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 600 IU 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 600 IU is indicated in adults only. There are insufficient paediatric data to recommend the administration of Prothromplex TOTAL 600 IU in children. **Dosage and administration:** Treatment should be initiated 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 dosing guidance, please refer to the SmPC. Should be administered via the intravenous route slowly and it is recommended not to administer more than 2 ml/min (60 IU/min). **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 600 IU should only be used when rapid correction of prothrombin complex levels 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 600 IU. 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 600 IU. 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 half-lives, 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 post-operative patients 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 are employed to prevent infections which can be transmitted by medicinal products made from human blood or plasma. However, infectious diseases due to transmission of infective agents cannot be totally excluded. The measures taken are considered effective for enveloped viruses such as HIV, HBV and HCV as well as against the non-enveloped HAV virus. 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. When a medicinal product prepared from human blood or plasma is administered regularly/repeatedly, appropriate vaccinations (hepatitis A and B) must be

considered. Sodium: This medicinal product contains 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. Interference with biological testing: 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 600 IU on fertility have not been established in clinical trials. There are no adequate data from the use of Prothromplex TOTAL 600 IU in pregnant or lactating women. Therefore, Prothromplex TOTAL 600 IU should be used during pregnancy and lactation only if clearly indicated.

Undesirable effects: *Common serious (≥1/100 to <1/10):* DIC, inhibitors to one or more of the prothrombin complex factors (development in patients with congenital deficient factors), anaphylactic shock, anaphylactic reaction, hypersensitivity, cerebrovascular accident, heart failure, acute myocardial infarction, arterial thrombosis, venous thrombosis, pulmonary embolism, nephrotic syndrome. *Common (≥1/100 to <1/10):* headache, tachycardia, hypotension, flushing, dyspnoea, wheezing, vomiting, nausea, urticaria, rash erythematous, pruritus and pyrexia. **Refer to the SmPC for details on full side effect profile and interactions**. **Pack Size:** 600 IU powder. **Basic UK NHS Cost:** £306 per pack. **Legal Category:** POM. **Marketing Authorisation (MA) Numbers and MA holder:** PL 34078/0009. Baxalta Innovations GmbH. Industriestrasse 67. A-1221 Vienna. Austria. Further information is available on request. **Email:** medinfoemea@takeda.com. **PI code:** pi-01124. **Date of preparation:** December 2020.

Adverse events should be reported. Reporting forms and information can be found at: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store. Adverse events should also be reported to Takeda UK Ltd. at: AE.GBR-IRL@takeda.com

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