Annex

Conditions or restrictions with regard to the safe and effective use of the medicinal product to be implemented by the Member States

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The Member States should ensure that all conditions or restrictions with regard to the safe and effective use of the medicinal product described below are implemented:

The Marketing Authorisation Holder (MAH) shall ensure that, at launch, a letter is sent to all expected and actual prescribers of NovoThirteen with an Educational Pack containing the following:

1. Physician brochure
2. Patient brochure

Both documents are to be used as part of an educational plan aiming to minimise risks of medication errors, risk of thromboembolic events due to increased levels of non-proteolytically activated rFXIII in connection with incorrect storage, and risk of off-label use for treatment of breakthrough bleeding. The MAH should ensure harmonisation between terminology used in the brochures and the product information.

The physician brochure should contain the following key elements and item:
- indication of the product
- the risks of off-label use within FXIII congenital deficiency
- appropriate diagnostic procedures to confirm FXIII A-subunit deficiency
- warning of the difference of both posology and concentration between NovoThirteen and other FXIII containing products (The recommended dose of NovoThirteen is 35 IU/kg body weight (bw) once monthly, administered as an intravenous bolus injection. The dose volume in millilitres should be calculated based on body weight for each patient using the following formula: Dose volume in ml = 0.042 x subject bw (kg).)
- correct handling and the risks associated with mishandling
- embolic and thrombotic events including the increased risk of vessel occlusion in patients at risk of thrombosis
- what to do in the event of incorrect storage, thrombosis or embolism
- contraindication of hypersensitivity
- warning and precautions regarding anaphylaxis
- the importance of collecting safety data and how to enrol patients in the PASS and other registries
- distribution and use of the patient brochure and the need to ensure that the patient has read and understood the brochure
- Summary of Product Characteristics

The patient brochure, to be distributed to patients by the prescribers, should contain the following key elements and item:
- indication of the product
- the risks of off-label use within FXIII congenital deficiency
- how to safely store, handle, reconstitute and administer the product
- the risks associated with incorrect storage and mishandling
- how to recognise the potential side effects (thrombosis and embolism)
- what to do in the event of incorrect storage, thrombosis or embolism
- Package Leaflet

The Marketing Authorisation Holder must implement this educational plan nationally, prior to marketing. The final content, format and distribution modalities of both documents should be agreed with the national competent authority in each Member State.