Who is Prothromplex TOTAL for?

Prothromplex TOTAL is indicated for the:

- Treatment of bleeding and perioperative prophylaxis of bleeding in acquired deficiency of prothrombin complex coagulation factors, such as a deficiency caused by treatment with vitamin K antagonists or, in case of overdose with vitamin K antagonists, when rapid correction of the deficiency is required

- Treatment and perioperative prophylaxis of haemorrhages in congenital deficiency of vitamin K-dependent coagulation factors, when purified specific coagulation factor concentrate is not available

Prothromplex TOTAL is indicated in adults. There are insufficient paediatric data to recommend the administration of Prothromplex TOTAL in children.

Prescribing and safety information

Presentation: Prothromplex TOTAL 600 IU powder and solvent for solution for injection (human prothrombin complex) PRESCRIBING INFORMATION (Please refer to the Summary of Product Characteristics (SmPC) before prescribing).

Presentation: Prothromplex TOTAL vials contain human prothrombin complex (human coagulation factors II, VII, IX, X) powder and solvent (20 ml water for injection). **Indications:** Treatment of bleeding and perioperative prophylaxis of bleeding in acquired deficiency of prothrombin complex coagulation factors, such as a deficiency caused by treatment with vitamin K antagonists or in case of overdose with vitamin K antagonists, when rapid correction of the deficiency is required; Treatment and perioperative prophylaxis of haemorrhages in congenital deficiency of vitamin K-dependent coagulation factors, when purified specific coagulation factor concentrate is not available. Prothromplex TOTAL is indicated in adults only. **Dosage and administration:** Treatment should be under the supervision of a physician experienced in the treatment of coagulation disorders. The dosage and duration of the substitution therapy depend on the severity of the coagulation disorder, on the location and extent of the bleeding and on the patient's clinical condition. Individual dosage requirements can only be identified on the basis of regular determinations of the individual plasma levels of the coagulation factors of interest or on the global test of the prothrombin complex level (e.g. Quick's time value, INR, prothrombin time) and continuous monitoring of the patient's clinical condition (please refer to the SmPC for dosage and frequency of administration calculations). In case of major surgical interventions precise monitoring of the substitution therapy by means of coagulation assays is essential (specific coagulation factor assays and/or global tests for prothrombin complex levels). For guidance on prophylaxis and on-demand treatment dosing, please refer to the SmPC. Should be administered via the intravenous route at a maximum rate of 2 ml/min (60 IU/min). The use of Prothromplex TOTAL in paediatric patients has not been established in clinical trials. **Contraindications:** Hypersensitivity to the active substance or to any of the excipients. Known allergy to heparin or history of heparin-induced thrombocytopenia. **Warnings and precautions:** Traceability: In order to improve the traceability of biological medicinal products, the name and the batch number of the administered product should be clearly recorded. The advice of a specialist experienced in the management of coagulation disorders should be sought. In patients with acquired deficiency of the vitamin K-dependent coagulation factors (e.g. as induced by treatment with vitamin K antagonists) Prothromplex TOTAL should only be used when rapid correction of prothrombin complex is necessary, such as major bleeding or emergency surgery. In other cases, reduction of the dose of vitamin K antagonist and/or administration of vitamin K is usually sufficient. Patients receiving a vitamin K antagonist may have an underlying hypercoagulable state and infusion of human prothrombin complex may exacerbate this. In congenital deficiency of any vitamin K-dependent factors, a specific coagulation factor product should be used when available. Hypersensitivity: Allergic-type hypersensitivity reactions including anaphylactic reactions and anaphylactic shock have been reported with Prothromplex TOTAL. If allergic/anaphylactic-type reactions occur, treatment should be stopped immediately and medical treatment sought. Thromboembolism, DIC, Fibrinolysis: Thrombosis and thromboembolic events, including disseminated intravascular coagulation (DIC), arterial and venous thromboembolic events including myocardial infarction, cerebrovascular accident, and pulmonary embolism have been reported with Prothromplex TOTAL. Patients, with either congenital or acquired deficiency, particularly with repeated dosing, are at risk of thrombosis and DIC. The risk may be higher in treatment of isolated FVII deficiency, since the other vitamin K-dependent coagulation factors, with longer halflives, may accumulate to levels considerably higher than normal. Patients should be observed closely for signs and symptoms of intravascular coagulation or thrombosis. Patients with history of coronary heart disease, liver disease, pre- or postoperative patients, neonates, or other patients at risk of thromboembolic events or DIC should have particularly close monitoring. In each of these situations, the potential benefit of treatment should be weighed against the risk of these complications. Virus safety: Standard measures for safety of plasma products are employed, but the risk of transmission of infective agents cannot be excluded. Parvovirus B19: The measures taken may be of limited value against non-enveloped viruses such as parvovirus B19. Parvovirus B19 infection may be serious for pregnant women and for individuals with immunodeficiency or increased erythropoiesis. Hepatitis A/B surface antibodies and test interpretation: When a medicinal product prepared from human blood or plasma is administered regularly/repeatedly, appropriate vaccinations (Hep A & B) must be considered. Sodium: This medicinal product contains the calculated value of 81.7 mg sodium per vial or 0.14 mg sodium per International Unit equivalent to 4.1% of the WHO recommended maximum daily intake of 2 g sodium for an adult. Heparin: Patients with history of heparin-induced allergic reactions should avoid the use of heparin containing medicines. **Interactions:** Human prothrombin complex products neutralise the effect of vitamin K antagonist treatment. No interaction studies have been performed. When performing clotting tests, which are sensitive to heparin in patients receiving high doses of human prothrombin complex, the heparin as a constituent of the administered product must be taken into account. **Fertility, pregnancy and lactation:** Effects of Prothromplex TOTAL on fertility have not been established in clinical trials. There are no adequate data from the use of Prothromplex TOTAL in pregnant or lactating women. Therefore Prothromplex TOTAL should be used during pregnancy and lactation only if clearly indicated. **Undesirable effects:** *Common (≥1/100 to <1/10)*: DIC [serious ADR], Inhibitors to one or more of the prothrombin complex factors (development in patients with congenital deficient factors) [serious ADR], anaphylactic shock [serious ADR], anaphylactic reaction [serious ADR], hypersensitivity [serious ADR], cerebrovascular accident [serious ADR], headache, heart failure [serious ADR], acute myocardial infarction [serious ADR], tachycardia, arterial thrombosis, venous thrombosis, hypotension, flushing, pulmonary embolism [serious ADR], dyspnoea, wheezing, vomiting, nausea, urticaria, rash erythematous, pruritus, nephrotic syndrome [serious ADR], and pyrexia. *Other serious undesirable effects*: Replacement therapy with human prothrombin complex concentrates, including Prothromplex TOTAL may result in the formation of circulating antibodies inhibiting one or more of the human prothrombin complex factors. If such inhibitors occur, the condition will manifest itself as a poor clinical response. There is a risk of thromboembolic episodes, and standard measures for safety of plasma products are employed but the risk of transmission of infective agents cannot be excluded. **Refer to the SmPC for details on full side effect profile and interactions. Pack Size:** 600 IU powder. **Legal Category:** POM **Marketing Authorisation (MA) Numbers and MA holder:** PA2004/005/001. Baxalta Innovations GmbH. Industriestrasse 67. A1221. Vienna. Austria. **Email:** medinfoemea@takeda.com. Further information is available on request. **PI code:** pi-01041. **Date of preparation:** November 2020.

Adverse events should be reported to the Pharmacovigilance Unit at the Health Products Regulatory Authority (HPRA) at: www.hpra.ie

Adverse events should also be reported to Shire Pharmaceuticals Ltd (now part of Takeda) at: drugsafety@shire.com

Reference

1. Prothromplex TOTAL 600 IU Summary of Product Characteristics. Available at www.medicines.ie.

PROTHROMPLEX TOTAL

For the treatment of bleeding and perioperative prophylaxis in acquired deficiency of prothrombin complex coagulation factors or congenital deficiency of vitamin K-dependent coagulation factors in adults

Administration guide

Practical information on how to store, prepare and administer Prothromplex TOTAL

Intended for healthcare professionals.
Prescribing information can be found on the back cover.

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How to store Prothromplex TOTAL

Pack contents

- 1 vial with Prothromplex TOTAL 600 IU powder
- 1 vial with 20 ml sterilised water
- 1 aeration needle
- 1 filter needle
- 1 transfer needle

Storage

- Store in a refrigerator (2–8°C). Do not freeze
- Store in the original package to protect from light
- Within the stated shelf life, Prothromplex TOTAL can be stored at room temperature (maximum 25°C) for one period of up to 6 months
  - Record the beginning and end of the room temperature storage period on the package
  - Do not return the product to the refrigerator and dispose within 6 months if not used

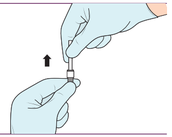
How to prepare Prothromplex TOTAL

***Only** reconstitute Prothromplex TOTAL **immediately** before use. Use aseptic technique.*

1. Warm the unopened water vial to room or body temperature (maximum 37°C).

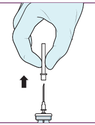
2. Remove the protective caps from the powder and water vials and clean both rubber stoppers.

3. Using a twisting motion, remove the protective covering from one end of the transfer needle.

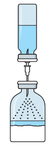


4. Insert the needle through the rubber stopper of the water vial.

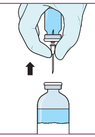
5. Remove the protective covering from the other end of the transfer needle – taking care not to touch the exposed end.



6. Invert the water vial over the powder vial and insert the end of the transfer needle through the rubber stopper of the powder vial. The water will be sucked into the powder by the vacuum created.



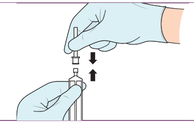
7. Remove the water vial together with the transfer needle. Gently swirl the powder vial to help the powder dissolve.



8. When all the powder has dissolved, insert the aeration needle to cause any foam to collapse. Remove the aeration needle.

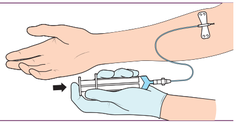
How to administer Prothromplex TOTAL

1. Remove the protective covering from one end of the filter needle by twisting. Fit the needle onto a sterile disposable syringe.



2. Draw the solution into the syringe.

3. Disconnect the filter needle from the syringe and slowly administer the solution intravenously (maximum infusion/injection rate: 2 ml/min).



After administration

- Discard all unsealed needles, together with the syringe and/or the infusion set in the product box
- Any unused Prothromplex TOTAL or waste material should be disposed of in accordance with your hospital requirements

***Before use,** inspect the solution for floating particles or discolouration – it should be clear or slightly opalescent. Dispose of any solutions that are cloudy or have deposits.*

Use aseptic technique.