HEMLIBRA® (EMICIZUMAB)
Solution for subcutaneous injection

Patient Card

Patient Card* for patients to ensure safe use of HEMLIBRA® for treatment of Hemophilia A

- These materials describe recommendations to minimize or prevent important risks of the drug.
- See the HEMLIBRA® Patient information leaflet for more information on possible side effects of HEMLIBRA®

Patients/carers should carry this Card at all times including emergencies. Please present the card at visits to doctors, hospital clinics, laboratory professionals or pharmacists to provide information on HEMLIBRA® treatment and risks.

SELECT IMPORTANT SAFETY INFORMATION

- In case of an emergency,
  - Contact an appropriate medical professional for immediate medical care
  - Should any questions related to your haemophilia A or current treatment arise, please have them contact your doctor
- Tell your doctor if you are using HEMLIBRA® before you have laboratory tests that measure how well your blood is clotting. This is because the presence of HEMLIBRA® in the blood may interfere with some of these laboratory tests, leading to inaccurate results.
- Serious and potentially life-threatening side effects have been observed when a “bypassing agent” called aPCC (FEIBA®) was used in patients who were also receiving HEMLIBRA®. These included,
  - **Thrombotic microangiopathy (TMA) -** this is a serious and potentially life-threatening condition where there is damage to the lining of blood vessels and formation of blood clots in small blood vessels. This can lead to damage in the kidneys and/or other organs.
  - **Thromboembolism** - Blood clots may form and in rare cases these blood clots may cause a life-threatening blockage of blood vessels.

*This educational material is mandatory as a condition of the marketing authorisation of subcutaneous HEMLIBRA® indicated for routine prophylaxis to prevent bleeding episodes in adults and children with haemophilia A (congenital factor VIII deficiency) with or without factor VIII inhibitors in order to further minimise important selected risks

Please read this information carefully before administering the product

In case of an emergency:

- **Contact** an appropriate medical professional for immediate medical care.
- Should any questions related to your hemophilia A or current treatment arise, please have them contact your doctor:
  Name of your Doctor:_____
- **Address:**_____
  Tel/Fax:_____
  Email:_____
  [*Your Hematologist's contact information*]

NOTICE TO HEALTHCARE PROFESSIONALS READING THIS PATIENT CARD

Please be aware of:

Thrombotic microangiopathy associated with HEMLIBRA® and aPCC

- Cases of thrombotic microangiopathy (TMA) were reported from a clinical trial in patients receiving HEMLIBRA® prophylaxis when on average a cumulative amount of >100U/kg/24 hours of activated prothrombin complex concentrate (aPCC) for 24 hours or more was administered
- Patients receiving HEMLIBRA®prophylaxis should be monitored for the development of TMA when administering aPCC

Thromboembolism associated with HEMLIBRA® and aPCC

- Thrombotic events (TE) were reported from a clinical trial in patients receiving HEMLIBRA® prophylaxis when on average a cumulative amount of >100U/kg/24 hours of activated prothrombin complex concentrate (aPCC) for 24 hours or more was administered
- Patients receiving HEMLIBRA® prophylaxis should be monitored for the development of thromboembolism when administering aPCC

Use of bypassing agents in patients receiving HEMLIBRA®

- Treatment with prophylactic bypassing agents should be discontinued the day before starting HEMLIBRA® therapy.
- Physicians should discuss with all patients and/or caregivers the exact dose and schedule of bypassing agents to use, if required while receiving HEMLIBRA® prophylaxis.
- HEMLIBRA® increases patients' coagulation potential. The bypassing agent dose required may therefore be lower than that used without HEMLIBRA®prophylaxis. The dose and duration of treatment with bypassing agents will depend on the location and extent of bleeding, and the patient's clinical condition.
- For all coagulation agents (aPCC, rFVIIa, FVIII, etc.), consideration should be given to verifying bleeds prior to repeated dosing.
- Use of aPCC should be avoided unless no other treatment options/alternatives are available.
  - If aPCC is the only option to treat bleeding for a patient receiving HEMLIBRA® prophylaxis, the initial dose should not exceed 50 U/kg and laboratory monitoring is recommended (including but not restricted to renal monitoring, platelet testing, and evaluation of thrombosis).
  - If bleeding is not controlled with the initial dose of aPCC up to 50 U/kg, additional aPCC doses should be administered under medical guidance or supervision, and the total aPCC dose should not exceed 100 U/kg in the first 24-hours of treatment.
  - Treating physicians must carefully weigh the risk of TMA and TE against the risk of bleeding when considering aPCC treatment beyond 100 U/kg in the first 24-hours.

- The safety and efficacy of emicizumab has not been formally evaluated in the surgical setting. If you require bypassing agents in the perioperative setting, it is recommended that the dosing guidance above for aPCC be followed by your doctor.

- In clinical trials, no cases of TMA or TE were observed with use of activated recombinant human FVII (rFVIIa) alone in patients receiving HEMLIBRA® prophylaxis.; however, the lowest dose expected to achieve hemostasis should be prescribed. Due to the long half-life of HEMLIBRA®[1], bypassing agent dosing guidance should be followed for at least 6 months following discontinuation of HEMLIBRA® prophylaxis.
- Please refer to section 4.4 of the HEMLIBRA® package insert for additional information and comprehensive instructions.

- **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
  - Therefore, aPTT-based coagulation laboratory test results in patients who have been treated with HEMLIBRA® prophylaxis should not be used to monitor HEMLIBRA® activity, determine dosing for factor replacement or anti-coagulation, or measure factor VIII inhibitors titers.
  - 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 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 utilizing a bovine-based factor VIII chromogenic test that is insensitive to emicizumab may be used.
  - Laboratory tests affected and 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, PT-based, single-factor assays - Chromogenic-based single-factor assays other than FVIII[1] - Immuno-based assays (e.g. ELISA, turbidimetric methods) - Bethesda assays (bovine chromogenic) for FVIII inhibitor titers - Genetic tests of coagulation factors (e.g. Factor V Leiden, Prothrombin 20210)

[1]Please refer to the HEMLIBRA® Package Insert section 4.5.

Contact the patient's Hematologist listed above for assistance in interpreting laboratory test results or for guidance on the use of bypassing agents in patients receiving HEMLIBRA® prophylaxis.

WHAT ADDITIONAL IMPORTANT INFORMATION SHOULD I KNOW?

Call for reporting

- Tell your doctor, nurse or pharmacist about any side effect you experience, bothers you or that does not go away. This includes any possible side effects not listed in the HEMLIBRA® patient information leaflet.The side effects listed in this brochure are not all of the possible side effects that you could experience with HEMLIBRA®.
- Talk to your doctor, nurse or pharmacist if you have any questions, problems or for more information.
- You can also report side effects directly via email or phone.
- By reporting side effects, you can help provide more information on the safety of this medicine.
- For information on possible adverse events, please see the patient information leaflet.
- For more information about **HEMLIBRA®** you can contact Roche Medical Information: e-mail: illovo.medinfo@roche.com Tel: +27 800 21 21 25
- **TO REPORT AN ADVERSE EVENT**: email: global.irt_sahubtcs@roche.com or Tel: +27 11 504 47 46

FURTHER INFORMATION

For more information about **HEMLIBRA®** you can contact Roche Medical Information:

Roche Medical Information
e-mail: illovo.medinfo@roche.com
Tel: +27 800 21 21 25

TO REPORT AN ADVERSE EVENT:

Roche Drug Safety
e-mail:
global.irt_sahubtcs@roche.com
Tel: +27 11 504 47 46

Reporting methods e.g., "Any suspected adverse reactions associated with the use of the HEMLIBRA® can be reported to MCAZ through the Adverse Drug Reaction (ADR) reporting form which can be obtained from the MCAZ offices at 106 Baines Avenue, Harare OR can be downloaded from the MCAZ website: www.mcaz.co.zw OR you can report using the ADR reporting platform found on the MCAZ website on the following link: https://primaryreporting.who-umc.org/ZW

HEMLIBRA® STANDARD BSS

S4 Hemlibra® 30 mg/1 mL, 60 mg/0,4 mL, 105 mg/0,7 mL, 150 mg/1 mL
Abbreviated product information: solution for injection. South Africa: 53/30.1/0071/2/3/4; Namibia: NS2 19/30/0033/4/5/6; Zimbabwe PP 2019/10.7/5815/4/3/2; Botswana S2 BOT2103738/7/6/0.
For full prescribing information, refer to the professional information approved by the Medicines Regulatory Authority.

COMPOSITION: Emicizumab, 30 mg/1 mL, 60 mg/0,4 mL, 105 mg/0,7 mL, 150 mg/1 mL per vial.

INDICATIONS: Hemlibra is indicated for routine prophylaxis to prevent bleeding or reduce the frequency of bleeding episodes in adults and children with haemophilia A (congenital factor VIII deficiency) with or without factor VIII inhibitors.
There are limited data in infants less than 1 year of age.

DOSAGE: The recommended loading dose is 3 mg/kg administered as a subcutaneous injection once weekly for the first 4 weeks, followed by a maintenance dose of either:
- 1,5 mg/kg once weekly, or
- 3 mg/kg every two weeks, or
- 6 mg/kg every four weeks

CONTRAINDICATIONS: Hypersensitivity to emicizumab or to any of the excipients.

WARNINGS AND PRECAUTIONS: ***Thrombotic microangiopathy (TMA) associated with Hemlibra and activated prothrombin complex concentrate (aPCC):*** Cases of TMA were reported when on average a cumulative amount of >100 U/kg/24 hours of activated prothrombin complex concentrate (aPCC) for 24 hours or more were administered. Monitor for the development of TMA when administering aPCC and immediately discontinue aPCC and interrupt Hemlibra therapy if clinical symptoms and/or laboratory findings consistent with TMA occur, and manage as clinically indicated. Consider the risks of resuming Hemlibra prophylaxis following complete resolution of TMA on a case-by-case basis. ***Thromboembolism associated with Hemlibra and activated prothrombin complex concentrate:*** Monitor for the development of thromboembolism when administering aPCC. Immediately discontinue aPCC and interrupt Hemlibra therapy if clinical symptoms, imaging, and/or laboratory findings consistent with thrombotic events occur, and manage as clinically indicated. Consider the risks of resuming Hemlibra prophylaxis following complete resolution of thrombotic events on a case-by-case basis. ***Guidance on the use of bypassing agents in patients receiving Hemlibra prophylaxis:*** Treatment with bypassing agents should be discontinued 24 hours before starting Hemlibra therapy. Discuss with all patients and/or caregivers the exact dose and schedule of bypassing agents to use. Avoid use of aPCC unless no other treatment options/alternatives are available. Weigh the risk of TMA and thromboembolism against the risk of bleeding when considering aPCC beyond 100 U/kg in first 24 hours. ***Immunogenicity:*** The presence of neutralising anti-hemlibra antibodies with decreasing Hemlibra concentration may be associated with loss of efficacy. In case of loss of efficacy, evaluate promptly to assess etiology and a possible change in treatment should be considered**.** ***Laboratory coagulation test interference:*** Hemlibra affects intrinsic pathway clotting-based laboratory tests, including the activated clotting time (ACT), activated partial thromboplastin time (aPTT) and all assays based on aPTT, such as one-stage factor VIII activity. Pregnant women are advised not to use Hemlibra. Women should not breastfeed while using Hemlibra. ***Traceability:*** Record batch number of the product and advise patients/caregivers to do the same to improve traceability.

SIDE EFFECTS: The most serious ADRs were TMA and thrombotic events, including cavernous sinus thrombosis and superficial vein thrombosis contemporaneous with skin necrosis. *General disorders and administration site conditions*: Injection site reactions, pyrexia. *Nervous system disorders*: Headache. *Gastrointestinal disorders*: Diarrhoea. *Musculoskeletal and connective tissue disorders*: Arthralgia, Myalgia. *Blood and Lymphatic system disorders*: Thrombotic microangiopathy. *Infections and Infestations*: Cavernous sinus thrombosis. *Skin and subcutaneous tissue disorders:* Skin necrosis. *Vascular Disorders*: Superficial thrombophlebitis.

PACK SIZE: 1 single-use 3 mL vial.

Full details are available from Roche Products (Pty) Ltd, P O Box 1469, Halfway House, 1685. Tel: 011 504 4746 or Toll-free on Roche Ethical Assistance Line (REAL): 0800 21 21 25. www.roche.co.za

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Based on approved date Professional Information: 20 Dec 2022

Last update to BSS: 20 Jan 2023 – Urgent safety update to CDS 7.0