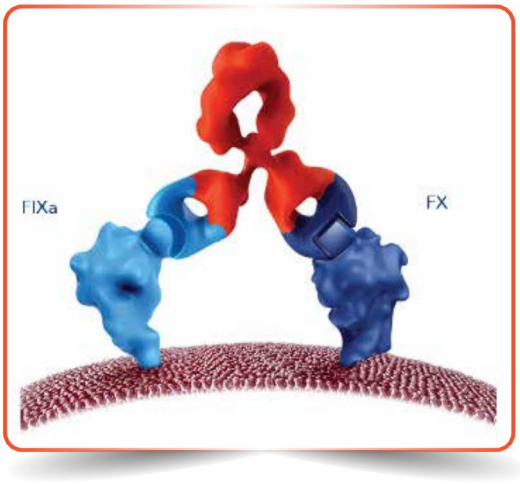
Healthcare Professional Guide



Emicizumab
Subcutaneous injection

Healthcare Professional Guide* for health care providers to ensure safe use of Emicizumab for treatment of Hemophilia A.

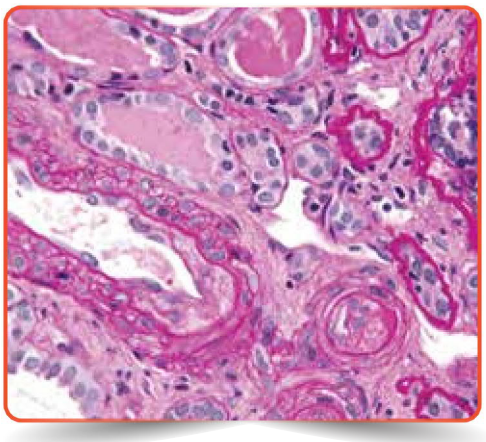
- Risk minimization materials for Emicizumab are assessed by the Drugs Controller General (India), Directorate General of Health Services, FDA Bhavan (CHEB Campus), Kotla Road, New Delhi 110 002.
- These materials describe recommendations to minimize or prevent important risks of the drug.
- See the Emicizumab local package insert for more information on possible side effects of Emicizumab.

SELECT IMPORTANT SAFETY INFORMATION

Note: In case a bypassing agent is indicated in a patient receiving Emicizumab prophylaxis, see below for dosing guidance on the use of bypassing agents.

Thrombotic microangiopathy associated with Emicizumab and aPCC

- Cases of thrombotic microangiopathy (TMA) were reported from a clinical trial in patients receiving Emicizumab prophylaxis and high cumulative doses of activated prothrombin complex concentrate (aPCC) were administered.
- Patients receiving Emicizumab prophylaxis should be monitored for the development of TMA when administering aPCC.



Thromboembolism associated with Emicizumab and aPCC

- Thrombotic events (TE) were reported from a clinical trial in patients receiving Emicizumab prophylaxis when high cumulative doses of aPCC were administered.
- Patients receiving Emicizumab prophylaxis should be monitored for the development of thromboembolism when administering aPCC.

Laboratory coagulation test interference

- Emicizumab 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 Emicizumab prophylaxis should not be used to monitor Emicizumab activity, determine dosing for factor replacement or anti-coagulation or measure Factor VIII inhibitor titres.

Healthcare professionals are requested to report any suspected adverse reactions. See final page for details on how to report.

Please read this information carefully before prescribing the product

Patient Alert Card and Patient/carer Guide

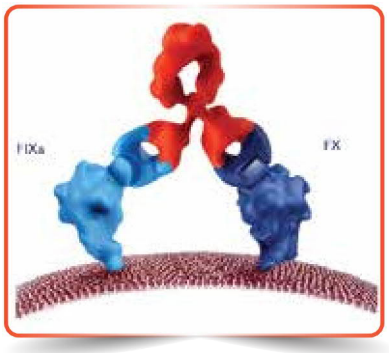
- All patients receiving treatment with Emicizumab should be given a Patient Alert Card and a Patient/caregiver Guide by their healthcare professional. This Patient Alert Card is to be carried by the patient at all times. These materials are to educate patients and their caregivers on the important risks, how to mitigate them, and the need to report any signs or symptoms of these potential adverse events to their treating doctor immediately.

- Treating doctors should advise their patients to keep the Patient Alert Card with them at all times and show it to any healthcare professional who may treat them. This includes any doctor, pharmacist, lab personnel, nurse or dentist they see - not just the specialist who prescribes their Emicizumab.
- To obtain copies of the Patient Alert Card and Patient/carer Guide, please contact Roche Medical Information department at india.medinfo@roche.com

What is Emicizumab?

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 Emicizumab 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

- Emicizumab is indicated for routine prophylaxis to prevent bleeding or reduce the frequency of bleeding episodes in patients with hemophilia A (congenital factor VIII deficiency) with or without factor VIII inhibitors.

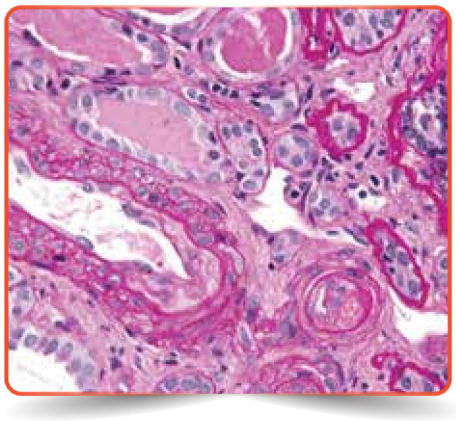
Method of administration

- Please refer to section 2.2 of the local package insert for additional information and comprehensive instructions.
- Emicizumab is intended for subcutaneous use only.
- Emicizumab should be administered using appropriate aseptic technique.
- Please refer to the local package insert for additional information and comprehensive instructions.

Important identified risks associated with Emicizumab use and how to mitigate them:

Thrombotic microangiopathy associated with Emicizumab and aPCC

- Cases of thrombotic microangiopathy (TMA) were reported from a clinical trial in patients receiving Emicizumab 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 [see local package insert of Emicizumab version 5.0 dated December 2019].



- Patients receiving Emicizumab prophylaxis should be monitored for the development of TMA when administering aPCC.

Thromboembolism associated with Emicizumab and aPCC

- Thrombotic events (TE) were reported from a clinical trial in patients receiving Emicizumab 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 [see local package insert of Emicizumab version 5.0 dated December 2019].

- Patients receiving Emicizumab prophylaxis should be monitored for the development of thromboembolism when administering aPCC.

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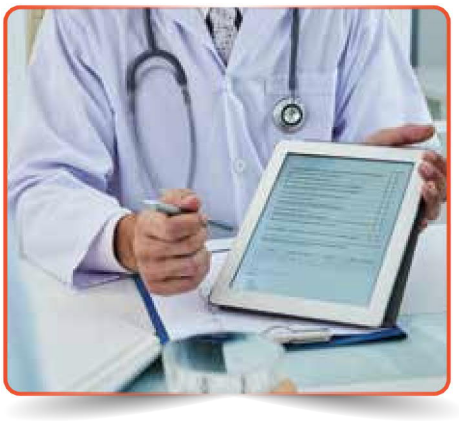
Guidance on the use of bypassing agents in patients receiving Emicizumab prophylaxis

- Treatment with prophylactic bypassing agents should be discontinued the day before starting Emicizumab therapy.
- Physicians should discuss with all patients and/or caregivers the exact dose and schedule of bypassing agents to use, if required while receiving Emicizumab prophylaxis.
- Emicizumab increases patients' coagulation potential. The bypassing agent dose required may therefore be lower than that used without Emicizumab 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 Emicizumab 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).



Sky Blue
30 mg/1 mL

Purple
60 mg/0.4 mL

- 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 for the diagnosis of TMA or thromboembolism and verification of bleeds prior to repeated dosing.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 patients require bypassing agents in the perioperative setting, it is recommended that the dosing guidance above for aPCC be followed.

- In clinical trials, no cases of TMA or TE were observed with use of activated recombinant human FVII (rFVIIa) alone in patients receiving Emicizumab prophylaxis; however, the lowest dose expected to achieve hemostasis should be prescribed. Due to the long half-life of Emicizumab, bypassing agent dosing guidance should be followed for at least 6 months following discontinuation of Emicizumab prophylaxis.

- Please refer to section 2.4 of the local package insert of Emicizumab for additional information and comprehensive instructions.

Laboratory coagulation test interference

- Emicizumab 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 Emicizumab prophylaxis should not be used to assess Emicizumab activity, determine dosing for factor replacement or anticoagulation, 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 Emicizumab are shown in Table 1 below.
- Due to the long half-life of Emicizumab, these effects on coagulation assays may persist for up to 6 months after the last dose (see section 3.2 of the local package insert).

Table 1: Coagulation Test Results Affected and Unaffected by Emicizumab

Results Affected by Emicizumab	Results Unaffected by Emicizumab
Activated Partial Thromboplastin Time (aPTT)	Thrombin Time (TT)
Activated Clotting Time (ACT)	One-stage, PT based, single-factor assays
One-stage, aPTT based, single-factor assays	Chromogenic based single-factor assays other than FVIII[1]
aPTT based Activated Protein C Resistance (APC-R)	Immuno-based assays (eg. ELISA, turbidometric methods)
Bethesda assays (clotting based) for FVIII inhibitor titers	Bethesda assays (bovine chromogenic) for FVIII inhibitor titers
	Genetic tests of coagulation factors (eg. Factor V Leiden, Prothrombin 20210)

[1]For important considerations regarding FVIII chromogenic activity assays, see section 2.8 of the local package insert.

Call for reporting

- Consult the local package insert before prescribing, preparing or administering Emicizumab.
- For full information on all possible adverse events please see the local package insert.
- Healthcare professionals are asked to report any suspected adverse reactions via Toll-Free No. PvPI: 1800-180-3024.
- Adverse reactions should also be reported to india.drugsafety@roche.com via the Company contact point, that is provided below.
- Healthcare Professionals treating patients at participating centers are encouraged to participate in and report the adverse events observed to the pharmacovigilance system.
- 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.

Company contact point - If you have any questions or problems:

Roche India Drug Safety:-
To report any Adverse Events (AE)

+91 98201 63752 | +91 22 33941422

india.drugsafety@roche.com

or

Medical Information - Queries

+91 8879021826 | +91 22 33941408

india.medinfo@roche.com

Visit: https://www.rocheindia.com/en/contact.html

Reference:
Data on file.

Disclaimer:
1. For the use of a Registered Medical Practitioner or a Hospital or a Laboratory only.
2. For scientific information on Roche Medicinal Product please write to india.medinfo@roche.com
3. For all Adverse Events/Special Situation Reports with Roche Medicinal Product please report the same to india.drugsafety@roche.com within one business day/24 hours.
4. This promotional input is not valid after 13/08/2021 or any update.

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Full prescribing information available on request.

Marketed in India by:
Roche Products (India) Pvt. Ltd.
1503, 15th Floor, "The Capital", Bandra Kurla Complex,
Bandra (East), Mumbai 400 051, India.
Tel.: +91 (22) 3394 1414 • Fax: +91 (22) 33941054