture C



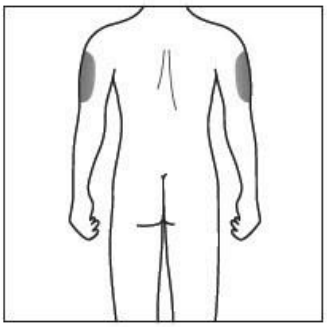
Choose and clean the injection site

- Areas of your body that you can use for injecting Kesimpta include:
  - the front of your thighs (**see Picture D**)
  - the lower stomach area (abdomen), but **not** the area 5 cm around your navel (belly button) (**see Picture D**)
  - your upper outer arms, if a caregiver or healthcare professional is giving you the injection (**see Picture E**).

Picture D



Picture E
(caregiver and healthcare professional only)



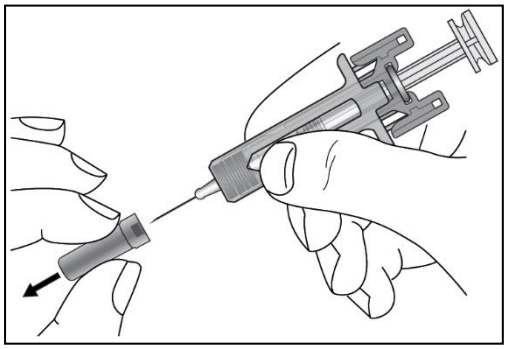
- Choose a different site each time you inject Kesimpta.
- **Do not inject** into areas where the skin is tender, bruised, red, scaly, or hard. Avoid areas with scars or stretch marks or infection sites.

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.

Giving your injection

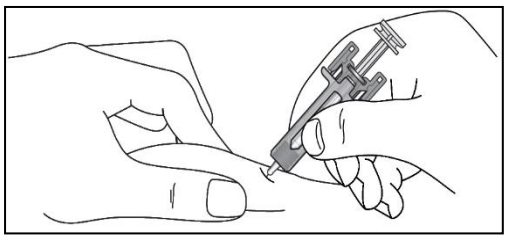
Step 9. Carefully remove the needle cap from the pre-filled syringe (**see Picture F**). Throw away the needle cap. You may see a drop of liquid at the end of the needle. This is normal.

Picture F



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 Picture G**). Push the needle all the way in to make sure that you inject your full dose.

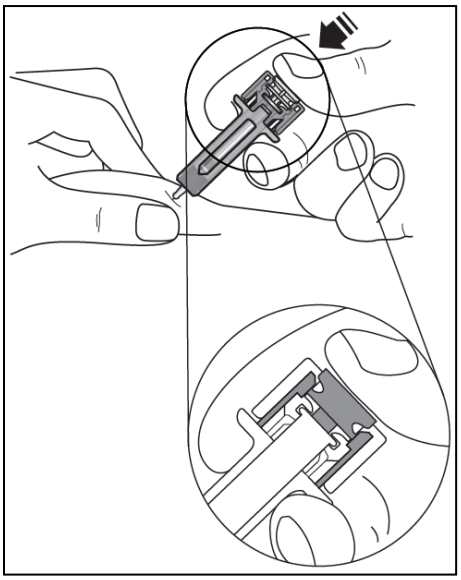
Picture G



Step 11. Hold the pre-filled syringe finger grips as shown (**see Picture 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 5 seconds while holding the syringe in place.

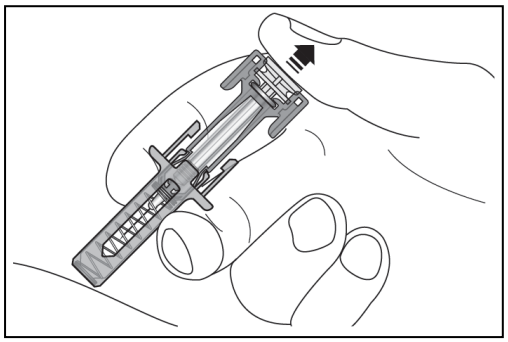
Picture H



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

Step 14. There may be a little 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 plaster, if the bleeding continues.

Picture I



How should I dispose of the used Kesimpta pre-filled syringe?

Step 15. Dispose of your used pre-filled syringe in a sharps disposal container (i.e. a puncture-resistant closable container, or similar) (**see Picture J**).

- **Do not dispose of** your used pre-filled syringe in your household waste.
- Never try to reuse your pre-filled syringe.

Keep the sharps container out of the reach of children.

Picture J

Package leaflet: Information for the patient

Kesimpta 20 mg solution for injection in pre-filled pen
ofatumumab

▼This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See the end of section 4 for how to report side effects.

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Kesimpta is and what it is used for

What Kesimpta is
Kesimpta contains the active substance ofatumumab. Ofatumumab belongs to a group of medicines called monoclonal antibodies.

What Kesimpta is used for
Kesimpta is used to treat adults with relapsing forms of multiple sclerosis (RMS).

How Kesimpta works
Kesimpta works by attaching to a target called CD20 on the surface of B cells. B cells are a type of white blood cell which are part of the immune system (the body's defences). In multiple sclerosis, the immune system attacks the protective layer around nerve cells. B cells are involved in this process. Kesimpta targets and removes the B cells and thereby reduces the chance of a relapse, relieves symptoms and slows down the progression of the disease.

2. What you need to know before you use Kesimpta

Do not use Kesimpta
- if you are allergic to ofatumumab or any of the other ingredients of this medicine (listed in section 6).
- if you have been told that you have severe problems with your immune system.
- if you are suffering from a severe infection.
- if you have cancer.

Warnings and precautions
Talk to your doctor before using Kesimpta
- Kesimpta may cause the hepatitis B virus to become active again. Your doctor will perform a blood test to check if you are at risk of hepatitis B infection. If this shows that you have had hepatitis B or are a carrier of the hepatitis B virus, your doctor will ask you to see a specialist.
- Before you start treatment with Kesimpta, your doctor may check your immune system.
- If you have an infection, your doctor may decide that you cannot be given Kesimpta or may delay your treatment with Kesimpta until the infection is resolved.
- Your doctor will check if you need any vaccinations before you start your treatment with Kesimpta. If you need a type of vaccine called a live or live-attenuated vaccine, it should be given at least 4 weeks before you start Kesimpta treatment. Other types of vaccines should be given at least 2 weeks before you start Kesimpta treatment.

While using Kesimpta
Tell your doctor:
- if you have a general injection-related reaction or a local injection-site reaction. These are the most common side effects of Kesimpta treatment and are described in section 4. They usually occur in the 24 hours after Kesimpta is injected, in particular after the first injection. The first injection should take place under the guidance of a healthcare professional.
- if you have an infection. 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. Infections could be serious and sometimes even life-threatening.
- if you plan to have any vaccinations. Your doctor will tell you whether the vaccination you need is a live vaccine, a live-attenuated vaccine, or another type of vaccine. You should not be given live or live-attenuated vaccines during treatment with Kesimpta as this may result in infection. Other types of vaccines may work less well if they are given during treatment with Kesimpta.

Tell your doctor straight away if you get any of the following during your treatment with Kesimpta, because they could be signs of a serious condition:
- if you have rash, hives, trouble breathing, swelling of the face, eyelids, lips, mouth, tongue or throat, chest tightness, or feel faint. These could be signs or symptoms of an allergic reaction.
- if you think your multiple sclerosis is getting worse (e.g. weakness or visual changes) or if you notice any new or unusual symptoms. These effects may indicate a rare brain disorder called progressive multifocal leukoencephalopathy (PML), which is caused by a virus infection.

Children and adolescents
Do not give this medicine to children and adolescents below 18 years of age because Kesimpta has not yet been studied in this age group.

Other medicines and Kesimpta
Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines.

In particular, tell your doctor or pharmacist:
- if you are taking, have recently taken or might take medicines that affect the immune system. This is because these may have an added effect on the immune system.
- if you plan to have any vaccinations (see “Warnings and Precautions” above).

Pregnancy and breast-feeding
If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor for advice before using this medicine.

Pregnancy
You should avoid becoming pregnant while using Kesimpta and for 6 months after you stop using it.

If there is a possibility that you could become pregnant you should use an effective birth control method during treatment and for 6 months after stopping Kesimpta. Ask your doctor about the available options.

If you do become pregnant or think you may be pregnant during treatment or within 6 months after the last dose, tell your doctor straight away. Your doctor will discuss with you the potential risks of Kesimpta on pregnancy. This is because Kesimpta can reduce the number of immune cells (B cells) in both the mother and the unborn baby. Your doctor should report your pregnancy to Novartis. You can also report your pregnancy by contacting the local representative of Novartis (see section 6), in addition to contacting your doctor.

Breast-feeding
Kesimpta can pass into breast milk. Talk to your doctor about the benefits and risks before breast-feeding your baby while using Kesimpta.

Vaccination of newborn babies
Ask your doctor or pharmacist for advice before vaccinating your newborn baby if you have used Kesimpta during your pregnancy (see "Warnings and precautions" above).

Driving and using machines
Kesimpta is unlikely to affect your ability to drive and use machines.

Kesimpta contains sodium
This medicine contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially 'sodium-free'.

Kesimpta contains polysorbate 80
This medicine contains 0.08 mg of polysorbate 80 per dose. Polysorbates may cause allergic reactions. Tell your doctor if you have any known allergies.

3. How to use Kesimpta

Always use this medicine exactly as your doctor has told you. Check with your doctor or pharmacist if you are not sure.

Kesimpta is given by subcutaneous injection (injection under your skin).

The first injection should take place under the guidance of a healthcare professional.

Kesimpta pre-filled pens are for single use only.

For detailed instructions on how to inject Kesimpta, see "Instructions for use of Kesimpta Sensoready Pen" at the end of this leaflet.

'QR code to be included' + www.kesimpta.eu

You can use Kesimpta at any time of day (morning, afternoon or evening).

How much Kesimpta to use and how often to use it

Do not exceed the dose prescribed by your doctor.

- The initial dosing is 20 mg Kesimpta administered on the first day of treatment (Week 0) and after 1 and 2 weeks (Week 1 and Week 2). After these first 3 injections, there is no injection in the following week (Week 3).
- Starting at Week 4 and then every month, the recommended dose is 20 mg Kesimpta.

Time	**Dose**
Week 0 (first day of treatment)	20 mg
Week 1	20 mg
Week 2	20 mg
Week 3	No injection
Week 4	20 mg
Every month afterwards	20 mg

How long to use Kesimpta
Continue using Kesimpta every month for as long as your doctor tells you to.

Your doctor will regularly check your condition to determine whether the treatment is having the desired effect.

If you have questions about how long to use Kesimpta, talk to your doctor, pharmacist or nurse.

If you use more Kesimpta than you should
If you have injected too much Kesimpta, contact your doctor right away.

If you forget to use Kesimpta
To get the full benefit of Kesimpta, it is important that you have every injection on time.

If you have forgotten an injection of Kesimpta, inject yourself as soon as possible. Do not wait until the next scheduled dose. The timing of future injections should then be calculated from the day you injected this dose and not based on the original schedule (see also “How much Kesimpta to use and how often to use it” above).

If you stop using Kesimpta
Do not stop using Kesimpta or change your dose without talking with your doctor.

Some side effects can be related to a low level of B cells in your blood. After you stop treatment with Kesimpta your blood level of B cells will gradually increase to normal. 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 doctor or pharmacist.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

The side effects of Kesimpta are listed below. If any of these side effects becomes severe, tell your doctor, pharmacist or nurse.

Very common (may affect more than 1 in 10 people)
- upper respiratory tract infections, with symptoms such as sore throat and runny nose
- injection-related reactions, such as fever, headache, muscle pain, chills and tiredness - these usually occur in the 24 hours after an injection of Kesimpta, in particular after the first injection
- urinary tract infections
- injection-site reactions, such as redness, pain, itching and swelling at the injection site

Common (may affect up to 1 in 10 people)
- decrease in the blood level of a protein called immunoglobulin M, which helps protect against infection
- oral herpes
- nausea, vomiting (have been reported in association with injection-related reactions)

Not known (frequency cannot be estimated from the available data)
- allergic reactions, with symptoms such as rash, hives, trouble breathing, swelling of the face, eyelids, lips, mouth, tongue or throat, chest tightness, or feeling faint

Reporting of side effects
If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Kesimpta

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the carton and label after EXP. The expiry date refers to the last day of that month.

Keep the pre-filled pen(s) in the outer carton in order to protect from light. Store in a refrigerator (2°C – 8°C). 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.

Do not use this medicine if you notice that the solution contains visible particules or is cloudy.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Kesimpta contains
- The active substance is ofatumumab. Each pre-filled pen contains 20 mg ofatumumab.
- The other ingredients are L-arginine, sodium acetate trihydrate, sodium chloride, polysorbate 80 (E 433), disodium edetate dihydrate, hydrochloric acid (for pH adjustment) and water for injections.

What Kesimpta looks like and contents of the pack
Kesimpta solution for injection is clear to slightly opalescent, and colourless to slightly brownish-yellow.

Kesimpta is available in unit packs containing 1 pre-filled Sensoready Pen and in multipacks comprising 3 cartons, each containing 1 pre-filled Sensoready Pen.

Not all pack sizes may be marketed.

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Other sources of information

Detailed information on this medicine is available on the European Medicines Agency web site: https://www.ema.europa.eu.

Instructions for use of Kesimpta Sensoready Pen

It is important that you understand and follow these instructions for use before injecting Kesimpta. Talk to your doctor, pharmacist or nurse if you have any questions before you use Kesimpta for the first time.

Remember:

- **Do not use** the pen if either the seal on the outer carton or the seal on the pen is broken. Keep the pen in the sealed outer carton until you are ready to use it.
- **Do not shake** the pen.
- If you drop your pen, **do not use** it if the pen looks damaged, or if you dropped it with the cap removed.
- Dispose of the used pen immediately after use. **Do not re-use a pen**. See "How should I dispose of the used Kesimpta Sensoready Pen?" at the end of these Instructions for Use.

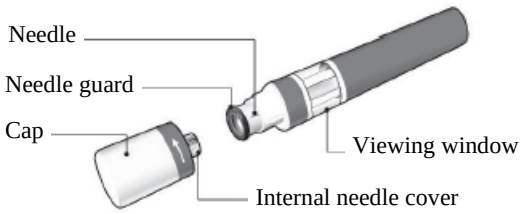
How should I store Kesimpta?

- Store the pen carton in a refrigerator between 2°C and 8°C.
- Keep the pen in the original carton until ready to use to protect from light.
- **Do not freeze** the pen.

Keep Kesimpta out of the sight and reach of children.

Kesimpta Sensoready Pen parts (see Picture A):

Picture A

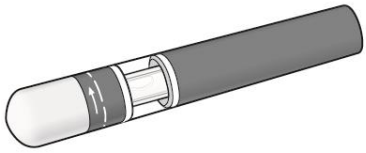


The Kesimpta Sensoready Pen is shown with the cap removed. **Do not** remove the cap until you are ready to inject.

What you need for your injection:
Included in the carton:

- A new Kesimpta Sensoready Pen (**see Picture B**)

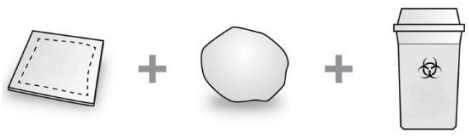
Picture B



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

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

Picture C



See "How should I dispose of the used Kesimpta Sensoready Pen?" at the end of these Instructions for Use.

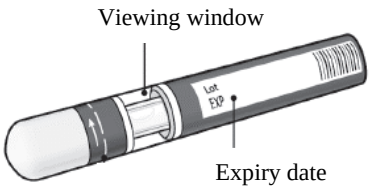
Before your injection:
Take the pen out of the refrigerator **15 to 30 minutes before injecting** to allow it to reach room temperature.

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

- Look through the viewing window. The liquid should be clear to slightly opalescent.
  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 **expiry date (EXP)** on your pen.
  Do not use your pen if the expiry date has passed.

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

Picture D

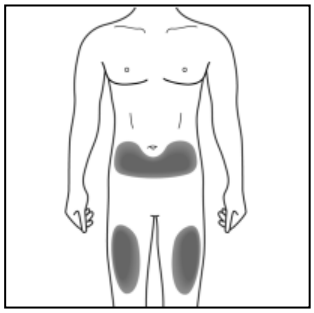


Step 2. Choose your injection site:

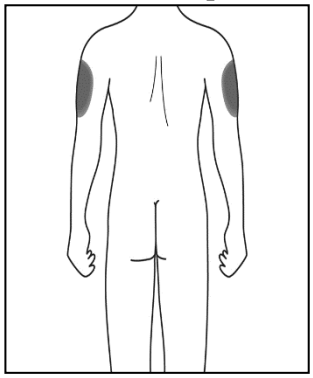
- The recommended site is the front of the thighs. You may also use the lower stomach area (lower abdomen), but **not** the area 5 cm around your navel (belly button) (**see Picture E**).
- Choose a different site each time you inject Kesimpta.
- **Do not inject** into areas where the skin is tender, bruised, red, scaly or hard. Avoid areas with scars or stretch marks or infection sites.

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

Picture E



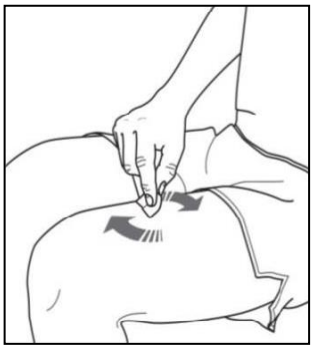
Picture F
(caregiver and healthcare professional only)



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 Picture G**).
- Do not touch the cleaned area again before injecting.

Picture G



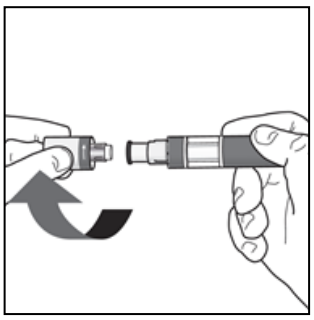
Your injection

Step 4. Remove the cap:

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

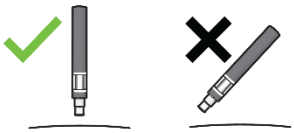
You may see a few drops of medicine come out of the needle. This is normal.

Picture H

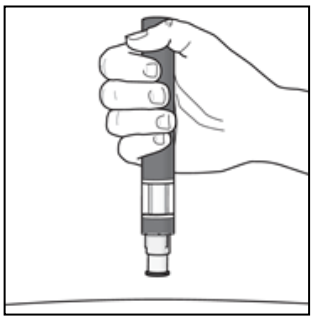


Step 5. Hold your pen:

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



Picture I



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

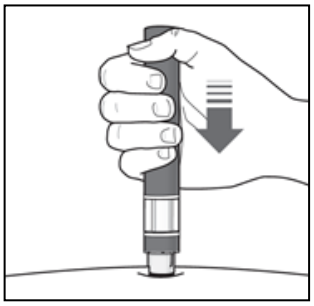
- The **first click** indicates that **the injection has started**.
- The **second click** indicates that **the injection is almost complete**.

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

Step 6. Start your injection:

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

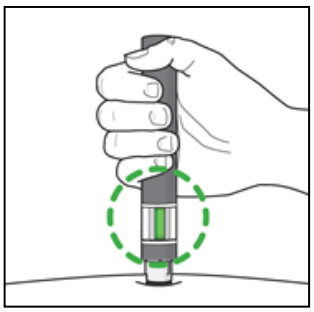
Picture J



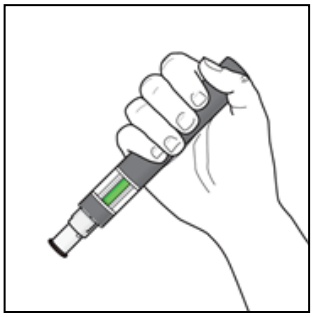
Step 7. Complete your injection:

- Listen for the **second click**. This indicates that the injection is **almost** complete.
- Check if the **green indicator** fills the window and has stopped moving (**see Picture K**).
- You can now remove the pen (**see Picture L**).

Picture K



Picture L



After your injection:

- If the green indicator does not fill the window, this means you have not received the full dose. Contact your doctor or pharmacist 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 plaster, if the bleeding continues.

How should I dispose of the used Kesimpta Sensoready Pen?

Step 8. Dispose of your Kesimpta Sensoready Pen:

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

Keep the sharps container out of the reach of children.

Picture M