World Federation of Hemophilia (WFH) Prophylaxis Guidelines

Recommendation for Pediatric Patients

"For pediatric patients with severe haemophilia A or B, the WFH recommends early initiation of prophylaxis with clotting factor concentrates (standard or extended half-life) or other hemostatic agent(s) prior to the onset of joint disease and ideally before age 3."

Recommendation for Adolescents & Adults

"For adolescents and adults with haemophilia who show evidence of joint damage and have not as yet been on prophylaxis, the WFH recommends commencing tertiary prophylaxis in order to reduce the number of hemarthroses, spontaneous and breakthrough bleeding, and slow down the progression of hemophilic arthropathy."

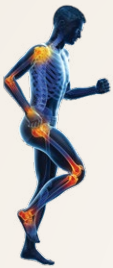
Srivastava et al. *Haemophilia* 2020;26(suppl 6):1-158.

Definition of Prophylaxis	
Primary prophylaxis	Regular continuous prophylaxis **started in the absence of documented joint disease**, determined by physical examination and/or imaging studies, and before the second clinically evident joint bleed and 3 years of age
Secondary prophylaxis	Regular continuous prophylaxis **initiated after 2 or more joint bleeds** but before the onset of joint disease; this is usually at 3 or more years of age
Tertiary prophylaxis	Regular continuous prophylaxis **initiated after the onset of documented joint disease**. Tertiary prophylaxis typically applies to prophylaxis commenced in adulthood

Prophylaxis Defined According to Intensity		
Prophylaxis Intensity	**Hemophilia A**	**Hemophilia B**
High-dose prophylaxis	25-40 IU FVIII/kg every 2 days (>4,000 IU/kg per year)	40-60 IU FIX/kg twice per wk (>4,000 IU/kg per year)
Intermediate-dose prophylaxis	15-25 IU FVIII/kg 3 days per wk (1,500-4,000 IU/kg per year)	20-40 IU FIX/kg twice per wk (2,000-4,000 IU/kg per year)
Low-dose prophylaxis (with escalation of dose intensity, as needed)	10-15 IU FVIII/kg 2-3 days per wk (1,000-1,500 IU/kg per year)	10-15 IU FIX/kg 2 days per wk (1,000-1,500 IU/kg per year)

Srivastava et al. *Haemophilia* 2020;26(suppl 6):1-158.

Factors to Consider When Personalizing Prophylaxis in Patients With Hemophilia A



- Adherence
- Age
- Venous access

- Timing of infusions

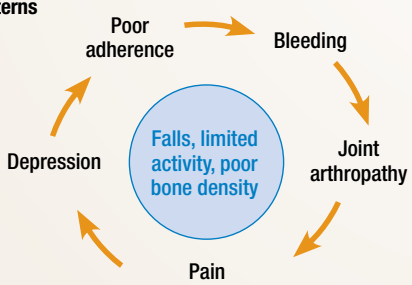
- Bleeding phenotype
- Peak/trough
- Factor half-life
- Joint status

- Activity type
- Activity pattern

Ar et al. *Expert Rev Hematol.* 2016;9:1203-1208.

Prophylaxis Therapies in Hemophilia A	
Standard Half-Life (SHL) Factor VIII Concentrates	Turoctocog alfa Lonoctocog alfa Octocog alfa Simoctocog alfa Moroctocog alfa
Extended Half-Life (EHL) Factor VIII Concentrates	Efmoroctocog alfa Rurioctocog alfa pegol Damoctocog alfa pegol Turoctocog alfa pegol
Non-Factor Therapies	Emicizumab-kxwh

Adherence Patterns



Thornburg and Duncan. *Patient Prefer Adherence* 2017;11:1677.

Adherence

Potential Barriers to Adherence	
Patient-related	Health beliefs
	Age
	Depression, anxiety
Condition-related	Bleeding frequency
Treatment-related	Costs and perceived costs
	Dosing regimen
	Frequency of infusions
	Venous access
	Ability to self-administer at home
Healthcare system-related	Access to hemophilia treatment center
	Insurance coverage
Socioeconomic	Acculturation
	Language
	Health literacy
	Balancing child's care with other family and social needs

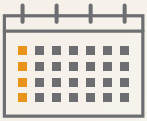
Ways to Improve Adherence	
Education about prophylaxis (peer-to-peer, multimedia; tailored to language, culture, and literacy level)	Prophylaxis benefits – Promote prophylaxis as a way to decrease inhibitors – Promote prophylaxis as a way to enhance activities – Increase awareness about important studies (Joint Outcome Study; Warren et al. *Blood Adv* 2020;4:2451-2459)
	Venous access – Improve ease of venous access – Psychological interventions to decrease anxiety – Training for independence
	Navigating healthcare system
	Patient e-health portals
Monitoring	Direct observation (mobile)
	Logs
	Diary
Communication/Reminders	Cell phone app
	Text messaging
	Phone calls
	More frequent visits
Incentives (age-appropriate)	Reward charts
	Financial
Social Support	Social workers for anxiety/depression screening

Thornburg and Duncan. *Patient Prefer Adherence* 2017;11:1677.
Thornburg. *Haemophilia* 2008;14(1):25-29.
Witkop et al. *Patient Prefer Adherence* 2019;13:1577.
De Moerloose et al. *Haemophilia* 2008;14:931-938.
Hacker et al. *Haemophilia* 2001;7:392-396.
Warren et al. *Blood Adv* 2020;4(110):2451-2459.

Emicizumab Prophylaxis: 3 Dosing Regimens

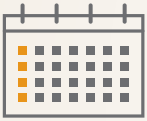
Indication: is a bispecific factor IXa- and factor X-directed antibody indicated for routine prophylaxis to prevent or reduce the frequency of bleeding episodes in adult and pediatric patients ages newborn and older with hemophilia A (congenital factor VIII deficiency) with or without factor VIII inhibitors.

Loading dose of 3 mg/kg by subcutaneous injection once weekly for the first 4 weeks

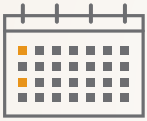


- The prophylactic use of FVIII products may be continued during the first week of prophylaxis
- Discontinue the prophylactic use of BPAs the day before starting prophylaxis

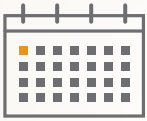
At Week 5, start on 1 of the maintenance dosing options



Every Week
1.5 mg/kg



Every 2 Weeks
3 mg/kg



Every 4 Weeks
6 mg/kg

BPA, bypassing agent.

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