FOR USE IN MALTA

Hemlibra (emicizumab):
Laboratory Professional Guide

This is additional risk minimisation material and is provided by Roche Products (Ireland) Limited as a condition of the Hemlibra marketing authorisation.

This material should be read in conjunction with the Summary of Product Characteristics (SmPC) which is available on www.ema.europa.eu

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What is Hemlibra?

Medicinal Product

- Emicizumab is a humanised monoclonal modified immunoglobulin G4 (IgG4) antibody with a bispecific antibody structure produced by recombinant DNA technology in Chinese hamster ovary (CHO) cells.
- Pharmacotherapeutic group: Antihemorrhagics, ATC code: B02BX06.

Mode of Action

- Emicizumab bridges activated factor IX and factor X to restore the function of missing activated factor VIII that is needed for effective haemostasis.
- Emicizumab has no structural relationship or sequence homology to factor VIII and, as such, does not induce or enhance the development of direct inhibitors to factor VIII.

Pharmacodynamics

- Prophylactic therapy with Hemlibra shortens the aPTT and increases the reported factor VIII activity (using a chromogenic assay with human coagulation factors). These two pharmacodynamic markers do not reflect the true haemostatic effect of emicizumab in vivo (aPTT is overly shortened and reported factor VIII activity may be overestimated) but provide a relative indication of the pro-coagulant effect of emicizumab.

Indication

- Hemlibra is indicated for routine prophylaxis of bleeding episodes in patients with haemophilia A (congenital factor VIII deficiency):
  - With factor VIII inhibitors.
  - Without factor VIII inhibitors who have:
    - Severe disease (FVIII < 1%)
    - Moderate disease (FVIII ≥ 1% and ≤ 5%) with severe bleeding phenotype.
- Hemlibra can be used in all age groups.

Laboratory coagulation test interference

- Hemlibra affects assays for activated partial thromboplastin time (aPTT) and all assays based on aPTT, such as one stage factor VIII activity (see Table 1 below).
- Therefore, aPTT and one-stage FVIII assay test results in patients who have been treated with Hemlibra prophylaxis should not be used to assess Hemlibra activity, determine dosing for factor replacement or anti coagulation, or measure factor VIII inhibitor titers (see below). Misinterpretation of their results may lead to under-treatment of patients experiencing bleeding episodes, which can potentially result in severe or life-threatening bleeds.
- However, single-factor assays utilising chromogenic or immuno-based methods are not affected by emicizumab and may be used to monitor coagulation parameters during treatment, with specific considerations for FVIII chromogenic activity assays.
- Chromogenic factor VIII activity assays containing bovine coagulation factors are insensitive to emicizumab (no activity measured) and can be used to monitor endogenous or infused factor VIII activity, or to measure anti-FVIII inhibitors. A chromogenic Bethesda assay utilising a bovine-based factor VIII chromogenic test that is insensitive to emicizumab may be used.
- Laboratory tests unaffected by Hemlibra are shown in Table 1 below.

Table 1 Coagulation Test Results Affected and Unaffected by Hemlibra

Results Affected by Hemlibra	Results Unaffected by Hemlibra
– Activated partial thromboplastin time (aPTT) – Activated clotting time (ACT) – One-stage, aPTT-based, single-factor assays – aPTT-based Activated Protein C Resistance (APC-R) – Bethesda assays (clotting-based) for FVIII inhibitor titers	– Thrombin time (TT) – One-stage, prothrombin time (PT)-based, single-factor assays – Chromogenic-based single-factor assays other than FVIII[1] – Immuno-based assays (e.g. ELISA, turbidometric methods) – Bethesda assays (bovine chromogenic) for FVIII inhibitor titers – Genetic tests of coagulation factors (e.g. Factor V Leiden, Prothrombin 20210)

[1]For important considerations regarding FVIII chromogenic activity assays, see section 4.4 of the Summary of Product Characteristics (SmPC).

- Due to the long half-life of Hemlibra, these effects on coagulation assays may persist for up to 6 months after the last dose (see section 5.2 of the SmPC).
- The laboratory director should contact the patient's treating physician to discuss any abnormal test results.

Reporting of suspected adverse events or reactions

Reporting suspected adverse events or 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 (see details below).

Where possible, healthcare professionals should report adverse events or reactions by brand name and batch number.

In the event of a suspected adverse event, please report it to:
Post: The Drug Surveillance Centre, Roche Products (Ireland) Limited, 3004 Lake Drive, Citywest, Naas Road, Dublin 24, Ireland.
Telephone: 00 353 (1) 469 0700;
Email: ireland.drug_surveillance_centre@roche.com

Alternatively, suspected adverse reactions (side effects) or medication errors may be reported using the Medicines Authority ADR reporting form, which is available online at: http://www.medicinesauthority.gov.mt/adrportal, and sent by post or email to:
Post: Pharmacovigilance Section at Post-Licensing Directorate, Medicines Authority, Sir Temi Żammit Buildings, Malta Life Sciences Park, San Ġwann SĠN 3000, Malta
Email: postlicensing.medicinesauthority@gov.mt

Further Information

For electronic copies of this risk minimisation material, refer to the Malta Medicines Authority website [http://www.medicinesauthority.gov.mt/rmm] and download the required material.
Alternatively if you would like hard copies, please contact Roche Products (Ireland) Limited, 3004 Lake Drive, Citywest, Naas Road, Dublin 24 by mail, telephone [00 353 (1) 469 0700], or email [ireland.drug_surveillance_centre@roche.com].

For further information about this medicine, please contact Medical Information at Roche Products (Ireland) Limited by telephone [00 353 (1) 469 0700], or email [Ireland.druginfo@roche.com].

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