Recombinant Factor VIII: Standard Half-Life

Product Specifics	KOVALTRY® Bayer	Kogenate® FS Bayer	Novoeight® Novo Nordisk	XYNTHA® Pfizer	Helixate® FS CSL Behring	Recombinate Shire	ADVATE Shire	Nuwiq Octapharma
Indications	Indicated for use in adults and children with hemophilia A (congenital Factor VIII deficiency) for: • On-demand treatment and control of bleeding episodes • Perioperative management of bleeding • Routine prophylaxis to reduce the frequency of bleeding episodes. KOVALTRY is not indicated for the treatment of von Willebrand disease	On-demand treatment and control of bleeding episodes in adults and children with hemophilia A. • Peri-operative management in adults and children with hemophilia A. • Routine prophylaxis to reduce the frequency of bleeding episodes in children with hemophilia A and to reduce the risk of joint damage in children without pre-existing joint damage. • Routine prophylaxis to reduce the frequency of bleeding episodes in adults with hemophilia A.	Indicated for use in adults and children with hemophilia A (congenital factor VIII deficiency or classic hemophilia) for: • Control and Prevention of bleeding • Perioperative management • Routine prophylaxis to prevent or reduce the frequency of bleeding episodes. Novoeight® is not indicated for the treatment of von Willebrand disease.	XYNTHA, Antihemophilic Factor (Recombinant), is indicated for use in adults and children with hemophilia A (congenital factor VIII deficiency) for control and prevention of bleeding episodes and for perioperative management. XYNTHA does not contain von Willebrand factor, and therefore is not indicated in von Willebrand's disease.	For control and prevention of bleeding episodes in adults and children with hemophilia A; peri-operative management in adults and children; and routine prophylaxis to 1) prevent or reduce the frequency of bleeding episodes and the risk of joint damage in children with hemophilia A with no pre-existing joint damage; 2) to prevent or reduce the frequency of bleeding in episodes in adults	RECOMBINATE is indicated in Hemophilia A for the prevention and control of hemorrhagic episodes. Also indicated in the perioperative management of patients with Hemophilia A.	Indicated for use in children and adults with hemophilia A (congenital factor VIII deficiency) for: • Control and prevention of bleeding episodes. • Perioperative management. • Routine prophylaxis to prevent or reduce the frequency of bleeding episodes. ADVATE is not indicated for the treatment of von Willebrand disease.	Nuwiq is a recombinant antihemophilic factor [blood coagulation factor VIII (Factor VIII)] indicated in adults and children with Hemophilia A for: • On-demand treatment and control of bleeding episodes • Perioperative management of bleeding • Routine prophylaxis to reduce the frequency of bleeding episodes Nuwiq is not indicated for the treatment of von Willebrand Disease.
Contraindications	Do not use in patients who have history of hypersensitivity reactions to the active substance, mouse or hamster protein, or other constituents of the product	Patients who have manifested life-threatening immediate hypersensitivity reactions, including anaphylaxis, to the product or its components, including mouse or hamster proteins	Do not use in patients who have had life-threatening hypersensitivity reactions, including anaphylaxis, to Novoeight or its components (including traces of hamster proteins)	Do not use in patients who have manifested life-threatening immediate hypersensitivity reactions, including anaphylaxis, to the product or its components, including hamster proteins.	Patients who have manifested life-threatening immediate hypersensitivity reactions, including anaphylaxis, to the product or its components, including mouse or hamster proteins	In patients who have manifested life-threatening immediate hypersensitivity reactions, including anaphylaxis, to the product or its components, including bovine, mouse, or hamster proteins.	ADVATE is contraindicated in patients who have life-threatening hypersensitivity reactions, including anaphylaxis, to mouse or hamster protein or other constituents of the product	Nuwiq is contraindicated in patients who have manifested life-threatening hypersensitivity reactions, including anaphylaxis, to the product or its components.
Nutrient in Cell Culture	Human- and animal-derived raw materials are not added to the cell culture, purification, or formulation processes	The cell culture medium contains human plasma protein solution and recombinant insulin, but does not contain any proteins derived from animal sources.	Novoeight® is produced using a defined cell culture medium which does not contain any proteins derived from human or animal sources	The cell line is grown in a chemically defined cell culture medium that contains recombinant insulin, but does not contain any materials derived from human or animal sources.	The cell culture medium contains Human Plasma Protein Solution (HPPS) and recombinant insulin, but does not contain any proteins derived from animal sources.	Bovine serum albumin and aprotinin	ADVATE is a purified glycoprotein consisting of 2,332 amino acids that is synthesized by a genetically engineered Chinese hamster ovary (CHO) cell line but does not contain plasma or albumin. The CHO cell line employed in the production of ADVATE is derived from that used in the biosynthesis of RECOMBINATE.	BDD-rFVIII is produced by recombinant DNA technology in genetically modified human embryonic kidney (HEK) cells with no animal or human derived materials added during the manufacturing process or to the final product.
Stabilizer in Final Formulation	2.2% glycine, 1% sucrose, 30 mM sodium chloride, 2.5 mM calcium chloride, 20 mM histidine and 80 ppm polysorbate 80.	Sucrose: 0.9-1.3% (250 IU, 500 IU, 1,000 IU); 0.9-1.2% (2,000 IU, 3,000 IU) Glycine: 21–25 mg/mL (250 IU, 500 IU, 1,000 IU); 20-24 mg/mL (2,000 IU, 3,000 IU) Histidine: 18–23 mmol/L(250 IU, 500 IU, 1,000 IU); 17–22 mmol/L (2,000 IU, 3,000 IU)	18 mg/mL sodium chloride 1.5 mg/mL L-histidine 3 mg/mL sucrose 0.1 mg/mL polysorbate 80 0.055 mg/mL L-methionine 0.25 mg/mL calcium chloride dihydrate	Sucrose	Sucrose (0.9-1.3%), Glycine (21-25 mg/mL), and Histidine (18-23 mM/L) in 250 IU, 500 IU, 1,000 IU Sucrose (0.9-1.2%), Glycine (20-24 mg/mL and Histidine (17-22 mM/L) in 2000 IU, 3000 IU	Human albumin, calcium, polyethylene glycol, sodium, histidine, polysorbate 80.	Mannitol, trehalose, sodium, histidine, Tris, calcium chloride, polysorbate-80, glutathione	The reconstituted product contains the following excipients per mL: 18 mg sodium chloride, 5.4 mg sucrose, 5.4 mg L-arginine hydrochloride, 0.3 mg calcium chloride dihydrate, 1.2 mg poloxamer 188, and 1.2 mg sodium citrate dihydrate.
Viral Safety Processes	The production process incorporates two dedicated viral clearance steps: (1) a detergent treatment step for inactivation and (2) a 20 nanometer filtration step for removal of viruses and potential protein aggregates.	The purification process includes a solvent/detergent virus inactivation step in addition to the use of the purification methods of ion exchange chromatography, monoclonal antibody immunoaffinity chromatography, along with other chromatographic steps designed to purify recombinant factor VIII and remove contaminating substances.	20-nm filtration. Solvent/Detergent Treatment.	The purification process uses a series of chromatography steps, one of which is based on affinity chromatography using a patented synthetic peptide affinity ligand. The process also includes a solvent-detergent viral inactivation step and a virus-retaining nanofiltration step.	The purification process includes a solvent/detergent virus inactivation step in addition to the use of the purification methods of ion exchange chromatography, monoclonal antibody immunoaffinity chromatography, along with other chromatographic steps designed to purify recombinant factor VIII and remove contaminating substances.	Immunoaffinity chromatography	Immunoaffinity chromatography. Solvent/Detergent Treatment.	The active substance is concentrated and purified by a series of chromatography steps, which also includes two dedicated viral clearance steps: solvent/detergent (S/D) treatment for virus inactivation and 20 nm nanofiltration for removal of viruses.
Product Half Life	0 to <6 yrs : 12.1 ± 2.7 hours 6 to <12 yrs: 12.0 ± 2.1 hours 12 to 17 yrs: 14.4 ± 5.5 hours ≥18 yrs: 14.2 ± 3.5 hours	13.74 ± 1.82 hours	Adults/adolescents with hemophilia A t½: 10.8-12 hours Children with hemophilia A t½ = 7.7-10 hours	11.2 + 5.0 hours (initial visit); 11.8 ± 6.2 (month 6); 16.7 ± 5.4 (pre-surgery). Compared to adults, the half-life of XYNTHA is shorter in children and the clearance (based on per kg body weight) is approximately 40% higher in children.	Adults: 13.7 ± 1.82 hours Children: 10.7 hours	14.6 ± 4.9 hours	Adults >16 years: 12.0 ± 4.2, infants 8.7 ± 1.4, 2 to < 5 year olds: 9.5 ± 1.8, 5 to <12 year olds 11..2 ± 3.5, 12 to <16 year olds 12.0 ± 2.9	In adults: 17.1 + 11.2 In children 2 to 5 years: 11.9 + 5.4 In children 6 to 12 years: 13.1 + 2.6
Product Recovery Percentage	0 to <6 yrs; 1.6 (IU/dL)/(IU/kg) 6 to 12 yrs; 1.7 (IU/dL)/(IU/kg) ≥12 yrs; 2.3 (IU/dL)/(IU/kg)	2.20 ± 0.34	Adults/adolescents with hemophilia A - incremental recovery: 0.02-0.028 (IU/mL)/(IU/kg) Children with hemophilia A - incremental recovery: 0.018-0.025 (IU/mL)/(IU/kg)	Incremental recovery: 2.15 ± 0.44 IU/dL per IU/kg (initial visit); 2.47 ± 0.84 (month 6); 2.17 ± 0.47 (pre-surgery)	2.1 ± 0.3 %/IU/kg in adults and 1.9 ± 1.25-2.76%/IU/kg in children	Calculated ratio of actual to expected recovery; 121.2 ± 48.9%. Actual baseline recovery observed was 123.9 ± 47.7 IU/dL.	Recovery IU/dL/IU/kg in vivo adults: 2.6 ± 0.5, IU/dL/IU/kg infants: 2.1 ± 0.5 2 to <5 years 1.8 ± 0.4, 5 to <12 years 2.1 ± 0.6, 12 to <16 years 2.1 ± 0.5	In adults: 2.1 + 0.3 In children 2 to 5 years: 1.6 + 0.2 In children 6 to 12 years: 1.6 + 0.4
Storage Requirements	Store KOVALTRY at +2°C to +8°C (36°F to 46°F) for up to 30 months from the date of manufacture. Do not freeze. Within this period, KOVALTRY may be stored for a single period of up to 12 months at temperatures up to +25°C or 77°FRecord the starting date of room temperature storage on the unopened product carton. Once stored at room temperature, do not return the product to the refrigerator. The shelf-life then expires after storage at room temperature for 12 months, or after the expiration date on the product vial, whichever is earlier. Do not use KOVALTRY after the expiration date indicated on the vial. Protect KOVALTRY from extreme exposure to light and store the vial with the lyophilized powder in the carton prior to use.	Product as Packaged for Sale: Store Kogenate® FS at +2°C to +8°C (36°F to 46°F) for up to 30 months from the date of manufacture. Within this period, Kogenate® FS may be stored for a period of up to 12 months at temperatures up to +25°C or 77°F, such as in home treatment situations. The starting date of room temperature storage should be clearly recorded on the unopened product carton. Once stored at room temperature, the product must not be returned to the refrigerator. The shelf-life then expires after the storage at room temperature, or the expiration date on the product vial, whichever is earlier. Do not use Kogenate® FS after the expiration date indicated on the vial. Do not freeze. Protect from extreme exposure to light and store the lyophilized powder in the carton prior to use. Product After Reconstitution: Administer Kogenate® FS within 3 hours after reconstitution. It is recommended to use the administration set provided.	Store Novoeight® in the original package to protect from light. Store under refrigeration at a temperature of 36–46°F (2-8°C) for up to 30 months from the date of manufacture until the expiration date stated on the label. Within the 30-month period, Novoeight® may also be stored at room temperature not to exceed 86°F (30°C) for up to 12 months. When stored at room temperature, clearly record the date when product was removed from the refrigerator in the space provided on the outer carton. Total storage time at room temperature should not exceed 12 months. Do not return the product to the refrigerator. Do not use Novoeight® after the end of the 12-month period at room temperature storage, or after the expiration date stated on the vial, whichever occurs earlier. Do not freeze Novoeight®. Use Novoeight® within 4 hours after reconstitution when stored at room temperature. Store reconstituted product in the vial. Discard any unused reconstituted product stored at room temperature for more than 4 hours.	XYNTHA: Store XYNTHA under refrigeration at a temperature of 2° to 8°C (36° to 46°F) for up to 36 months from the date of manufacture until the expiration date stated on the label. XYNTHA may also be stored at room temperature not to exceed 25°C (77°F) for up to 3 months. After room temperature storage, XYNTHA can be returned to the refrigerator until the expiration date. Do not store XYNTHA at room temperature and return it to the refrigerator more than once. Clearly record the starting date at room temperature storage in the space provided on the outer carton. At the end of the 3-month period, immediately use, discard, or return the product to refrigerated storage. The diluent syringe may be stored at 2° to 25°C (36° to 77°F). Do not freeze, to prevent damage to the pre-filled syringe. During storage, avoid prolonged exposure of XYNTHA to light. XYNTHA SOLOFUSE: Store XYNTHA® SOLOFUSE™ under refrigeration at a temperature of 2° to 8°C (36° to 46°F) for up to 36 months from the date of manufacture until the expiration date stated on the label. Within the expiration date, XYNTHA® SOLOFUSE™ also may be stored at room temperature not to exceed 25°C (77°F) for up to 3 months. Clearly record the starting date at room temperature storage in the space provided on the outer carton. At the end of the 3-month period, immediately use or discard the product. Do not put the product back into the refrigerator.	Store in refrigerator at 2-8°C (36-46°F) for period indicated by the expiration date on the label. Within this period, Helixate FS may also be stored at room temperature, not to exceed 25°C (77°F), for up to 12 months. Once stored at room temperature, do not return the product to the refrigerator. Do not freeze. Protect from extreme exposure to light and store the lyophilized powder in the carton prior to use.	RECOMBINATE can be refrigerated [2° - 8°C (36° - 46°F)] or stored at room temperature, not to exceed 30°C (86°F). Avoid freezing to prevent damage to the diluent vial. Do not use beyond the expiration date printed on the box.	2°-8°C (36°-46°F). May be stored at room temperature, up to 30°C (86°F) for up to 6 months not to exceed the expiration date. Do not freeze.	Protect from light. Store at 2 – 8°C (35 – 46°F) for up to 24 months. Do not freeze. During the shelf life, the product may be kept at room temperature [up to 25°C (77°F)] for a single period not exceeding 3 months. After storage at room temperature, do not return the product to the refrigerator. Do not use after the expiration date. Keep the reconstituted solution at room temperature. Do not refrigerate after reconstitution. Use the reconstituted solution immediately or within 3 hours after reconstitution. Discard any remaining solution.
Shelf Life from Date of Manufacture	30 months	30 months	30 months (may also be stored at room temperature not to exceed 86°F (30°C) for up to twelve (12) months)	Shelf life for both vial and Dual Chamber Syringe presentations are 36 months at the recommended storage conditions.	30 months under refrigeration	36 months	24 months	24 months
How Supplied / Diluent Volume	250 IU - 2.5mL, 500 IU - 2.5mL, 1000 IU - 2.5mL, 2000 IU - 5mL, 3000 IU - 5mL	250 IU - 2.5 mL, 500 IU - 2.5 mL, 1,000 IU - 2.5 mL, 2,000 IU - 5 mL, 3,000 IU - 5 mL	The diluent for reconstitution of Novoeight® is 4 mL of 0.9% sodium chloride solution and is supplied as a clear colorless solution in a pre-filled diluent syringe.	250 IU - 4 mL, 500 IU - 4 mL, 1,000 IU - 4 mL, 2,000 IU - 4 mL, 3,000 IU - 4 mL	250 IU - 2.5 mL, 500 IU - 2.5 mL, 1,000 IU - 2.5 mL, 2,000 IU - 5 mL, 3,000 IU - 5mL	5 mL	2 mL, 5 mL	250, 500, 1000, 2000 IU; 2.5mL