Direct healthcare professional communication (DHPC)

Remsima (infliximab): New IV formulation (100 mg and 350 mg concentrate for solution for infusion) contains sorbitol and is therefore contraindicated in patients with hereditary fructose intolerance

Dear Healthcare Professional,

The marketing authorisation holder, Celltrion Healthcare Hungary Kft. ("Celltrion"), in agreement with the European Medicines Agency (EMA) and the <*National Competent Authority*>, would like to inform you of the following:

Summary

Risk of serious metabolic harm in patients with hereditary fructose intolerance (HFI) due to sorbitol content of new IV Remsima formulation.

- **Remsima 100 mg and 350 mg concentrate for solution for infusion is a new intravenous (IV) formulation of infliximab; it contains 45mg of sorbitol per 1 mL.**
- **Intravenously administered medicines containing sorbitol are contraindicated in patients with HFI.**
- **In patients with HFI, even small amounts of intravenously administered sorbitol can result in severe adverse reactions, including hypoglycaemia, acute hepatic failure, haemorrhagic syndrome, renal failure, and death.**
- **The approved Remsima subcutaneous (SC) formulation also contains sorbitol, but is considered safe for patients with HFI due to the SC administration route.**
- **The previously available IV formulation of Remsima 100 mg powder for concentrate for solution for infusion does not contain sorbitol.**

Interchangeability of Remsima 100 mg and 350 mg concentrate for solution for infusion

< Optional national information on interchangeability of Remsima 100 mg and 350 mg concentrate for solution for infusion, (e.g., Remsima 100 mg and 350 mg concentrate for solution for infusion is not freely interchangeable with other intravenous formulations of infliximab in patients with HFI)>

Background

Remsima (infliximab) is a biosimilar which has been authorised in the European Union (EU) since 10 September 2013 for the treatment of the following conditions:

In adults:

- rheumatoid arthritis
- ankylosing spondylitis
- psoriatic arthritis
- psoriasis
- Crohn's disease
- ulcerative colitis.

In pediatric patients (≥6 years):

- severe, active Crohn's disease
- severely active ulcerative colitis.

A new IV liquid formulation of Remsima has been authorised, which contains sorbitol as an excipient: Remsima 100 mg and 350 mg concentrate for solution for infusion. Intravenous medicines containing sorbitol are contraindicated in patients with HFI. Remsima 100 mg powder for concentrate for solution for infusion, which does not include sorbitol, will continue to be available for prescription for patients who might require it.

HFI is a rare hereditary autosomal recessive deficit in the main enzyme responsible for hepatic metabolism of fructose. The condition is normally diagnosed in infancy. Administration of sorbitol to patients with HFI may lead to intracellular accumulation of fructose 1-phosphate, which is highly toxic.

The product information and patient reminder card for Remsima have been updated to include the information that Remsima 100 mg and 350 mg concentrate for solution for infusion contains sorbitol and must not be given to patients with HFI.

Health care professionals must:
- confirm that the patient does not have HFI before administration of Remsima 100 mg or 350 mg concentrate for solution for infusion;
- be aware that Remsima 100 mg and 350 mg concentrate for solution for infusion is not freely interchangeable with other intravenous formulations of infliximab in patients with HFI;
- make sure that patients receive the updated patient card; and
- make HFI patients aware of the contraindication of the new formulation.

Call for reporting
Healthcare professionals are asked to report any suspected adverse drug reactions in patients treated with Remsima (infliximab) 100mg and 350mg concentrate for solution for infusion, in accordance with the national spontaneous reporting system and include batch/lot number if available.
<include the details (e.g. name, postal address, fax number, website address) on how to access the national spontaneous reporting system>.

Company contact point
<Contact point details for access to further information, including relevant website address(es), telephone numbers and a postal address>.

DHPC Communication Plan	
Medicinal product(s)/active substance(s)	Remsima 100mg and 350mg concentrate for solution for infusion (Infliximab)
Marketing authorisation holder	Celltrion Healthcare Hungary Kft.
Safety concern and purpose of the communication	Contraindication in patients with hereditary fructose intolerance (HFI) for Remsima 100mg and 350mg concentrate for solution for infusion (IV liquid formulation) only
DHPC recipients	Specialists in rheumatology, gastroenterology, dermatology, paediatricians, and Pharmacies/hospital pharmacists. Target groups will be further defined at national level, in agreement with the respective national competent authority.
Member States where the DHPC will be distributed	All EU/EEA Member states where the medicinal product is marketed.

Timetable	Date
DHPC and communication plan (in English) agreed by PRAC	04 Sep 2025
DHPC and communication plan (in English) agreed by CHMP	18 Sep 2025
Submission of translated DHPCs to the national competent authorities for review	18 Oct 2025
Agreement of translations by national competent authorities	18 Nov 2025
Dissemination of DHPC	Subject to each member state's launch date of the new formulation