Policy Number	RX501.160
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Wilate

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Disclaimer

Medical policies are a set of written guidelines that support current standards of practice. They are based on current generally accepted standards of care developed by: nonprofit professional association(s) for the relevant clinical specialty, third-party entities that develop treatment criteria, or other federal or state governmental agencies. A requested therapy must be proven effective for the relevant diagnosis or procedure. For drug therapy, the proposed dose, frequency and duration of therapy must be consistent with recommendations in at least one authoritative source. This medical policy is supported by FDA-approved labeling and/or nationally recognized authoritative references to major drug compendia, peer reviewed scientific literature and generally accepted standards of medical care. These references include, but are not limited to: MCG care guidelines, DrugDex (IIa level of evidence or higher), NCCN Guidelines (IIb level of evidence or higher), NCCN Compendia (IIb level of evidence or higher), professional society guidelines, and CMS coverage policy.

Carefully check state regulations and/or the member contract.

Each benefit plan, summary plan description or contract defines which services are covered, which services are excluded, and which services are subject to dollar caps or other limitations, conditions or exclusions. Members and their providers have the responsibility for consulting the member's benefit plan, summary plan description or contract to determine if there are any exclusions or other benefit limitations applicable to this service or supply. **If there is a discrepancy between a Medical Policy and a member's benefit plan, summary plan description or contract, the benefit plan, summary plan description or contract will govern.**

Legislative Mandates

EXCEPTION: For members residing in the state of Ohio, § 3923.60 requires any group or individual policy (Small, Mid-Market, Large Groups, Municipalities/Counties/Schools, State Employees, Fully-Insured, PPO, HMO, POS, EPO) that covers prescription drugs to provide for the coverage of any drug approved by the U. S. Food and Drug Administration (FDA) when it is prescribed for a use recognized as safe and effective for the treatment of a given indication in one or more of the standard medical reference compendia adopted by the United States Department of Health and Human Services or in medical literature even if the FDA has not approved the drug for that indication. Medical literature support is only satisfied when safety and efficacy has been confirmed in two articles from major peer-reviewed professional medical journals that present data supporting the proposed off-label use or uses as generally safe and effective. Examples of accepted journals include, but are not limited to, Journal of

American Medical Association (JAMA), New England Journal of Medicine (NEJM), and Lancet. Accepted study designs may include, but are not limited to, randomized, double blind, placebo controlled clinical trials. Evidence limited to case studies or case series is not sufficient to meet the standard of this criterion. Coverage is never required where the FDA has recognized a use to be contraindicated, and coverage is not required for non-formulary drugs.

Coverage

von Willebrand Disease

Wilate (von Willebrand Factor/Coagulation Factor VIII Complex [Human]) **may be considered medically necessary** when the following criteria are met:

- Documentation of von Willebrand disease (any type) that is unresponsive or intolerant or contraindicated to treatment with desmopressin; AND
- Any of the following:
  - On-demand treatment and control of bleeding episodes in children and adults; or
  - Perioperative management of bleeding in children and adults; or
  - Routine prophylaxis to reduce the frequency of bleeding episodes in children 6 years of age and older and adults.

Hemophilia A

Wilate (von Willebrand Factor/Coagulation Factor VIII Complex [Human]) **may be considered medically necessary** in individuals ≥12 years of age with hemophilia A for the following indications:

- Routine prophylaxis to reduce the frequency of bleeding episodes; or
- On-demand treatment and control of bleeding episodes.

Wilate (von Willebrand Factor/Coagulation Factor VIII Complex [Human]) **is considered experimental, investigational and/or unproven** for all other non-Food and Drug Administration approved indications.

Policy Guidelines

None.

Description

von Willebrand Disease (VWD)

von Willebrand disease is an inheritable bleeding disorder, and one of the most common, affecting up to 1% of the population in the United States (U.S.). According to the Centers for Disease Control and Prevention (CDC), approximately 3.2 million people in the U.S. have VWD. (2, 3) Individuals with VWD are either missing or low in the clotting protein von Willebrand factor (VWF). VWF binds to factor VIII, another clotting protein, and platelets in blood vessel

walls. This process helps to form a platelet plug during the clotting process; individuals with VWD are unable to form this plug, or it takes longer to form. (2)

Types of VWD

There are three main types of VWD: (2, 3)

- Type 1: The most common type, it is found in 60%-80% of individuals who have low levels of VWF in their blood, ranging from 20%-50% of normal; symptoms are usually mild.
- Type 2: Found in 15%-30% of individuals who have normal levels of VWF, but the factor does not function as it should. Type 2 is broken down into four subtypes: type 2A, type 2B, type 2M, and type 2N, depending on the specific way the VWF is defective. These individuals experience mild to moderate symptoms.
- Type 3: This type is found in 5%-10% of individuals; they have very low levels or no VWF in their blood. Some may also have low factor VIII. Symptoms are typically severe, and include spontaneous bleeding episodes, often into joints or muscles.

Another type of VWD is acquired VMD, where there is a lack of prior personal bleeding, a negative family history of VWD and nongenetic cause such as after a diagnosis of an autoimmune disease such as lupus, or from heart disease or some types of cancer. It can also occur after taking certain medications. (2, 3)

Symptoms (2, 3)

Individuals with VWD may become symptomatic at any age. Individuals with mild or moderate disease may experience the following symptoms:

- Frequent (more than 5/year) epistaxis (nosebleeds) lasting longer than 10 minutes;
- Bleeding from cuts or injuries that last longer than 10 minutes;
- Bruising easily, with bruises that are raised and larger than a quarter;
- Low iron or have been treated for anemia;
- Heavy bleeding after any surgery including dental surgery, following childbirth or miscarriage;
- History of family members having any of these symptoms, or have been diagnosed with a bleeding disorder such as von Willebrand disease or hemophilia;
- Heavy menstrual bleeding requiring changing of pad or tampon hourly or lasting longer than 7 days.

Treatment

Treatment options for individuals with VWD include:

- Desmopressin (DDAVP), which is a synthetic analogue of vasopressin. It may be administered subcutaneously, intravenously, or via intranasal spray. DDVAP leads to increased von Willebrand factor and factor VIII levels.
- von Willebrand factor/factor VIII (VWF/FVIII) concentrates, which are purified plasma-derived concentrates of VWF/FVIII used for treatment of bleeds and for surgical prophylaxis when DDAVP is ineffective or contraindicated.

- Tranexamic acid can also be used as an anti-fibrinolytic agent. It prevents the breakdown of fibrin clots.
- Cryoprecipitate and fresh frozen plasma (FFP) can be used in life-threatening scenarios. (4)

Hemophilia A

Hemophilia A is a genetic bleeding disorder caused by insufficient levels of factor VIII (factor 8) resulting in poor blood clotting. It is an X-linked recessive disorder predominately affecting males, although some females who carry the gene may have mild or rarely, severe symptoms of bleeding. (5, 6) Hemophilia A occurs in approximately 1 in 4000 to 1 in 5000 live male births, with about half to two-thirds having severe disease (factor VIII activity <1% of normal). (6) The age of onset and frequency of bleeding episodes depend on the amount of factor VIII protein and overall clotting ability of the blood. Regardless of severity, in most individuals, bleeding episodes tend to be more frequent in childhood and adolescence than in adulthood. (5)

Symptoms

In mild hemophilia A, individuals may experience bruising and bleeding from the mucous membranes such as nosebleed or bleeding from the gums. More serious or prolonged bleeding may occur after surgery or dental procedures, injury, or trauma and is out of proportion for the procedure or trauma. Mild hemophilia A may go undiagnosed until a surgical procedure is needed, or the individual suffers an injury or trauma. (5)

Individuals with moderate hemophilia A are at risk for prolonged bleeding following surgery, dental procedures, or trauma. These individuals rarely experience spontaneous bleeding (bleeding episodes that occur without any apparent cause). Moderate hemophilia A is often diagnosed by 5 or 6 years of age. (5, 6)

Severe hemophilia A is associated with spontaneous bleeding episodes. This can often result in bleeding into the deep muscles or joints (hemarthroses), causing pain and swelling along with restricted movement of the joint. These cases usually become apparent during infancy and a diagnosis is often made by 2 years of age. Without prophylactic treatment, these individuals may experience bleeding from minor mouth injuries. They can experience spontaneous bleeding into any organ system including the kidneys, the gastrointestinal tract, and the brain. Genitourinary and gastrointestinal bleeding may respectively cause blood in the urine (hematuria) and black or bloody stools (melena, hematochezia). Intracranial bleeding may cause headaches, stiff neck, vomiting, seizures, mental status changes including excessive sleepiness and poor arousability. If untreated, these frequently occurring spontaneous bleeding events can be life-threatening. (5)

Treatment

There is no cure for hemophilia A. Treatment consists of replacing the missing clotting factor protein (factor VIII) and preventing complications associated with the disorder. Replacement of this protein may be obtained using recombinant factor VIII, which is artificially created in a lab, and does not contain components derived from human blood. Factor VIII can also be obtained from frozen plasma. Individuals with mild or moderate hemophilia A can be treated with

replacement therapy as needed to treat specific bleeding episodes. Affected individuals and family members can be trained to administer infusions at home. This is especially important for individuals with severe disease because infusion of factor VIII concentrate is most effective within one hour of the onset of a bleeding episode. In general, rapid treatment is important because it reduces pain and damage to the joints, muscle or other affected tissues or organs. (5)

Regulatory Status
Wilate is a human plasma-derived, sterile, purified, double virus inactivated von Willebrand Factor/Coagulation Factor VIII Complex. It was approved by the U.S. Food and Drug Administration (FDA) in 2009. It is currently indicated in children and adults with VWD for on-demand treatment and control of bleeding episodes and perioperative management of bleeding. Wilate is labeled for routine prophylaxis to reduce the frequency of bleeding episodes in children 6 years of age and older as well as adults with VWD. It is indicated in adolescents and adults with hemophilia A for routine prophylaxis to reduce the frequency of bleeding episodes as well as on-demand treatment and control of bleeding episodes.

The safety and effectiveness of Wilate have not been established for pediatric patients <12 years of age with hemophilia A. (1)

Rationale

This policy is based on the U.S. Food and Drug Administration labeled indications for Wilate (von Willebrand Factor/Coagulation Factor VIII Complex [Human]).

von Willebrand Disease (1)
Treatment of Bleeding Episodes
Clinical efficacy of Wilate in the control of bleeding in subjects with von Willebrand disease (VWD) was determined in four prospective, open-label, non-controlled clinical studies excluding pharmacokinetic (PK) study. For inclusion in the studies, subjects had to have inherited VWD (any type) that did not respond to desmopressin acetate. Subjects aged ≥12 to ≤65 years were eligible to enter three of the four studies, and subjects aged ≥6 to ≤85 years were eligible for one study. Exclusion criteria included the administration of other plasma-derived or blood products or desmopressin acetate 15 days before study entry, administration of acetylsalicylic acid 7 days before study entry, symptomatic infection, past or present inhibitor activity (3 studies), and severe liver or kidney disease (3 studies). A total of 70 VWD subjects with a mean age of 37 years (range 5–77 years) were enrolled in the studies, of whom 37 were type 3 and 30 were male. The total number of exposure days to Wilate for all investigations across the four studies ranged from 202 to 4917 days. Treated bleeding episodes (BEs) were analyzed for efficacy using a set of objective criteria in addition to a subjective 4-point hemostatic efficacy scale (excellent, good, moderate and none) which was determined at the discretion of the investigator. In assessing efficacy using the objective criteria, treatment of a bleeding episode was classified as a success when none of the criteria listed below were met:

- The episode was additionally treated with another VWF-containing product (excluding whole blood).
- The subject received a blood transfusion during the episode.
- Follow-up treatment with a daily dosage of Wilate that was greater than or equal to 50% (≥50%) above the initial dose (for bleeding episodes with more than 1 day of treatment).
- Treatment duration of more than 4 days (> 4 days) in cases of severe bleeding (other than gastrointestinal).
- Treatment duration of more than 3 days (> 3 days) in cases of moderate bleeding (other than gastrointestinal).
- Treatment duration of more than 2 days (> 2 days) in cases of minor bleeding (other than gastrointestinal).
- The last efficacy rating of the bleeding episode was 'moderate' or 'none.'

BEs treated with Wilate are summarized for all subjects (n=45) and subjects aged 5–16 years (n=11) in Table 1. Among the 70 VWD subjects administered Wilate in clinical studies (excluding the PK study), 45 received on demand treatment for 1068 BEs. Using the above objective criteria, corresponding efficacy for each bleeding event was rated as being successful in 84% of the episodes. In these 45 subjects with BEs, 93% of the successfully treated BEs occurred in VWD type 3 subjects (n=25). In 11 pediatric subjects aged 5–16 years, efficacy was rated as being successful in 87.6% of BEs.

Table 1. Proportion of Successful Treatments of Bleeding Episodes with Wilate

	Number of BEs[a]	**Number of Successfully Treated BEs**	**% Success (95% CI)**
All subjects (n=45)	1068	898	84.1 (81.8-86.2)
Subjects 5-16 years (n=11)	234	205	87.6 (82.7-91.5)

BEs: bleeding episodes; CI: confidence interval.

[a] A “bleeding episode” may involve bleeding in multiple sites in this analysis.

Dosing information for 972 successfully treated “bleeding episodes” (1423 infusions), and 211 successfully treated BEs (289 infusions) in subjects aged 5–16 years, for regional bleeding is summarized in Table 2. For the purpose of assigning success/failure to regional bleeding that occurred at the same time, bleeding at different sites over the same time span was counted as separate BEs. Thus, the number of these “episodes” is different from that in the overall evaluation for success/failure of Wilate in the treatment of BEs in Table 1. The majority of BEs were treated for 1-3 days. In subjects with gastrointestinal (GI) bleeds, the duration for product use to control bleeding was longer (up to 7 days).

Table 2. Administered Dosages (VWF:RCo in IU/kg) in Bleeding Episodes[a] Successfully Treated with Wilate: Mean ± SD (Range)

Location	**All Subjects (n=45)**		**Subjects 5-16 years (n=11)**	
	Initial Dose	**Subsequent Doses**	**Initial Dose**	**Subsequent Doses**

	# of Infusions	Dose: Mean ± SD (Range)	# of Infusions	Dose: Mean ± SD (Range)	# of Infusions	Dose: Mean ± SD (Range)	# of Infusions	Dose: Mean ± SD (Range)
Joints	542	28 ± 13 (7 - 69)	259	21 ± 10 (7 - 60)	117	32 ± 13 (14 -69)	41	25 ± 9 (12 - 62)
Epistaxis	91	25 ± 10 (13 -78)	41	22 ± 14 (8 - 77)	25	25 ± 10 (14 -52)	5	37 ± 25 (12 - 77)
GI Tract	64	43 ± 19 (9 - 76)	61	36 ± 21 (9 - 76)	1	22 (N/A)	0	N/A
Oral	33	27 ± 14 (10 -80)	8	24 ± 18 (8 - 60)	21	24 ± 8 (16 -52)	2	25 ± 13 (16 - 35)
Gynecological	52	28 ± 17 (12 -77)	35	26 ± 9 (9 - 52)	33	27 ± 16 (12 -69)	25	26 ± 8 (12 - 52)
Other[b]	189	24 ± 12 (12 -95)	48	20 ± 13 (10 -95)	14	27 ± 7 (19 -37)	5	19 ± 4 (16 - 26)

VWF:RCo: von Willebrand factors and ristocetin cofactor; IU/kg: international units per kilogram; SD: standard deviation; N/A: not applicable

[a] For the purpose of this analysis, bleeding at each site is counted as a separate "episode."

[b] "Other" includes mostly muscle bleeds, hematuria, ecchymosis, hematoma, and other miscellaneous sites of bleeding.

Prevention of Bleeding in Surgery (Perioperative Management)

A prospective, open-label, single-arm, uncontrolled, multi-center clinical study was conducted to investigate the safety and hemostatic efficacy of Wilate in 28 subjects (19 female and 9 male) who underwent 30 surgeries. Two female subjects underwent 2 surgeries each. Subjects ranged in age from 12 to 74 years (median=36). Three subjects were between 12 and 17 years old and 4 were 65 years or older. Six subjects had type 1 VWD, 1 had type 2A, 1 type 2B, and 20 had type 3 VWD. One type 1 and one type 3 subject had 2 surgeries each.

Twenty-one surgeries were classified as major (e.g., orthopedic joint replacement, cesarean section and vaginal deliveries, laminectomy, tonsillectomy, appendectomy, 3rd molar extractions) and 9 were classified as minor (e.g., meniscectomy, teeth extractions other than 3rd molars, septoplasty, biopsy). Seven surgeries (3 major, 4 minor) were performed in type 1 VWD subjects, 2 surgeries (1 major, 1 minor) were performed in type 2 (A/B) VWD subjects, and 21 surgeries (17 major, 4 minor) were performed in type 3 VWD subjects. The types of surgery for the 9 minor procedures were: dental (n=5, 55.6%); orthopedic (n=2, 22.2%); ophthalmologic (n=1, 11.1%); and ear, nose and throat (n=1, 11.1%). The types of surgery for the 21 major procedures were: orthopedic (n=8, 38.1%); obstetric/gynecological (n=5, 23.8%); gastrointestinal (n=4, 19.0%); dental (n=2, 9.5%); and ear, nose and throat (n=2, 9.5%). The type of surgery according to VWD type were: VWD type 1 (n=7) – dental (n=4, 57.1%), orthopedic (n=2, 28.6%), and ear, nose and throat (n=1, 14.3%); VWD type 2 (A/B) (n=2) – orthopedic (n=1, 50%), and obstetric/gynecological (n=1, 50%); VWD type 3 (n=21) – orthopedic (n=7, 33.3%), gastrointestinal (n=4, 19.0%), obstetric/gynecological (n=4, 19.0%), dental (n=3, 14.3%), ear, nose and throat (n=2, 9.5%), and ophthalmologic (n=1, 4.8%).

Dosing was individualized based on *in-vivo* recovery results performed before surgery. Mean total loading dose per infusion was 51.4 IU/kg (median 52.1 IU/kg; range 27-77 IU/kg). Major surgeries required a mean loading dose of 54.7 IU/kg (median 55.5 IU/kg; range 36-69 IU/kg) in comparison with a mean loading dose of 41.9 IU/kg (median 37.5 IU/kg; range 27−77 IU/kg) for minor surgeries. Mean total maintenance dose per infusion was 28.5 IU/kg (median 28.5 IU/kg; range 8-63 IU/kg). Major surgeries required a mean maintenance infusion of 29.6 IU/kg (median 30 IU/kg; range 8-63 IU/kg) in comparison with a mean maintenance infusion of 21.6 IU/kg (median 20.6 IU/kg; range 14-38 IU/kg) for minor surgeries.

Efficacy of Wilate in surgical procedures was assessed by the surgeon at the conclusion of surgery and by the investigator-hematologist at 24 hours following completion of the final maintenance dose. Efficacy of Wilate was assessed using a stringent and objective 4-point ordinal efficacy scale (excellent, good, moderate, or none) based on estimated expected versus actual blood loss, transfusion requirements and post-operative bleeding and oozing. A rating of excellent or good was required to declare the outcome a success. An independent data monitoring committee (IDMC) additionally conducted an independent *post hoc* adjudication of intra-and post-operative assessments made by the surgeon/investigator-hematologist. In situations where the IDMC's assessment differed from that of the surgeon and/or investigator-hematologist, the IDMC assessment took priority.

The overall efficacy of Wilate treatment for surgical procedures in this study was 96.7%. Treatment with Wilate was successful in all minor surgeries and in 95.2% of major surgeries (Table 3). It was also successful in all surgical procedures in VWD type 3 and type 2 subjects and in 85.7% of procedures in VWD type 1 subjects (Table 4). One failure was reported in a VWD type 1 subject undergoing lumbar laminectomy (major surgery) who experienced slightly greater blood loss (25 mL) than the expected maximum (20 mL).

Table 3. Hemostatic Efficacy Assessments by Severity of Surgery as Adjudicated by the IDMC (n=30)

Efficacy Grade	Minor (n=9)			Major (n=21)			All Surgeries (n=30)		
	n (%)	Rate	98.75% CI	n (%)	Rate	98.75% CI	n (%)	Rate	98.75% CI
Success	9 (100)	1.000	0.569, 1.000	20 (95.2)	0.952	0.704, 1.000	29 (96.7)	0.967	0.784, 1.000
Failure	0			1 (4.8)			1 (3.3)		

IDMC: independent data monitoring committee; CI: confidence interval; n: number of surgeries; rate: overall success rate.

Table 4. Hemostatic Efficacy Assessment by Type of VWD as Adjudicated by the IDMC (n=30)

Efficacy Grade	VWD type 1			VWD type 2			VWD type 3		
	n (%)	Rate	98.75% CI	n (%)	Rate	98.75% CI	n (%)	Rate	98.75% CI
Overall IDMC Assessment									

Success	6 (85.7)	0.857	0.328, 0.999	2 (100)	1.000	0.079, 1.000	21 (100)	1.000	0.785, 1.000
Failure	1 (14.3)			0			0		

VWD: von Willebrand Disease; IDMC: independent data monitoring committee; CI: confidence interval; n: number of surgeries; rate: overall success rate.

In this study, actual blood loss (median) was lower than the expected maximal estimated blood loss in all types of surgeries. The actual blood loss was also lower than the average predicted blood loss in minor surgeries and equal in major surgeries (Table 5).

Table 5. Expected and Estimated Blood Loss During Surgery

Estimated Blood Loss	Minor Surgery (n=9)	Major Surgery (n=21)
Expected Maximum - Median (range) mL	50 (1-200)	500 (20-2000)
Expected Average – Median (range) mL	20 (1-100)	100 (5-1500)
Actual - Median (range) mL	15 (1-50)	100 (0-1200)

Intra-operative transfusion was predicted in 5 subjects, but actually given in only 2. One subject received platelets intra-operatively for previously existing thrombocytopenia and one subject who underwent abdominal hysterectomy received one infusion of rejuvenated (in biochemical solution) packed red blood cells intraoperatively which was planned pre-surgery.

Three subjects received transfusions following surgery due to anemia and low hemoglobin values seen post-operatively.

Routine Prophylaxis

A prospective, non-controlled, international, multi-center clinical study was conducted to demonstrate that Wilate is efficacious in bleeding prophylaxis in 33 evaluable subjects with VWD. The total annualized bleeding rates under prophylactic treatment in this study was compared to the annualized bleeding rates recorded for the same patients during a previous, non-interventional, on-demand treatment study. Annualized bleeding rates for all bleeding episodes, treated and untreated, for the on-demand treatment and the prophylaxis treatment are summarized in Table 6.

Subjects ranged in age from 7 to 61 years (median=18); 19 (57.6%) were male and 14 (42.4%) were female; 97% were White and 3% Black or African American. Nine subjects were between 6 and 11 years old, 6 were between 12 and 17 years old and 18 were 17 years or older. Six subjects had severe type 1 VWD, 5 had type 2A, and 22 had type 3 VWD. Subjects were treated for 12 months of prophylaxis with a dose of 20-40 IU/kg Wilate, mean dose=30.57 IU/kg.

There were 10 (30.3%) subjects with 0 bleeding episodes and 15 (45.5%) subjects with 0 spontaneous bleeding episodes.

Table 6. Annualized Bleeding Rate in Adult Subjects and in Pediatric Subjects (6-17 Years Old) under Prophylaxis

	On-demand treatment (n=33)	Prophylaxis treatment (n=33)	Ratio of ABRs (95% confidence interval)
Annualized bleeding rate (± SD) per subject for all types of bleeds (excluding menstrual bleeds)	33.38 ± 23.61 (median 24, range 11-114.5)	5.24 ± 7.75 (median 2, range 0-35.8)	0.16 (0.1, 0.27)
Annualized bleeding rate (± SD) per subject - spontaneous bleeds	24.42 ± 20.05 (median 19, range 4.9-92.8)	3.23 ± 5.92 (median 1, range 0-24.6)	0.14 (0.08, 0.25)
Annualized bleeding rate (± SD) per subject – joint bleeds	7.56 ± 11.51 (median 3.43, range 0-39.1)	0.53 ± 1.48 (median 0, range 0-6.9)	0.08 (0.03, 0.18)

ABRs: annualized bleeding rates; SD: standard deviation.

Hemophilia A (1)

Routine Prophylaxis

The efficacy of Wilate in routine prophylaxis was evaluated in a prospective, open-label, multicenter clinical study in which adults and adolescents aged 12-15 years were treated during 6 months of prophylaxis with 20-40 IU/kg Wilate, mean dose 32 IU/kg. Within the group of 55 subjects, of which 50 adults and 5 adolescents, there were 30 (54.6%) subjects with 0 bleeding episodes, 12 (21.8%) subjects with 1 bleeding episode, 4 (7.3%) subjects with 2 bleeding episodes, 4 (7.3%) subjects with 3 bleeding episodes, and 5 (9%) subjects with 5 or more bleeding episodes. Annualized bleeding rates for all bleeding episodes, treated and untreated, are summarized in Table 7.

Table 7. Annualized Bleeding Rate in Adults and Pediatric Subjects under Prophylaxis

	Adults (n=50)	Adolescents (n=5)
Annualized bleeding rate (per subject) - spontaneous bleeds	1.67 ± 3.11 (median 0, range 0-11.76)	0 (median 0, range 0-0)
Annualized bleeding rate (per subject) for all types of bleeds	2.39 ± 3.77 (median 0, range 0-15.69)	0.4 ± 0.89 (median 0, range 0-2)

Treatment of Bleeding Episodes

The study presented above also provided data on the efficacy of Wilate in the treatment of bleeding episodes. The break-through bleeds were treated with Wilate doses adjusted to the severity of the bleed. Treatment efficacy was assessed by the patient or the patient's parents (together with the investigator in case of on-site treatment) using the predefined criteria using

an ordinal scale of excellent (abrupt pain relief and/or unequivocal improvement in objective signs of bleeding within approximately 8 hours after a single injection), good (definite pain relief and/or improvement in signs of bleeding within approximately 8–12 hours after an injection, requiring up to two injections for complete resolution), moderate (probable or slight beneficial effect within approximately 12 hours after the first injection, requiring more than two symptoms, requiring more than two injections for complete resolution), or none (no improvement within 12 hours, or worsening of symptoms, requiring more than two injections for complete resolution).

In the per protocol population (n=52) of the study performed in adults and adolescents aged 12-15 years, 57 bleeding episodes were treated with Wilate, of which 15 (26.3%) bleeding episodes were minor (e.g., early onset muscle and joint bleeds with no visible symptoms, such as little or no change in the range of motion of affected joint, mild restriction of mobility and activity, scrapes, superficial cuts, bruises, superficial mouth bleeds, and most nose bleeds), 32 (56.1%) were moderate (e.g., advanced soft tissue and muscle bleeds into the limbs, bleeding into the joint space, such as the elbow, knee, ankle, wrist, shoulder, hip, foot, or finger), 10 (17.5%) were major (e.g., complicated joint bleeds, bleeds of the pelvic muscles, eyes), and 0 (0%) were life-threatening (e.g., bleedings in the abdomen, digestive system or chest, central nervous system bleeds, bleedings in the area of the neck or throat or pharynx, or other major trauma). Forty-one bleeds (71.9%) were spontaneous and 16 (28.1%) were traumatic. Thirty-six bleeding episodes (63.2%) were managed with one Wilate injection, 12 (21.1%) were managed with two injections, 7 (12.3%) were managed with 3 injections, and 2 (3.6%) required more than 3 injections. The mean dose of Wilate per injection was 34 IU/kg. Treatment efficacy was judged as excellent for 16 (28.1%) bleeding episodes, good for 32 (56.1%) bleeding episodes and moderate for 9 (15.8%) bleeding episodes. Therefore, 84.2% of all bleeding episodes were treated successfully. The one bleeding episode in one subject younger than 16 years (bleeding in finger) was treated with a single injection of 62.81 IU/kg of Wilate with excellent efficacy (successful treatment).

Further efficacy data in the treatment of bleeding episodes is available from a pooled analysis of 37 subjects with hemophilia A included in 3 additional clinical studies. These subjects had at least 150 exposure days at the time of enrollment into the study and had been treated for at least 50 exposure days and 6 months in the study. The analysis encompassed 973 bleeding episodes, of which 924 (95%) were treated successfully.

Coding

Procedure codes on Medical Policy documents are included **only** as a general reference tool for each policy. **They may not be all-inclusive.**

The presence or absence of procedure, service, supply, or device codes in a Medical Policy document has no relevance for determination of benefit coverage for members or reimbursement for providers. **Only the written coverage position in a Medical Policy should be used for such determinations.**

Benefit coverage determinations based on written Medical Policy coverage positions must include review of the member's benefit contract or Summary Plan Description (SPD) for defined coverage vs. non-coverage, benefit exclusions, and benefit limitations such as dollar or duration caps.

CPT Codes	None
HCPCS Codes	J7183

*Current Procedural Terminology (CPT®) ©2025 American Medical Association: Chicago, IL.

References

U.S. Food and Drug Administration Label:

1. Prescribing Label: Wilate (von Willebrand Factor/Coagulation Factor VIII Complex [Human]) November 2024. Available at <https://www.accessdata.fda.gov> (accessed February 25, 2026).

Other:

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Centers for Medicare and Medicaid Services (CMS)

The information contained in this section is for informational purposes only. HCSC makes no representation as to the accuracy of this information. It is not to be used for claims adjudication for HCSC Plans.

The Centers for Medicare and Medicaid Services (CMS) does not have a national Medicare coverage position. Coverage may be subject to local carrier discretion.

A national coverage position for Medicare may have been developed since this medical policy document was written. See Medicare's National Coverage at <https://www.cms.hhs.gov>.

Policy History/Revision

Date	Description of Change

09/01/2026	Policy updated. The following change was made to Coverage: Hemophilia A Coverage statement revised, removing "adolescents and adults" and replacing with "individuals ≥12 years of age". Reference 4 added; one removed.
10/01/2025	Policy updated with literature review. The following changes were made to Coverage: 1) Revised Coverage statement for von Willebrand disease to align with the current FDA label for Wilate (von Willebrand Factor/Coagulation Factor VIII Complex [Human]), including new indication for routine prophylaxis to reduce the frequency of bleeding episodes in children 6 years of age and older and adults; 2) Added "non-Food and Drug Administration approved" to the existing experimental, investigational and/or unproven statement. No new references added; others updated.
10/15/2024	Reviewed. No changes.
04/01/2024	New medical document. Wilate (von Willebrand Factor/Coagulation Factor VIII Complex [Human]) may be considered medically necessary in children and adults for on-demand treatment and control of bleeding episodes or perioperative management of bleeding for individuals with mild or moderate von Willebrand disease (Type 1 or 2) in whom the use of desmopressin is known or suspected to be ineffective or contraindicated, or individuals with severe von Willebrand disease (Type 3). Wilate (von Willebrand Factor/Coagulation Factor VIII Complex [Human]) may be considered medically necessary in adolescents and adults with Hemophilia A for routine prophylaxis to reduce the frequency of bleeding episodes; or on-demand treatment and control of bleeding episodes. It is considered experimental, investigational and/or unproven for all other indications.