ADVATE 250, 500, 1000, 1500, 2000, 3000 IU powder and solvent for solution for injection (Human coagulation factor VIII (rDNA) octocog alfa) PRESCRIBING INFORMATION (Please refer to the Summary of Product Characteristics (SmPC) before prescribing). **Presentation:** ADVATE vials contain human coagulation factor VIII (rDNA) octocog alfa powder and solvent (5 ml and 2 ml sterilised water for injection). After reconstitution, nominally 250, 500, 1000, 1500, 2000 and 3000 IU per vial. **Indication:** Treatment and prophylaxis of bleeding in patients with haemophilia A (congenital factor VIII deficiency). ADVATE is indicated in all age groups. **Dosage and Administration:** Treatment should be initiated under the supervision of a physician experienced in the treatment of haemophilia and with resuscitation support immediately available in case of anaphylaxis. In case of administration by a non-healthcare professional appropriate training is needed. Dosage and duration depend on the severity of the factor VIII deficiency, location and extent of bleeding and on the patient's clinical condition (please refer to the SmPC guide for dosing and frequency of administration for on-demand treatment (bleeding episodes and surgery) and prophylaxis). Should be administered via the intravenous route at a maximum rate 10 ml/min. **Contraindications:** Hypersensitivity to the active substance or to any of the excipients or to mouse or hamster proteins. **Warnings and Precautions:** Determination of plasma factor VIII levels is also advised during treatment to guide dosing and frequency of repeated injections. For major surgical interventions, precise monitoring of the substitution therapy by means of plasma factor VIII activity assay is indispensable. Hypersensitivity: Allergic type hypersensitivity reactions, including anaphylaxis, have been reported with ADVATE. Cease treatment and seek medical attention if such reactions occur. Caution advised during injection of ADVATE reconstituted in 2 ml solvent, especially in children, if hypersensitivity reactions occur there is less time to react by stopping the injection. Misapplication (intra-arterially or paravenously): May lead to mild, short-term injection site reactions. Inhibitors: The formation of neutralising antibodies (inhibitors) to factor VIII is a known complication in the management of individuals with haemophilia A. All patients should be carefully monitored for the development of inhibitors. The risk of developing inhibitors is correlated to the severity of the disease as well as the exposure to factor VIII, this risk being highest within the first 20 exposure days. In patients with high levels of inhibitor, factor VIII therapy may not be effective and other therapeutic options should be considered. Catheter-related complications in treatment: If central venous access device (CVAD) is required, risk of CVAD related complications including local infections and catheter site thrombosis should be considered. Excipient-related considerations: After reconstitution this medicinal product contains 0.45 mmol sodium (10 mg) per vial. To be taken into consideration by patients on a controlled sodium diet. With each administration of ADVATE, the product name and batch number should be recorded. Paediatric: The listed warnings and precautions apply to both adults and children. **Interactions:** No interaction studies have been performed with ADVATE. **Pregnancy and Lactation:** No data available, therefore factor VIII should be used during pregnancy and lactation only if clearly indicated. **Undesirable effects:** Very common (≥1/10): Factor VIII inhibition (PUPs, previously-untreated patients). Common (≥1/100 to <1/10): Headache, Pyrexia. Other serious undesirable effects: Uncommon frequency (≥1/1,000 to <1/100): Post procedural haemorrhage, Lymphangitis, Factor VIII inhibition (PTPs, previously-treated patients); Unknown frequency: Anaphylactic reaction, Hypersensitivity. **Refer to the SmPC for details on full side effect profile and interactions**. **Pack Size:** Single vials of ADVATE with 2 ml solvent for injection containing 250, 500, 1000, or 1500 IU powder. Single vials of ADVATE with 5 ml solvent for injection containing 250, 500, 1000, 1500 2000 or 3000 IU powder. **Basic UK NHS Cost**: 71p per IU. **Legal Category:** POM **Marketing Authorisation Numbers and holder:** EU/1/03/271/001-020. Takeda Manufacturing Austria AG, Industriestrasse 67, A-1221 Vienna, Austria. Further information is available on request: **Email:** medinfoEMEA@shire.com. **PI approval code:** pi-00822 **Date of Revision:** April 2020.

UK: 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
Ireland: Adverse events should be reported to the Pharmacovigilance Unit at the Health Products Regulatory Authority (HPRA) at: www.hpra.ie
UK and Ireland: Adverse events should also be reported to Shire Pharmaceuticals Ltd. (now part of Takeda) at: drugsafety@shire.com

ADYNOVI® ▼ (rurioctocog alfa pegol) powder and solvent for solution for injection

PRESCRIBING INFORMATION FOR GREAT BRITAIN (ENGLAND, SCOTLAND, WALES)

Refer to the Summary of Product Characteristics (SmPC) before prescribing
Presentation: ADYNOVI vials contain human coagulation factor VIII (rDNA), rurioctocog alfa pegol powder and solvent (2 or 5 ml sterilised water for injection). After reconstitution, nominally 250 IU/2 ml, 500 IU/2 ml, 1000 IU/2 ml, and 2000 IU/5 ml per vial.
Indication: Treatment and prophylaxis of bleeding in patients 12 years and above with haemophilia A (congenital factor VIII deficiency).
Dosage and administration: Treatment should be under the supervision of a physician experienced in the treatment of haemophilia. The dose and duration of the substitution therapy depend on the severity of the factor VIII (FVIII) deficiency, on the location and extent of the bleeding and on the patient's clinical condition. For guidance on prophylactic and on-demand treatment dosing, please refer to the SmPC. Should be administered via the intravenous route at a maximum rate of 10 ml/min.
Contraindications: Hypersensitivity to the active substance, to the parent molecule octocog alfa or to any of the excipients. Known allergic reaction to mouse or hamster protein.
Warnings and precautions: Traceability: Name and the batch number of the administered product should be clearly recorded. Hypersensitivity: Allergic type hypersensitivity reactions are possible with ADYNOVI. If symptoms occur, patients should be advised to discontinue use of the medicinal product immediately and contact their physician. In case of anaphylactic shock, standard medical treatment for shock should be implemented. Inhibitors: Development of neutralising antibodies (inhibitors) may occur in patients with haemophilia A treated with FVIII, including with ADYNOVI. If such inhibitors occur, the condition will manifest itself as an insufficient clinical response. In such cases, management of such patients should be directed by physicians with experience in the care of haemophilia and FVIII inhibitors. All patients should be monitored for the development of inhibitors especially following any product switch, if plasma levels are not attained or if bleeding is not controlled with an appropriate dose. Immune tolerance induction (ITI): No clinical data for use of ADYNOVI in ITI are available. Cardiovascular events: In patients with existing cardiovascular risk factors, substitution therapy with FVIII may increase the cardiovascular risk. Catheter-related complications: If a central venous access device (CVAD) is required, risk of CVAD-related complications including local infections, bacteraemia and catheter site thrombosis should be considered. Excipient-related considerations: ADYNOVI contains less than 1 mmol sodium (23 mg) per vial. Paediatric population: The listed warnings and precautions apply both to adults and children (12 to 18 years of age).
Interactions: None reported.
Fertility, pregnancy and lactation: Based on the rare occurrence of haemophilia A in women, experience regarding the use of FVIII during pregnancy and breastfeeding is not available. Therefore, FVIII should be used during pregnancy and lactation only if clearly indicated.
Undesirable effects: Very common (≥1/10): Headache. Common (≥1/100 to <1/10): dizziness, diarrhoea, nausea and rash. Uncommon (≥1/1000 to <1/100): FVIII inhibition (in previously treated patients), hypersensitivity, ocular hyperaemia, flushing, drug eruption, eosinophil count increased and infusion related reaction. **Refer to the SmPC for details on full side effect profile and interactions**. **Legal classification:** POM.
Marketing authorisation (MA) numbers: 250 IU/2ml: PLGB 34078/0020; 500 IU/2ml: PLGB 34078/0022; 1000 IU/2ml: PLGB 34078/0017; 2000 IU/5ml: PLGB 34078/0019. **UK basic NHS price:** 85p per IU. **Name and address of MA holder:** Takeda UK Ltd, 1 Kingdom Street, London, W2 6BD, United Kingdom. **PI approval code:** pi-01601. **Date of preparation:** August 2021.

▼ This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Adverse events should be reported. Reporting forms and information can be found at: www.mhra.gov.uk/yellowcard. Adverse events should also be reported to Takeda at: AE.GBR-IRL@takeda.com

ADYNOVI® ▼ (rurioctocog alfa pegol) powder and solvent for solution for injection

PRESCRIBING INFORMATION FOR NORTHERN IRELAND

Refer to the Summary of Product Characteristics (SmPC) before prescribing
Presentation: ADYNOVI vials contain human coagulation factor VIII (rDNA), rurioctocog alfa pegol powder and solvent (2 and 5 ml sterilised water for injection). After reconstitution, nominally 250 IU/2ml, 500 IU/2ml, 1000 IU/2ml, and 2000 IU/5ml per vial. **Indication:** Treatment and prophylaxis of bleeding in patients 12 years and above with haemophilia A (congenital factor VIII deficiency).
Dosage and administration: Treatment should be under the supervision of a physician experienced in the treatment of haemophilia. The dose and duration of the substitution therapy depend on the severity of the factor VIII (FVIII) deficiency, on the location and extent of the bleeding and on the patient's clinical condition. For guidance on prophylactic and on-demand treatment dosing, please refer to the SmPC. Should be administered via the intravenous route at a maximum rate of 10 ml/min. **Contraindications:** Hypersensitivity to the active substance, to the parent molecule octocog alfa or to any of the excipients. Known allergic reaction to mouse or hamster protein.
Warnings and precautions: Traceability: Name and the batch number of the administered product should be clearly recorded. Hypersensitivity: Allergic type hypersensitivity reactions are possible with ADYNOVI. If symptoms occur, patients should be advised to discontinue use of the medicinal product immediately and contact their physician. In case of anaphylactic shock, standard medical treatment for shock should be implemented. Inhibitors: Development of neutralising antibodies (inhibitors) may occur in patients with haemophilia A treated with FVIII, including with ADYNOVI. If such inhibitors occur, the condition will manifest itself as an insufficient clinical response. In such cases, it is recommended that a specialised haemophilia centre be contacted. All patients should be monitored for the development of inhibitors especially following any product switch, if plasma levels are not attained or if bleeding is not controlled with an appropriate dose. Immune tolerance induction (ITI): No clinical data for use of ADYNOVI in ITI are available. Cardiovascular events: In patients with existing cardiovascular risk factors, substitution therapy with FVIII may increase the cardiovascular risk. Catheter- related complications: If a central venous access device (CVAD) is required, risk of CVAD-related complications including local infections, bacteraemia and catheter site thrombosis should be considered. Excipient-related considerations: ADYNOVI contains less than 1 mmol sodium (23 mg) per vial. Paediatric population: The listed warnings and precautions apply both to adults and children (12 to 18 years of age). **Interactions:** None reported. **Fertility, pregnancy and lactation:** Based on the rare occurrence of haemophilia A in women, experience regarding the use of FVIII during pregnancy and breastfeeding is not available. Therefore, FVIII should be used during pregnancy and lactation only if clearly indicated. **Undesirable effects:** Very common (≥1/10): Headache. Common (≥1/100 to <1/10): dizziness, diarrhoea, nausea and rash. Uncommon (≥1/1000 to <1/100): FVIII inhibition (in previously treated patients), hypersensitivity, ocular hyperaemia, flushing, drug eruption, eosinophil count increased and infusion related reaction. **Refer to the SmPC for details on full side effect profile and interactions**. **Legal classification:** POM. **Marketing authorisation (MA) numbers:** 250 IU/2ml: EU/1/17/1247/002; 500 IU/2ml: EU/1/17/1247/006; 1000 IU/2ml: EU/1/17/1247/010; 2000 IU/5ml: EU/1/17/1247/014. **UK basic NHS price:** 85p per IU. **Name and address of MA holder:** Baxalta Innovations GmbH. Industriestrasse 67. A-1221. Vienna. Austria. **PI approval code:** pi-01449. **Date of preparation:** May 2021.

Adverse events should be reported. Reporting forms and information can be found at: www.mhra.gov.uk/yellowcard. Adverse events should also be reported to Takeda at: AE.GBR-IRL@takeda.com