Unit: Technical Assessment Unit

Public assessment report for biological products

Ocrevus 920 mg

Administrative information:

Trade name of the medicinal product:	Ocrevus 920 mg
INN (or common name) of the active substance(s):	Ocrelizumab 920 mg/23ml
Manufacturer of the finished product	Roche Diagnostics GmbH, Sand Hofer Strasse 116, 68305 Mannheim, - Germany
Marketing Authorization holder	Roche Registration GmbH, Emil-Barell-Strasse 1, 79639 Grenzach-Wyhlen - Germany
Applied Indication(s):	1-Adults with relapsing forms of multiple sclerosis (RMS), with active disease defined by clinical or imaging features. 2-Adults with early primary progressive multiple sclerosis (PPMS) in terms of disease duration and level of disability, and with imaging features characteristic of inflammatory activity.
Pharmaceutical form(s) and strength(s):	Solution for injection 920 mg/23ml
Route of administration	S.C
Approved pack	Carton box containing Type I borosilicate, colorless glass vial closed with gray butyl rubber stopper laminated with fluororesin film (contact polymer) sealed with aluminum seal fitted with orange plastic flip-off cap and inner leaflet
Registration track	Reliance level 1
Type of registration (EMA/FDA – Local)	EMA approved

List of abbreviations

RMS	relapsing forms of multiple sclerosis
DP	Drug Product
DS	Drug substance
PPMS	primary progressive multiple sclerosis
GMP	Good manufacturing practice
IV	intravenus
SC	Subcutaneous
rHuPH20	Recombinant human hyaluronidase PH20

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Dossier initial submission and evaluation process:

- The product was submitted for registration via reliance level I.
- The dossier evaluation by the registration administration units was started on 6.3.2025 after providing all the required documents (**Unredacted assessment report** along with Full CTD for the product)

1. General introduction about the product including brief description of the AI, its mode of action and indications

Ocrelizumab is a recombinant humanized, glycosylated, monoclonal IgG1 antibody that selectively targets and depletes CD20-expressing B cells, while preserving the capacity of B cell reconstitution and preexisting humoral immunity. Ocrevus IV was first approved then the applicant has developed a subcutaneous (SC)

formulation. The ocrelizumab active ingredient is the same for the ocrelizumab SC and commercial ocrelizumab IV formulations

The SC formulation is a combination of ocrelizumab with rHuPH20 (human recombinant hyaluronidase) to improve dispersion of large SC injection volumes (i.e., it functions as a permeation enhancer).

Each 50 mL single-dose vial contains 920 mg/23 mL (nominal) of ocrelizumab and 1000 U/mL rHuPH20 at target pH 5.3. rHuPH20 is the permeation enhancer to increase the dispersion and absorption of large drug volumes administered via the SC route.

2. **Quality aspects:**

- **Manufacturer**
- **Drug Substance**

Manufacture of drug substance in Genentech Inc. 1000 New Horizons Way, Vasaville, CA, 95688 –United States of America

- **Drug Product:**

Manufacturer of the Drug Product

Roche Diagnostics GmbH, Sandhofer Strasse 116, 68305 Mannheim, -GERMANY

Batch releaser site is

F.Hoffman-La Roche AG, Wurmisweg, 4303 Kaiseraugst, - Switzerland

- **Stability**

Drug substance:

- Required Shelf Life: 3 years

-Suggested Storage Conditions: Store at ≤ -20 °C

Drug Product:

Required Shelf Life: 2 years

Suggested Storage Conditions: Store in a refrigerator (2 °C – 8 °C).

Do not freeze.

Do not shake.

Keep the vials in the outer carton in order to protect from light.

3.Non –Clinical aspect & Clinical aspect:

- Overall, there were no macroscopic dermal observations or systemic effects attributed to ocrelizumab SC administration. SC administration was locally and systemically well tolerated in rats and minipigs. The results are in line with the toxicity profile for ocrelizumab IV.

-The local tolerance studies in monkeys, rats and minipigs demonstrated that while ocrelizumab is not tolerated at high dose levels without the co-administration of rHuPH20, lower levels are well tolerated when co-administered with rHuPH20. Overall, dose levels of up to 40 mg/mL, the proposed clinical SC, were well tolerated in non-clinical species, when co-administered with rHuPH20.

- Therefore, the NOAEL levels were considered 40 mg/mL in both rats and minipigs. By converting the NOAEL values to body weight normalized doses, the Applicant demonstrated sufficient safety margins (5.22 and 1.57 for the rat and minipig respectively), relative to the projected nominal SC human dose of 960 mg, supporting that the treatment should be locally well tolerated.

-Overall conclusion The available nonclinical safety data for ocrelizumab SC demonstrates that changing from IV to SC administration does not alter the overall safety profile of the drug.

-In conclusion the overall benefit/risk of Ocrevus 920 mg solution for injection, SC is favorable in the treatment of:
adult patients with relapsing forms of multiple sclerosis (RMS) with active disease defined by clinical or imaging features,
adult patients with early primary progressive multiple sclerosis (PPMS) in terms of disease duration and level of disability, and with imaging features characteristic of inflammatory activity.

4.General Conclusion and Recommendations if any:
Based on the review of CTD modules and other supplementary documents, the product is approved.
For more information, please visit EMA published assessment report link:

https://www.ema.europa.eu/en/documents/product-information/ocrevus-epar-product-information_en.pdf