LABORATORY PROFESSIONAL GUIDE

Hemlibra (emicizumab)

Laboratory Professional Guide to ensure safe use of HEMLIBRA for treatment of Hemophilia A

- Risk minimization materials for HEMLIBRA (emicizumab) are assessed by the Saudi Food and Drug Authority
- These materials describe recommendations to minimize or prevent important risks of the drug.
- See the HEMLIBRA SPC for more information on possible side effects of HEMLIBRA

*This educational material is mandatory as a condition of the marketing authorisation of subcutaneous HEMLIBRA in the treatment of patients with hemophilia A in order to further minimise important selected risks.

Please read this information carefully before prescribing the product.

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.

Therapeutic indication

- HEMLIBRA is indicated for routine prophylaxis to prevent or reduce the frequency of bleeding episodes in adult and pediatric patients ages newborn and older with hemophilia A (congenital factor VIII deficiency) with or without factor VIII inhibitors.

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)

- However, single-factor assays utilizing 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 tests may be manufactured with either human or bovine coagulation proteins.
  - Assays containing human coagulation factors are responsive to emicizumab but may overestimate the clinical hemostatic potential of emicizumab.
  - 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.
- Laboratory tests unaffected by HEMLIBRA are shown in Table 1 below.
- 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 3.2 of the SPC).

Table1 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, 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 the SPC

- The laboratory director should contact the Healthcare Provider to discuss any abnormal test results.

Call for reporting

- For full information on all possible adverse events please see the SPC
- Healthcare professionals are asked to report any suspected adverse reactions via the National reporting system that is provided below.
- Adverse reactions should also be reported to Roche Medical Information via the Company contact point that is provided below.
- Healthcare Professionals are also encouraged to inform the laboratory director which laboratory tests are affected or unaffected by emicizumab. The Healthcare Professional should be contacted by the laboratory director to discuss any abnormal test results.
- In case of any adverse events – including any possible side effects not listed in the leaflet – or product complaints associated with the use of HEMLIBRA, please talk to the HCP or report the details in accordance with the national requirements via the national spontaneous reporting systems to:

The National Pharmacovigilance Centre
Land Line: 19999.
Fax: +966112057662
Email: npc.drug@sfda.gov.sa

Roche Products Saudi Arabia L.L.C.
Direct Tel. +966 12211 4618
Mobile: +966 5678 44 692
Email: jeddah.drug_safety@roche.com

Company contact point

Should you have any questions regarding the use of HEMLIBRA, please feel free to contact us at jeddah.medinfo@roche.com

Roche Products Saudi Arabia

This document has been reviewed and approved by The Saudi Food and Drug Authority (SFDA)