PATIENT ALERT CARD

▼HEMLIBRA (emicizumab)

Subcutaneous injection

Patient Alert Card* for patients 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 package leaflet for more information on possible side effects of HEMLIBRA

▼*This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions. See final page for details on how to report.*

*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.

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

Please read this information carefully before administering the product.

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SELECT IMPORTANT SAFETY INFORMATION

- 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-threating blockage of blood vessels.

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:_____
  Tel/Fax:_____
  Email:_____
  [*Your Hematologist's contact information***]**

NOTICE TO HEALTH CARE PROFESSIONALS READING THIS ALERT 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 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 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, bypassing agent dosing guidance should be followed for at least 6 months following discontinuation of HEMLIBRA prophylaxis.
- Please refer to section 2.4 of the CDS 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, turbidometric methods) - Bethesda assays (bovine chromogenic) for FVIII inhibitor titers - Genetic tests of coagulation factors (e.g. Factor V Leiden, Prothrombin 20210)

Please refer to the CDS for additional information (section 2.4)

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

or

Refer to Patient Information Leaflet (PIL) for additional information and guidance

Loss of efficacy due to suspect anti-emicizumab antibodies

Loss of efficacy of emicizumab due to anti-emicizumab antibodies may manifest as an increase in breakthrough bleeding events. Patients and caregivers concerned about a loss of efficacy should seek prompt evaluation by their healthcare professional.

WHAT ADDITIONAL IMPORTANT INFORMATION SHOULD I KNOW?

Call for reporting

- **This medicinal product is subject to additional monitoring**. This will allow quick identification of new safety information.
- **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 package 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 in accordance with your country's national spontaneous reporting system directly that is provided below. By reporting side effects you can help provide more information on the safety of this medicine.
- Adverse reactions should also be reported to Roche Medical Information at Company contact point below.
- 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 (NPC)	**Roche Products Saudi Arabia L.L.C.**
Land Line: 19999.	**Direct Tel.** +966 12211 4618
Fax: +966112057662	**Mobile:** +966 5678 44 692
Email: npc.drug@sfda.gov.sa	**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)

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