ADVATE (octocog alfa) 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: ADVATE vials contain human coagulation factor VIII (rDNA) octocog alfa powder and solvent (5 ml or 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 (FVIII) 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). Determination of plasma FVIII 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 FVIII activity assay is indispensable. 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:** 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 FVIII 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 FVIII, this risk being highest within the first 20 exposure days. In patients with high levels of inhibitor, FVIII 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 10 mg sodium 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. Paediatrics: The listed warnings and precautions apply to both adults and children. **Interactions:** Not known. **Fertility, pregnancy and lactation:** No data available, therefore FVIII should be used during pregnancy and lactation only if clearly indicated. **Undesirable effects:** *Very common (≥1/10)*: FVIII inhibition (PUPs, previously untreated patients). *Common (≥1/100 to <1/10):* Headache, pyrexia. Other serious undesirable effects: *Uncommon (≥1/1,000 to <1/100)*: Post-procedural haemorrhage, lymphangitis, FVIII inhibition (PTPs, previously treated patients), syncope, haematoma, dyspnoea, peripheral oedema; *Unknown frequency*: Anaphylactic reaction, hypersensitivity. **Refer to the SmPC for details on full side effect profile and interactions**. **Basic UK NHS cost**: 71p per IU. **Legal classification:** POM. **Marketing Authorisation (MA):** *2 ml solvent*: PLGB 06009/0028 (250 IU), PLGB 06009/0031 (500 IU); *5 ml solvent*: PLGB 06009/0029 (250 IU), PLGB 06009/0032 (500 IU), PLGB 06009/0024 (1000 IU), PLGB 06009/0026 (1500 IU), PLGB 06009/0027 (2000 IU), PLGB 06009/0030 (3000 IU). **Business responsible for sale and supply:** Takeda UK Limited, 1 Kingdom Street, London, W2 6BD, United Kingdom. **PI approval code:** pi-01980. **Date of preparation:** April 2022.

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

ADVATE (octocog alfa) powder and solvent for solution for injection

PRESCRIBING INFORMATION FOR NORTHERN IRELAND

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 or 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 (FVIII) 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). Determination of plasma FVIII 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 FVIII activity assay is indispensable. 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:** 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 FVIII 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 FVIII, this risk being highest within the first 20 exposure days. In patients with high levels of inhibitor, FVIII 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 10 mg sodium 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. Paediatrics: The listed warnings and precautions apply to both adults and children. **Interactions:** Not known. **Fertility, pregnancy and lactation:** No data available, therefore FVIII should be used during pregnancy and lactation only if clearly indicated. **Undesirable effects:** *Very common (≥1/10)*: FVIII inhibition (PUPs, previously untreated patients). *Common (≥1/100 to <1/10):* Headache, pyrexia. Other serious undesirable effects: *Uncommon (≥1/1,000 to <1/100)*: Post-procedural haemorrhage, lymphangitis, FVIII inhibition (PTPs, previously treated patients), syncope, haematoma, dyspnoea, peripheral oedema; *Unknown frequency*: Anaphylactic reaction, hypersensitivity. **Refer to the SmPC for details on full side effect profile and interactions**. **Basic UK NHS cost**: 71p per IU. **Legal classification:** POM. **Marketing authorisation numbers:** *2 ml solvent*: EU/1/03/271/007 (250 IU), EU/1/03/271/008 (500 IU); *5 ml solvent*: EU/1/03/271/001 (250 IU), EU/1/03/271/002 (500 IU), EU/1/03/271/003 (1000 IU), EU/1/03/271/004 (1500 IU), EU/1/03/271/005 (2000 IU), EU/1/03/271/006 (3000 IU). **Business responsible for sale and supply:** Takeda UK Limited, 1 Kingdom Street, London W2 6BD, United Kingdom. **PI approval code:** pi-01979. **Date of preparation:** April 2022.

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 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, rash and urticaria. 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-02023. **Date of preparation:** August 2022.

▼ 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 or 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 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 up to 12.42 mg sodium per vial, equivalent to 0.62% of the World Health Organisation (WHO) recommended maximum daily intake of 2 g sodium for an adult. Depending on the body weight and posology, the patient could receive more than one vial. This should be taken into consideration by patients on a controlled sodium diet. It is strongly recommended that every time that ADYNOVI is administered to a patient, the name and batch number of ADYNOVI is recorded in order to maintain a link between the patient and the batch of ADYNOVI. 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, rash and urticaria. *Uncommon* (≥1/1000 to <1/100): FVIII inhibition (in previously treated patients), hypersensitivity, ocular hyperaemia, flushing, rash pruritic, 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 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.

Business responsible for sale and supply: Takeda UK Limited, 1 Kingdom Street, London, W2 6BD, United Kingdom.

PI approval code: pi-02205

Date of preparation: November 2022

▼ This medicinal product is subject to additional monitoring.

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

FEIBA (Factor VIII Inhibitor Bypassing Activity) 25 U/ml or 50 U/ml powder and solvent for solution for infusion
PRESCRIBING INFORMATION for UNITED KINGDOM
Refer to the Summary of Product Characteristics (SmPC) before prescribing

Presentation: 1 vial of FEIBA 25 U/ml contains 500 U factor VIII inhibitor bypassing activity. 1 vial of FEIBA 50 U/ml contains 500 U, 1000 U or 2500 U factor VIII inhibitor bypassing activity.

Indications: Treatment of spontaneous bleeding and cover of surgical interventions in haemophilia A patients with factor VIII inhibitors and in non-haemophiliacs with acquired factor VIII inhibitors. Prophylaxis in haemophilia A patients with high responding inhibitors and frequent joint bleeding.

Dosage and administration: Treatment should be initiated and supervised by a physician experienced in the management of haemophilia. Posology: The dosage and duration of the therapy is dependent upon the severity of the disorder, the location and extent of the bleeding and the patient's clinical condition. As a general guide a dose of 50 to 100 U of FEIBA per kg body weight is recommended, repeated every 6 – 12 hours depending on type of bleed and degree of response (for further information on dosage please refer to the SmPC). Dosage and frequency of administration should always be guided by the clinical efficacy in each individual case. FEIBA should be administered via the intravenous route at a maximum rate of 2 U/kg body weight per minute. A single dose of 100 U/kg body weight and a daily dose of 200 U/kg body weight should not be exceeded unless the severity of bleeding warrants and justifies the use of higher doses. Bleeding prophylaxis: For prevention of bleeding episodes during prophylaxis, dose 70 to 100 U/kg body weight every other day. Adjust dose based on the patient's clinical response. Paediatrics: The experience in children under 6 years of age is limited; the same dose regimen as in adults should be adapted to the child's clinical condition. Monitoring: In case of inadequate response to treatment with the product, it is recommended that a platelet count be performed because a sufficient number of functionally intact platelets are considered to be necessary for the efficacy of the product. Results of routine coagulation tests may not correlate with clinical improvement – no direct monitoring is possible. Global haemostatic tests such as thromboelastogram (TEG) or thrombin generation assay (TGA) may be useful tools to monitor and optimise the treatment. **Contraindications:** FEIBA must not be used in the following situations if therapeutic alternatives to FEIBA are available: Hypersensitivity to the active substance or to any of the excipients. Disseminated intravascular coagulation (DIC). Acute thrombosis or embolism (including myocardial infarction). **Warnings and precautions:** Traceability: Name and the batch number of the administered product should be clearly recorded. Thromboembolic events: Have occurred, including DIC, venous thrombosis, pulmonary embolism, myocardial infarction, and stroke. Some occurred with doses above 200 U/kg/day or in patients with other risk factors for thromboembolic events (including DIC, advanced atherosclerotic disease, crush injury or septicaemia). FEIBA should be used with particular caution in patients at risk of DIC, arterial or venous thrombosis. Thrombotic microangiopathy (TMA) has not been reported in FEIBA clinical studies. Cases of TMAs were reported in an emicizumab clinical trial where subjects received FEIBA as part of a treatment regimen for breakthrough bleeding. If treatment with FEIBA is considered required for patients receiving emicizumab, patients must be closely monitored. At the first signs or symptoms of thromboembolic events, the infusion should be stopped immediately, and appropriate diagnostic and therapeutic measures initiated. A single dose of 100 U/kg body weight and a daily dose of 200 U/kg body weight should not be exceeded. When used to stop bleeding, the product should be given only for as long as absolutely necessary to achieve the therapeutic goal. Allergic-type hypersensitivity reactions: FEIBA can precipitate allergic-type hypersensitivity reactions that have included, urticaria, angioedema, gastrointestinal manifestations, bronchospasm, and hypotension; these reactions can be severe and can be systemic (e.g. anaphylaxis with urticaria and angioedema, bronchospasm, and circulatory shock). At the first sign or symptom of an infusion/hypersensitivity reaction, FEIBA administration should be stopped and medical care initiated as appropriate. Measures to prevent transmission of infectious agents: Standard measures for safety of plasma products are employed but the risk of transmission of infective agents cannot be excluded. The measures taken may be of limited value against nonenveloped viruses such as parvovirus B19. Parvovirus B19 infection may be serious for pregnant women (foetal infection) and for individuals with immunodeficiency or increased erythropoiesis (e.g. haemolytic anaemia). Appropriate vaccination (against hepatitis A and B) should be considered for patients in regular/repeated receipt of plasma-derived products. Discordant response to bypassing agents: Due to patient-specific factors the response to a bypassing agent can vary, in case of insufficient response to one bypassing agent, use of another agent should be considered. Anamnestic responses: Patients with inhibitors may result in an initial "anamnestic" rise in the inhibitor levels. Continuous administration of FEIBA may decrease the inhibitors over time. Interference with laboratory tests: High doses of FEIBA may result in misleading interpretation of positive results in serological testing. Sodium content: FEIBA contains approximately 4 mg sodium (calculated) per ml. To be taken into consideration in patients on a low sodium diet. **Interactions:** No adequate and well-controlled studies of the combined or sequential use of FEIBA and recombinant factor VIIa (rFVIIa), antifibrinolytics or emicizumab have been conducted. The possibility of thromboembolic events should be considered when systemic antifibrinolytics are used. Therefore, antifibrinolytics and FEIBA should be administered at least 6 hours apart. In cases of concomitant rFVIIa use, a potential drug interaction may occur (potentially resulting in adverse events such as a thromboembolic event). Clinical experience from an emicizumab clinical trial suggests that a potential drug interaction may exist with emicizumab when FEIBA was used as part of a treatment regimen for breakthrough bleeding. **Fertility, pregnancy and lactation:** There are no adequate data from the use of FEIBA in pregnant or lactating women. **Undesirable effects:** Common (≥1/100 to <1/10): Hypersensitivity, headache, dizziness, hypotension, rash, and hepatitis B surface antibody positive. Other

serious undesirable effects (unknown frequency): DIC, anamnestic response, anaphylactic reaction, embolic stroke, thrombotic stroke, cardiac infarction, arterial thrombosis, hypertension, thrombosis, venous thrombosis, bronchospasm, dyspnoea, pulmonary embolism, angioedema, pyrexia, tachycardia. **Refer to the SmPC for details on full side effect profile and interactions**. **UK basic NHS price:** 25 U/ml powder/solvent: 500 U/20ml – £390; 50 U/ml powder/solvent: 500 U/10 ml – £390, 1000 U/20 ml – £780, 2500 U/50 ml – £1950. **Legal classification:** POM. **Marketing authorisation (MA) numbers:** 25 U/ml: PL 34078/0002, 50 U/ml: PL 34078/0003. **Name and address of MA holder:** Baxalta Innovations GmbH, Industriestrasse 67, A-1221 Vienna, Austria. **PI approval code:** pi-01419. **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

OBIZUR ▼ (susoctocog alfa) 500 U 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: 500 U of B domain deleted antihaemophilic factor VIII (rDNA), porcine sequence, susoctocog alfa powder in a vial and solvent in pre-filled syringe (1 ml water for injection).

Indication: Treatment of bleeding episodes in patients with acquired haemophilia caused by antibodies to factor VIII. OBIZUR is indicated in adults.

Dosage and administration: Treatment with OBIZUR should be under the supervision of a physician experienced in the treatment of haemophilia. Treatment monitoring: The product is for in-patient administration only. Requires clinical supervision of the bleeding status of the patient. Dose based on bodyweight may require adjustment in underweight or overweight patients. In the case of major surgical interventions in particular, precise monitoring of the substitution therapy by means of coagulation analysis (plasma factor VIII activity) is indispensable. When using aPTT-based one-stage clotting assay results can be significantly affected by both the type of aPTT reagent and the reference standard. Also, there can be significant discrepancies between assay results obtained by aPTT-based one stage clotting assay and the chromogenic assay according to Ph. Eur. Posology: The dose, frequency, and duration of the therapy with OBIZUR depend on the location, extent and severity of the bleeding episode, target factor FVIII (FVIII) activity, and on the patient´s clinical condition. The recommended initial dose is 200 U/kg body weight, given by intravenous injection - titrate subsequent doses based on clinical response and to maintain target FVIII trough activity. Monitor FVIII activity and clinical condition 30 minutes after the first injection and 3 hours after administering OBIZUR. Monitor FVIII activity immediately prior to and 30 minutes after subsequent doses. If testing of anti-rpFVIII antibodies is negative at baseline, a dose lower than the recommended 200 U/kg may be used as the initial treatment dose. Clinical response should be closely monitored as dosing below 200 U/kg has been associated with a lack of efficacy. Refer to the SmPC guide for dosing and frequency of administration. The total volume of reconstituted OBIZUR should be administered via the intravenous route at a rate of 1 to 2 mL per minute. **Contraindications:** Hypersensitivity to the active substance, hamster protein, or to any of the excipients. Congenital haemophilia A with inhibitors (CHAWI). **Warnings and precautions:** Dosing: Initial dosing below the recommended 200 U/kg has been associated with lack of efficacy. Traceability: Name and the batch number of the administered medicinal product should be clearly recorded. Hypersensitivity: Allergic-type hypersensitivity reactions are possible with OBIZUR. The medicinal product contains trace amounts of hamster proteins. Cease treatment and seek medical attention if such reactions occur. Inhibitors: It is recommended to test for anti-rpFVIII antibodies prior to initiation of treatment.

Treatment may be started at physician's discretion prior to receiving the result of this test. Treatment decisions can be further supported by monitoring FVIII levels. Inhibitory antibodies against porcine FVIII were detected before and after exposure to OBIZUR. Inhibitor titres of up to 29 Bethesda units were recorded at baseline yet patients responded positively to OBIZUR. Lack of efficacy could be due to inhibitory antibodies to OBIZUR. It is recommended that treatment should be based on clinical judgement and not based on detection of inhibitory antibodies by the Bethesda assay. Anamnestic reactions with rise in human FVIII and/or porcine FVIII inhibitors have also been reported. These anamnestic rises may result in lack of efficacy. There is a lack of clinical information on the development of inhibitory antibodies to OBIZUR following repeated administration. Therefore, OBIZUR must only be administered when considered clinically necessary. Cardiovascular events: In patients with existing cardiovascular risk factors, substitution therapy with FVIII may increase the cardiovascular risk. Thromboembolic Events: High and sustained FVIII activity in blood may predispose to thromboembolic events. Those with pre-existing cardiovascular disease and the elderly are at particular risk. Treatment Monitoring: FVIII activity determined by the chromogenic assay is generally lower than FVIII activity determined by the one stage clotting assay. Measurement of FVIII activity must always be carried out using the same assay methodology on any one patient. The one stage assay is recommended. Sodium content: OBIZUR contains 4.6 mg sodium in 1 mL of reconstituted solution in each vial. Multiple vials must be taken per dose. **Interactions:** None reported. **Fertility, pregnancy and lactation:** No clinical experience in pregnant or lactating women, therefore OBIZUR should only be used during pregnancy and lactation, if clearly indicated.

Undesirable effects: *Very common* (≥1/10): Anamnestic reaction; *Common* (≥1/100 to <1/10): Positive test for inhibitory antibodies against porcine FVIII. *Other serious undesirable effects:* Hypersensitivity or allergic reactions (which may include angioedema, burning and stinging at the injection site, chills, flushing, generalised urticaria, headache, hives, hypotension, lethargy, nausea, restlessness, tachycardia, tightness of the chest, tingling, vomiting, wheezing) are possible and may progress to severe anaphylaxis (including shock). **Refer to the SmPC for details on full side effect profile and interactions. Basic UK NHS Cost:** £2.29 per IU. **Legal Category:** POM. **Marketing authorisation (MA) number:** PLGB 34078/0025. **Business responsible for sale and supply:** Takeda UK Limited, 1 Kingdom Street, London, W2 6BD, United Kingdom. **PI approval code:** pi-02113. **Date of preparation:** September 2022.

▼This medicinal product is subject to additional monitoring. 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 UK Ltd at: AE.GBR-IRL@takeda.com

OBIZUR ▼ (susoctocog alfa) 500 U powder and solvent for solution for injection

PRESCRIBING INFORMATION FOR NORTHERN IRELAND

Refer to the Summary of Product Characteristics (SmPC) before prescribing.

Presentation: 500 U of B domain deleted antihaemophilic factor VIII (rDNA), porcine sequence, susoctocog alfa powder in a vial and solvent in pre-filled syringe (1 ml water for injection).

Indication: Treatment of bleeding episodes in patients with acquired haemophilia caused by antibodies to factor VIII. OBIZUR is indicated in adults.

Dosage and administration: Treatment with OBIZUR should be under the supervision of a physician experienced in the treatment of haemophilia. Treatment monitoring: The product is for in-patient administration only. Requires clinical supervision of the bleeding status of the patient. Dose based on bodyweight may require adjustment in underweight or overweight patients. In the case of major surgical interventions in particular, precise monitoring of the substitution therapy by means of coagulation analysis (plasma factor VIII activity) is indispensable. When using aPTT-based one-stage clotting assay results can be significantly affected by both the type of aPTT reagent and the reference standard. Also, there can be significant discrepancies between assay results obtained by aPTT-based one stage clotting assay and the chromogenic assay according to Ph. Eur. Posology: The dose, frequency, and duration of the therapy with OBIZUR depend on the location, extent and severity of the bleeding episode, target factor FVIII (FVIII) activity, and on the patient´s clinical condition. The recommended initial dose is 200 U/kg body weight, given by intravenous injection - titrate subsequent doses based on clinical response and to maintain target FVIII trough activity. Monitor FVIII activity and clinical condition 30 minutes after the first injection and 3 hours after administering OBIZUR. Monitor FVIII activity immediately prior to and 30 minutes after subsequent doses. If testing of anti-rpFVIII antibodies is negative at baseline, a dose lower than the recommended 200 U/kg may be used as the initial treatment dose. Clinical response should be closely monitored as dosing below 200 U/kg has been associated with a lack of efficacy. Refer to the SmPC guide for dosing and frequency of administration. The total volume of reconstituted OBIZUR should be administered via the intravenous route at a rate of 1 to 2 mL per minute.

Contraindications: Hypersensitivity to the active substance, hamster protein, or to any of the excipients. Congenital haemophilia A with inhibitors (CHAWI).

Warnings and precautions: Dosing: Initial dosing below the recommended 200 U/kg has been associated with lack of efficacy. Traceability: Name and the batch number of the administered medicinal product should be clearly recorded. Hypersensitivity: Allergic type hypersensitivity reactions are possible with OBIZUR. The medicinal product contains trace amounts of hamster proteins. Cease treatment and seek medical attention if such reactions occur. Inhibitors: It is recommended to test for anti-rpFVIII antibodies prior to initiation of treatment. Treatment may be started at physician's discretion prior to receiving the result of this test. Treatment decisions can be further supported by monitoring FVIII levels. Inhibitory antibodies against porcine FVIII were detected before and after exposure to OBIZUR. Inhibitor titres of up to 29 Bethesda units were recorded at baseline yet patients responded positively to OBIZUR. Lack of efficacy could be due to inhibitory antibodies to OBIZUR. It is recommended that treatment should be based on clinical judgement and not based on detection of inhibitory antibodies by the Bethesda assay. Anamnestic reactions with rise in human FVIII and/or porcine FVIII inhibitors have also been reported. These anamnestic rises may result in lack of efficacy. There is a lack of clinical information on the development of inhibitory antibodies to OBIZUR following repeated administration. Therefore, OBIZUR must only be administered when considered clinically necessary. Cardiovascular events: In patients with existing cardiovascular risk factors, substitution therapy with FVIII may increase the cardiovascular risk. Thromboembolic Events: High and sustained FVIII activity in blood may predispose to thromboembolic events. Those with pre-existing cardiovascular disease and the elderly are at particular risk. Treatment Monitoring: FVIII activity determined by the chromogenic assay is generally lower than FVIII activity determined by the one stage clotting assay. Measurement of FVIII activity must always be carried out using the same assay methodology on any one patient. The one stage assay is recommended. Sodium content: OBIZUR contains 4.6 mg sodium in 1 mL of reconstituted solution in each vial. Multiple vials must be taken per dose.

Interactions: None reported.

Fertility, pregnancy and lactation: No clinical experience in pregnant or lactating women, therefore OBIZUR should only be used during pregnancy and lactation, if clearly indicated.

Undesirable effects: *Very common* (≥1/10): Anamnestic reaction; *Common* (≥1/100 to <1/10): Positive test for inhibitory antibodies against porcine FVIII. *Other serious undesirable effects:* Hypersensitivity or allergic reactions (which may include angioedema, burning and stinging at the injection site, chills, flushing, generalised urticaria, headache, hives, hypotension, lethargy, nausea, restlessness, tachycardia, tightness of the chest, tingling, vomiting, wheezing) are possible and may progress to severe anaphylaxis (including shock). **Refer to the SmPC for details on full side effect profile and interactions.**

Basic UK NHS Cost: £2.29 per IU. **Legal Category:** POM. **Marketing authorisation numbers:** EU/1/15/1035/001-003. **Business responsible for sale and supply:** Takeda UK Limited, 1 Kingdom Street, London, W2 6BD, United Kingdom. **PI approval code:** pi-02027. **Date of preparation:** July 2022.

▼This medicinal product is subject to additional monitoring. 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 UK Ltd at: AE.GBR-IRL@takeda.com

RIXUBIS® (nonacog gamma) 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: RIXUBIS vials contain nonacog gamma, recombinant human coagulation factor IX (rDNA) powder and solvent (5 ml sterilised water for injection). After reconstitution, nominally 250, 500, 1000, 2000 and 3000 IU per vial. **Indication:** Treatment and prophylaxis of bleeding in patients with haemophilia B (congenital factor IX deficiency) in all age groups. **Dosage and administration:** Treatment should be under the supervision of a physician experienced in the treatment of haemophilia. Dose and duration of the substitution therapy depends on the severity of the factor IX (FIX) deficiency, on the location and extent of the bleeding, and on the patient's clinical condition, age and pharmacokinetic parameters of FIX, such as incremental recovery and half-life (refer to the SmPC for dosing calculations). Should be administered via the intravenous route at a maximum rate of 10 ml/min. Do not administer RIXUBIS by continuous infusion. **Contraindications:** Hypersensitivity to the active substance or to any of the excipients or known allergic reaction to hamster protein. **Warnings and precautions:** Traceability: Name and the batch number of the administered product should be recorded. Hypersensitivity: Allergic type hypersensitivity reactions, including anaphylaxis, have been reported with RIXUBIS. The risk is highest during the early phases of initial exposure to FIX concentrates in previously untreated patients (PUPs), in particular, in patients with high-risk gene mutations. Cease treatment and seek medical attention if such reactions occur. Inhibitors: After repeated treatment, all patients should be monitored for the development of inhibitors. Nephrotic syndrome: Has been reported following attempted immune tolerance induction in haemophilia B patients with FIX inhibitors. Thromboembolism: Due to the potential risk of thrombotic complications, clinical surveillance for early signs of thrombotic and consumptive coagulopathy should be initiated when administering to patients with liver disease, postoperatively, new-born infants, or to patients at risk of thrombotic phenomena or DIC (disseminated intravascular coagulation). Cardiovascular events: In patients with existing cardiovascular risk factors, substitution therapy with FIX 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: After reconstitution this medicinal product contains less than 1 mmol (23 mg) sodium per vial. To be taken into consideration in patients on a controlled sodium diet. Elderly: Clinical studies of RIXUBIS did not include subjects aged 65 and over. It is not known whether they respond differently from younger subjects. As for all patients, dose selection should be individualised. Paediatric population: The listed warnings and precautions apply both to adults and children. **Interactions:** None reported. **Fertility, pregnancy and lactation:** There are no or limited amount of data from the use of FIX in pregnant women. It is unknown whether FIX/metabolites are excreted in human milk. FIX should be used during pregnancy and breast-feeding only if clearly indicated. **Undesirable effects:** *Common* (≥1/100 to <1/10): Dysgeusia, pain in extremity. *Other serious undesirable effects* (unknown frequency): Hypersensitivity. The low purity FIX has been associated with instances of myocardial infarction, DIC, venous thrombosis and pulmonary embolism. High purity FIX is rarely associated with such adverse reactions. **Refer to the SmPC for details on full side effect profile and interactions. Legal classification:** POM. **Marketing authorisation numbers:** 250 IU: PLGB 34078/0028, 500 IU: PLGB 34078/0030, 1000 IU: PLGB 34078/0026, 2000IU: PLGB 34078/0027, 3000 IU: PLGB 34078/0029. **UK basic NHS price:** 60.72p per IU. **Business Responsible for Sale and Supply:** Takeda UK Ltd, 1 Kingdom Street, W2 6BD, United Kingdom. **PI approval code**: pi-01812. **Date of preparation:** December 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

VEYVONDI® ▼ (vonicog alfa) 650 IU and 1300 IU powder and solvent for solution for injection
PRESCRIBING INFORMATION FOR UNITED KINGDOM (ENGLAND, SCOTLAND, WALES AND NORTHERN IRELAND).
Refer to the Summary of Product Characteristics (SmPC) before prescribing
Presentation: Each vial contains nominally 650 IU and 1300 IU vonicog alfa powder. After reconstitution with 5 mL or 10 mL, respectively, of solvent provided, VEYVONDI contains approximately 130 IU/mL of vonicog alfa. **Indication:** VEYVONDI is indicated in adults (age 18 and older) with von Willebrand disease (VWD), when desmopressin (DDAVP) treatment alone is ineffective or not indicated, for the treatment of haemorrhage and surgical bleeding and prevention of surgical bleeding. VEYVONDI should not be used in the treatment of Haemophilia A. **Dosage and administration:** Treatment of VWD should be supervised by a physician experienced in the treatment of haemostatic disorders. Dosage and frequency of administration must be individualised according to clinical judgement and based on the patient´s weight, type and severity of the bleeding episodes/surgical intervention and based on monitoring of appropriate clinical and laboratory measures. Dose based on body weight may require adjustment in underweight or overweight patients (refer to the SmPC for dosing calculations). Generally, 1 IU/kg of VEYVONDI raises the plasma VWF:RCo by 0.02 IU/mL (2%). If the patient's baseline plasma FVIII:C level is <40% or is unknown and in all situations where a rapid correction of haemostasis should be achieved, it is necessary to administer a recombinant factor VIII (rFVIII) product with the first infusion of VEYVONDI, in order to achieve a haemostatic plasma level of FVIII:C. However, if an immediate rise in FVIII:C is not necessary, or if the baseline FVIII:C level is sufficient to ensure haemostasis, the physician may decide to omit the co-administration of rFVIII at the first infusion with VEYVONDI. In case of major bleeding events or major surgeries requiring repeated, frequent infusions, monitoring of FVIII:C levels is recommended, to decide if rFVIII is required for subsequent infusions to avoid excessive rise of FVIII:C. For guidance on the treatment of bleeding episodes (on-demand treatment) and prevention of bleeding / haemorrhage and treatment in case of elective surgery, please refer to the SmPC. VEYVONDI should be administered via the intravenous route up to a maximum rate of 4 mL/min. If any reaction, such as tachycardia, occurs that might be related to the administration of the product, the rate of infusion should be reduced or stopped as required by the clinical condition of the patient. **Contraindications:** Hypersensitivity to the active substance or to any of the excipients. Known allergic reaction to mouse or hamster proteins. **Warnings and precautions:** In actively bleeding patients it is recommended to co-administer a FVIII product with VEYVONDI as a first line treatment and depending on the FVIII activity levels. Traceability: Name and the batch number of the administered product should be clearly recorded. Hypersensitivity reactions: Hypersensitivity reactions (including anaphylaxis) have occurred. Patients should be closely monitored and carefully observed for any symptoms throughout the infusion period. If signs and symptoms occur, patients should immediately discontinue use of VEYVONDI and be provided with appropriate supportive care. VEYVONDI contains traces of mouse immunoglobulin and hamster proteins, and rFVIII. Thrombosis and embolism: There is a risk of occurrence of thrombotic events, particularly in patients with known clinical or laboratory risk factors for thrombosis including low ADAMTS13 levels. Therefore, patients at risk have to be monitored for early signs of thrombosis, and prophylaxis measures against thromboembolism should be instituted according to current recommendations and standard of care. In patients requiring frequent doses of VEYVONDI in combination with rFVIII, FVIII:C activity should be monitored to avoid sustained excessive FVIII:C plasma levels, which may increase the risk of thrombotic events. Any FVIII that would be administered along with VEYVONDI should be a pure FVIII product. A combination with a FVIII product containing von Willebrand factor (VWF) would pose an additional risk of thrombotic events. Inhibitors: Patients with VWD, especially type 3, may develop neutralising antibodies (inhibitors) to VWF. If the expected plasma levels of VWF:RCo are not attained, or if bleeding is not controlled with an appropriate dose, an appropriate assay should be performed to determine if a VWF inhibitor is present. In patients with high levels of anti-VWF antibodies, von Willebrand factor therapy may not be effective and other therapeutic options should be considered. Patients who have high-titre binding antibodies (due to previous treatment with plasma-derived VWF) may require a higher dose to overcome the binding antibody effect and such patients could be managed clinically by administration of higher doses of VEYVONDI based on the PK data for each individual patient. Excipient-related considerations: VEYVONDI contains 5.2 mg sodium in each 650 IU vial or 10.4 mg sodium in each 1300 IU vial. To be taken into consideration by patients on a controlled sodium diet. **Interactions:** None known. **Fertility, pregnancy and lactation:** Pregnancy: Experience in the treatment of pregnant or breast-feeding women is not available. VEYVONDI should be administered to pregnant women only if clearly indicated, taking into consideration that delivery confers an increased risk of haemorrhagic events in these patients. Breast-feeding: It is unknown whether VEYVONDI is excreted in human milk. VEYVONDI should be administered to lactating VWF-deficient women only if clearly indicated. Healthcare professionals should balance the potential risks and only prescribe VEYVONDI if needed. Fertility: The effects of VEYVONDI on fertility have not been established. **Undesirable effects:** Common (≥1/100 to <1/10): Dizziness, vertigo, dysgeusia, tremor, tachycardia, deep venous thrombosis (*serious*), hypertension, hot flush, vomiting, nausea, pruritus generalised, chest discomfort, infusion site

paraesthesia, electrocardiogram T wave inversion and heart rate increased. Other serious undesirable effects (unknown frequency): Anaphylactic reaction, infusion-related reaction (including tachycardia, flushing, rash, dyspnoea, blurred vision). **Refer to the SmPC for details on full side effect profile and interactions**. **Legal classification:** POM. **UK basic NHS price:** 92p per IU. **Marketing authorisation (MA) numbers:** 650 IU: PLGB 34078/0031 / EU/1/18/1298/001, 1300 IU: PLGB 34078/0032 / EU/1/18/1298/002. **Name and address of MA holder:** Takeda UK Ltd, 1 Kingdom Street, London, W2 6BD, United Kingdom**. PI approval code:** pi-01692. **Date of preparation:** September 2021.

▼ This medicinal product is subject to additional monitoring. 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