PATIENT/CARER GUIDE

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 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 administering the product.

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-threating blockage of blood vessels.

WHAT YOU SHOULD KNOW ABOUT HEMLIBRA

What is HEMLIBRA?

HEMLIBRA, otherwise known as emicizumab, belongs to a group of medicines called "monoclonal antibodies".

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.

How has HEMLIBRA been studied in Hemophilia A?

HEMLIBRA has been studied in adults and children with Hemophilia A.

How is HEMLIBRA used in Hemophilia A?

HEMLIBRA is injected under the skin (subcutaneously) and is present in the blood at stable levels when used as prescribed. Your doctor or nurse will show you and/or your carer how to inject HEMLIBRA. Once you and/or your caregiver have been trained, you should be able to inject this medicine at home, by yourself or with the help of a caregiver.

This medicine is used to prevent bleeding or reduce the number of bleeding episodes in people with this condition. This medicine is not to be used to treat a bleeding episode.

If I am on HEMLIBRA, can I continue to use bypassing agents (such as NovoSeven or FEIBA) to prevent bleeding?

A patient on emicizumab can use “bypassing agents” (BPA) to treat break through bleeds based on the guidance on the use of BPA provided in the prescribing information.

Before you start using HEMLIBRA, it is very important you talk to your doctor about when and how to use “bypassing agents” while receiving HEMLIBRA, as this may differ from before. Serious and potentially life threatening side effects have been observed when aPCC (FEIBA) was used in patients who were also receiving HEMLIBRA.

What do I do if I develop a break-through bleed while on HEMLIBRA?

When You Think You May Be Having a Breakthrough Bleed, tell your doctor or pharmacist if you are using, have recently used or might use any other medicines.

Using a bypassing agent while receiving HEMLIBRA

- Before you start using HEMLIBRA, talk to your doctor and carefully follow their instructions regarding when to use a bypassing agent and the dose and schedule you should use.
- Treatment with prophylactic bypassing agents should be discontinued the day before starting HEMLIBRA therapy.
- Your doctor should discuss with you or your caregiver the exact dose and schedule of bypassing agents to use, if required while receiving HEMLIBRA.
- HEMLIBRA increases the ability of your blood to clot. The bypassing agent dose required may therefore be lower than that used before starting HEMLIBRA. The dose and duration of treatment with bypassing agents will depend on the location and extent of bleeding, and on your 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 with consideration made to laboratory monitoring and verification of bleeds prior to repeated dosing. The total aPCC dose should not exceed 100 U/kg in -24hours of treatment.
- Treating physicians must carefully weigh the risk of TMA and thromboembolism against the risk of bleeding when considering aPCC treatment beyond a maximum of 100 U/kg in -24hours.

- The safety and efficacy of HEMLIBRA 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.

What important information should I always tell healthcare providers to help them take care of me?

- Tell your doctor that you are receiving HEMLIBRA for the treatment of Haemophilia A.
- 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, and lead to unreliable results. Your doctor may refer to these laboratory tests as “coagulation tests” and “inhibitor assays.”
- 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 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 unaffected by HEMLIBRA are shown in Table 1 below.

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)

WHAT IS THE PATIENT ALERT CARD?

The Patient Card contains important safety information that you need to know before, during and after treatment with HEMLIBRA.

- Your doctor, pharmacist or nurse should give you a HEMLIBRA Patient Alert Card prior to starting HEMLIBRA.
- Keep the Patient Alert Card with you all the time - you can keep it in your wallet or purse.
- Show the Patient Card to anyone who is giving you medical care. This includes any doctor, pharmacist, lab personnel, nurse or dentist you see - not just the specialist who prescribes your HEMLIBRA.
- Tell your partner or caregiver about your treatment and show them the Patient Card because they may notice side effects that you are not aware of.
- Keep the Patient Card with you for 6 months after your last dose of HEMLIBRA. This is because the effects of HEMLIBRA can last for several months, so side effects can occur even when you are no longer being treated with HEMLIBRA

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 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
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)