CALL FOR STAKEHOLDER COMMENTS ON THE PRELIMINARY RECOMMENDATION OF THE HEALTH TECHNOLOGY ASSESSMENT (HTA) COUNCIL ON COAGULATION FACTOR VIII *for Hemophilia A* AND FACTOR VIII INHIBITOR BYPASSING ACTIVITY *for Hemophilia A with inhibitors and Hemophilia B with inhibitors*

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As of 10 April 2025, the Health Technology Assessment Council hereby makes public its **preliminary recommendations** on the possible financing of the following health technologies by the Department of Health (DOH) and the Philippine Health Insurance Corporation (PhilHealth), **for stakeholder feedback/comments**.

These health technologies were reviewed against clinical practice guidelines (CPGs) *[local and approved by the DOH, such as the DOH Omnibus Health Guidelines (OHG); and/or international, but locally adopted guidelines*], and existing recommendations by the World Health Organization (WHO). Further, costing analyses of these health technologies were performed. The specific recommendations and the supporting evidence reviewed and considered by the HTA Council are shown in ***Annex A***.

	Health Technology	Preliminary HTAC Recommendation *(further details in Annex A)*
1	**Plasma-derived Coagulation Factor VIII** [500 units/10mL (50 units/mL); 1000 units/20mL (50 units/mL); 2500 units/50mL (50 units/mL) powder solution for IV] for prophylaxis/prevention of bleeding in the pediatric population with hemophilia A	**Positive** recommendation for the **prophylaxis or prevention** of bleeding episodes in pediatric patients with hemophilia A Plasma-derived Coagulation Factor VIII is a standard of care based on the World Federation of Hemophilia (WFH) Guidelines for the Management of Hemophilia, 3rd edition (2020) *(High rating in the AGREE II tool)* for the prophylaxis of bleeding episodes in pediatric patients with Hemophilia A *(No Strength of recommendation stated)*. The WFH guidelines have been locally adopted by the Philippine Society of Hematology and Blood Transfusion (PSHBT) and the Philippine College of Hematology and Transfusion (PCHTM). The Philippine Society of Pediatric Hematology concurs with the use of CF VIII for pediatric patients with hemophilia A. Plasma-derived CF VIII is also included in the WHO EML for hemophilia A for all age groups. Furthermore, coagulation factor replacement therapy has long been the standard of care and a life-sustaining treatment to prevent bleeding episodes in individuals with hemophilia A. Although plasma-derived CF

		VIII is already listed in the PNF, the listed indication is only for adults with acquired hemophilia A. Alternative options (i.e., Recombinant CF VIII, Emicizumab) received marketing authorization in the Philippines; however, these alternative options are not financed by the government and not included in the WHO EML. Using this health technology for the prophylaxis or prevention of bleeding episodes, the cost ranges from PHP 522,020.00 to PHP 2,236,564.00 per patient per year. *(Note: Range of cost depends on various factors, including different volumes of preparation, brand, and patient weight*).
2	**Plasma-derived Coagulation Factor VIII** [500 units/10mL (50 units/mL); 1000 units/20mL (50 units/mL); 2500 units/50mL (50 units/mL) powder solution for IV] for treatment of bleeding in the pediatric population with hemophilia A	**Positive** recommendation for the **treatment** of bleeding episodes or hemorrhages in pediatric patients with hemophilia A Plasma-derived Coagulation Factor (CF) VIII is a standard of care based on the World Federation of Hemophilia (WFH) Guidelines for the Management of Hemophilia, 3rd edition (2020) *(High rating in the AGREE II tool)* for the treatment of bleeding episodes or hemorrhages in pediatric patients with hemophilia A *(No Strength of recommendation stated)*. The WFH guidelines are locally adopted by the PSHBT and the PCHTM. The Philippine Society of Pediatric Hematology concurs with the use of CF VIII for pediatric patients with hemophilia A. Plasma-derived CF VIII is also included in the WHO EML for hemophilia A for all age groups. Furthermore, coagulation factor replacement therapy has long been the standard of care and a life-saving treatment for bleeding episodes in individuals with hemophilia A. Although plasma-derived CF VIII is already listed in the PNF, the listed indication is only for adults with acquired hemophilia A. An alternative option (i.e., Recombinant CF VIII) is available in the Philippine Market; however, it is not financed by the government and not included in the WHO EML. Using this health technology for the treatment for major hemorrhages (i.e., iliopsoas or deep muscle bleeding, gastrointestinal bleeding, and intracranial bleeding), the cost ranges from PHP 320,360.00 to PHP 1,329,840.00 per patient per year *(Note: Range of cost depends on various factors, including different volumes of preparation, brand, bleeding site, and patient weight*). However, it is important to note that this estimated cost only covers costs directly related to the use of the health technology and does not cover other costs related to the general treatment of symptoms or complications related to bleeding episodes (e.g., hospitalization, surgical cost).
3	**Factor VIII Inhibitor Bypassing Activity** *[500U/10mL; 1000U/20mL; 2500U/50mL powder solution for infusion*	**Positive** recommendation for the treatment of bleeding events in hemophilia A patients with inhibitors Factor VIII Inhibitor Bypassing Activity is the standard of care for the treatment of bleeding events in hemophilia A patients with inhibitors based on the World Federation of Hemophilia (WFH) Guidelines for the

	(IV)] for hemophilia A with inhibitors (for treatment of bleeding)	Management of Hemophilia, 3rd edition (2020) *(High rating in the AGREE II tool)*. The WFH guidelines have been locally adopted by the PSHBT and the PCHTM. In addition, the Philippine Society of Pediatric Hematology (PSPH) supports the inclusion of Factor VIII Inhibitor Bypassing Activity in the PNF, as it has long been the standard treatment. Its inclusion will address significant gaps in the treatment and management of hemophilia A patients with inhibitors, providing them access to this life-saving medication. An alternative treatment (i.e., recombinant factor VIIa), although available in the Philippine market, is not listed in the PNF nor financed by the government. Using this health technology, the total cost of treatment is presented below, which varies per age group *(Note: the range of values depends on various factors, including the required dosage depending on the severity of the bleed and the cost of management of adverse events.)* However, it is important to note that this estimated cost only covers costs directly related to the use of the health technology and does not cover other costs related to the general treatment of symptoms or complications related to bleeding episodes (e.g., hospitalization, surgical cost: ● **1-4 years old:** PHP 142,098.33 to PHP 310,127.32 per patient per year. ● **5-13 years old:** PHP 234,216.62 to PHP 494,363.92 per patient per year. ● **14-18 years old:** PHP 418,453.22 to PHP 862,837.11 per patient per year. ● **19 years old and above:** PHP 556,630.67 to PHP 1,185,251.15 per patient per year
4	**Factor VIII Inhibitor Bypassing Activity** *[500U/10mL; 1000U/20mL; 2500U/50mL powder solution for infusion (IV)]* for hemophilia B with inhibitors (for treatment of bleeding)	**Positive** recommendation for the treatment of bleeding events in hemophilia B patients with inhibitors Factor VIII Inhibitor Bypassing Activity is the standard of care for the treatment of bleeding events in hemophilia B patients with inhibitors based on the World Federation of Hemophilia (WFH) Guidelines for the Management of Hemophilia, 3rd edition (2020) *(High rating in the AGREE II tool)*. The WFH guidelines were locally adopted by the PSHBT and the PCHTM. In addition, the PSPH supports the inclusion of Factor VIII Inhibitor Bypassing Activity in the PNF, as it has long been the standard treatment. Its inclusion will address significant gaps in the treatment and management of hemophilia B patients with inhibitors, providing them access to this life-saving medication. An alternative treatment (i.e., recombinant factor VIIa), although available in the Philippine market, is not listed in the PNF nor financed by the government. Using this health technology, the total cost of treatment varies per age group *(Note: the range of values depends on various factors, including the required dosage depending on the severity of the bleed and the cost of management of adverse events.)* However, it is important to note that this estimated cost only covers costs directly related to the use of the health technology and does not cover other costs related to the general treatment of symptoms or complications related to bleeding episodes (e.g., hospitalization, surgical cost):

		• **1-4 years old:** PHP 142,098.33 to PHP 310,127.32 per patient per year. • **5-13 years old:** PHP 234,216.62 to PHP 494,363.92 per patient per year. • **14-18 years old:** PHP 418,453.22 to PHP 862,837.11 per patient per year. • **19 years old and above:** PHP 556,630.67 to PHP 1,185,251.15 per patient per year

All comments, inputs, and/or appeals on the above preliminary recommendation may be submitted until **17 April 2025** *(Thursday)*, for the consideration of the HTA Council through email at hta@dost.gov.ph.

Please use the prescribed form for appeals indicated on the official HTA Philippines website [https://hta.dost.gov.ph/appeals-2/]. **Appeals not following the prescribed format, and those submitted beyond the deadline shall not be entertained**.

Should you have any questions or concerns regarding the preliminary recommendation, please do not hesitate to contact us through the same email address or via telephone call at (02) 8837-2071 local 4100.

Thank you very much and best regards.

On behalf of the HTA Philippines:

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Annex A. Summary of Evidence for the Preliminary Recommendation of Priority Topics

Health technology	Clinical Practice Guidelines	WHO recommendation	Costing
Plasma-derived Coagulation Factor VIII *[500 units/10mL (50 units/mL); 1000 units/20mL (50 units/mL); 2500 units/50mL (50 units/mL) powder solution for IV]* for prophylaxis of hemophilia A in the pediatric population	Included in the WFH Guidelines for the Management of Hemophilia, 3rd edition (2020): *"For pediatric patients with severe hemophilia A or B, the WFH recommends early initiation of prophylaxis with clotting factor concentrates (standard or extended half-life FVIII/FIX) or other hemostatic agent(s) prior to the onset of joint disease and ideally before age 3, in order to prevent spontaneous and break-through bleeding including hemarthroses which can lead to joint disease."* Per consultation with PSHBT, in the context of prophylaxis low dose prophylaxis is used (i.e., 1000-1500 IU/kg per year or 10-15 IU FVIII/kg 2-3 days per week due to limited availability and high cost of CF concentrates.	Included in the WHO EML for Hemophilia A: *"Parenteral > General injections > IV: 250 IU in vial powder for injection; 500 IU in vial powder for injection; 1000 IU in vial powder for injection"* Included in the WHO Selection of Essential Drugs (1979): *"Factor IX complex (coagulation factors II, VII, IX, X, concentrate) (c) (2,8) (dried)"*	The annual cost of prophylaxis for a pediatric Hemophilia A patient using lyophilized plasma-derived Coagulation Factor VIII is estimated to range from PHP 522,020.00 to PHP 2,236,564.00. The variation in cost depends on the patient's weight, the brand of the drug, and the available volume of the preparation. The cost of Coagulation Factor VIII is the main driver of the cost of prophylaxis in the majority of pediatric age groups, followed by the cost of treatment monitoring. Details on the costing: ● [Evidence Slides] Coagulation Factor VIII.pdf
Plasma-derived Coagulation Factor VIII *[500 units/10mL (50 units/mL); 1000 units/20mL (50 units/mL); 2500 units/50mL (50 units/mL) powder solution for IV]* for treatment of	Included in the WFH Guidelines for the Management of Hemophilia, 3rd edition (2020): *"In hemophilia patients presenting with suspected central nervous system bleeds or bleed-related symptoms, clotting factor replacement therapy should be administered immediately before investigations are performed".* *"In patients with hemophilia presenting with*	Included in the WHO EML for Hemophilia A: *"Parenteral > General injections > IV: 250 IU in vial powder for injection; 500 IU in vial powder for injection; 1000 IU in vial powder for*	The annual cost of treatment of major hemorrhages (i.e., iliopsoas or deep muscle bleeding, gastrointestinal bleeding, intracranial bleeding) for a pediatric Hemophilia A patient using lyophilized plasma-derived Coagulation Factor VIII is estimated to range from PHP 320,360.00 to PHP 1,329,840.00. The variation in cost depends on the patient's weight, site of bleeding, the brand of the drug, and the available volume of the preparation. However, it is important to note that this estimated cost only covers costs directly related to the use of the health technology and does not cover other costs related to the general treatment of

hemophilia A in the pediatric population	*suspected central nervous system bleeding that could be life-threatening, clotting factor replacement therapy should be administered immediately before investigations are performed and continued until the bleed resolves".* ● *"In patients with hemophilia who have been treated for central nervous system bleeding, secondary prophylaxis is recommended to prevent bleed recurrence".* *"In patients with throat and neck bleeding, clotting factor replacement therapy should be administered immediately and critical care evaluation sought".* *"In patients with lacerations and abrasions, clotting factor replacement therapy should be administered and the wound sutured immediately, if appropriate, in consultation with appropriate surgeons".* Per consultation with PSHBT, in the context of treatment of hemorrhage, the following low dose practice pattern treatment regimen per bleeding episode is followed: Iliopsoas or deep muscle bleeding ● Initial dose: maintain 20 IU/dL peak factor level for 1-2 days ● Maintenance dose: maintain 10 IU/dL peak factor level for 3 days Gastrointestinal bleeding ● Initial dose: maintain 30 IU/dL peak factor level for 3 days ● Maintenance dose: maintain 10 IU/dL peak factor level for 4 days	*injection"* Included in the WHO Selection of Essential Drugs (1979): *"Factor IX complex (coagulation factors II, VII, IX, X, concentrate) (c) (2,8) (dried)"*	symptoms or complications related to bleeding episodes (e.g., hospitalization, surgical cost). For older children, the main cost driver is the drug regimen while for younger children, the main cost driver is treatment monitoring cost. Details on the costing: ● [Evidence Slides] Coagulation Factor VIII.pdf

	Intracranial bleeding • Initial dose: maintain 50 IU/dL peak factor level for 3 days • Maintenance dose: maintain 30 IU/dL peak factor level for 4 days		
Factor VIII Inhibitor Bypassing Activity *[500U/10mL; 1000U/20mL; 2500U/50mL powder solution for infusion (IV)] for hemophilia A with inhibitors (for treatment of bleeding)*	Included in the International CPG from WFH Guidelines for the Management of Hemophilia, 3rd edition (2020) (pp. 109-115) *"For patients with hemophilia A and inhibitors who have acute bleeds, the WFH recommends FVIII concentrate for those with low-responding inhibitors, and a bypassing agent (recombinant factor VIIa [rFVIIa] or aPCC) for those with high-responding inhibitors"*	*None*	The cost of this health technology varies per age group: • **1-4 years old:** PHP 142,098.33 to PHP 310,127.32 per patient per year. • **5-13 years old:** PHP 234,216.62 to PHP 494,363.92 per patient per year. • **14-18 years old:** PHP 418,453.22 to PHP 862,837.11 per patient per year. • **19 years old and above:** PHP 556,630.67 to PHP 1,185,251.15 per patient per year Details on the costing • [Evidence Slides] Factor VIII Inhibitor Bypass…
Factor VIII Inhibitor Bypassing Activity *[500U/10mL; 1000U/20mL; 2500U/50mL powder solution for infusion (IV)] for hemophilia B with inhibitors (for treatment of bleeding)*	Recommended by the World Federation of Hemophilia (WFH) Guidelines for the Management of Hemophilia, 3rd edition (2020) (pp. 115-119) *"For patients with hemophilia B and low-responding FIX inhibitors, the WFH recommends use of a FIX-containing product to treat acute bleeds, as long as there is no allergic reaction to FIX"*	*None*	The cost of this health technology varies per age group: • **1-4 years old:** PHP 142,098.33 to PHP 310,127.32 per patient per year. • **5-13 years old:** PHP 234,216.62 to PHP 494,363.92 per patient per year. • **14-18 years old:** PHP 418,453.22 to PHP 862,837.11 per patient per year. • **19 years old and above:** PHP 556,630.67 to PHP 1,185,251.15 per patient per year Details on the costing: • [Evidence Slides] Factor VIII Inhibitor Bypass…