WFH
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Chapter 6
PROPHYLAXIS IN HEMOPHILIA

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PROPHYLAXIS

Prophylaxis is the **Standard of Care** everywhere around the world

Prophylaxis is the regular administration of a hemostatic agent with the goal of preventing bleeding in people with hemophilia while allowing them to lead active lives and achieve quality of life comparable to non-hemophilic individuals.

Early initiation of prophylaxis, ideally before age 3 years

Prophylaxis should be individualized*, and sufficient to prevent all bleeds at all times

*Individualizing prophylaxis means that if patients continue to experience bleeds, their prophylaxis regimen should be escalated (in dose/frequency or both) to prevent bleeding. See the PK characteristics of the CFC product used in Table 6.3.

Prophylaxis treatment includes standard half-life factor, extended half-life factor and non-factor replacement therapy

In countries with significant healthcare constraints, the WFH advocates for the use of prophylaxis over episodic (on demand) therapy but recognizes that less intensive prophylaxis with CFCs may be used.

Conventional factor prophylaxis with **standard half-life clotting factor** is defined by intensity (these categories have not (as yet) been revised for use of EHL clotting factors or non-factor therapies)

Prophylaxis intensity	Hemophilia A	Hemophilia B
High-dose prophylaxis	25 - 40 IU FVIII/kg every 2 days (>4000 IU/kg per year	40 - 60 IU FIX/kg twice per week (>4000 IU/kg per year)
Intermediate-dose prophylaxis	15 - 25 IU FVIII/kg 3 days per week (1500- 4000 IU/kg per year)	20 - 40 IU FIX/kg twice per week (2000- 4000 IU/kg per year)
Low-dose prophylaxis*	10 - 15 IU FVIII/kg 2- 3 days per week (1000- 1500 IU/kg per year)	10 - 15 IU FIX/kg 2 days per week (1000- 1500 IU/kg per year)

*Should only be taken as the starting point of replacement therapy to be tailored, as possible, to prevent bleeding.

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Variables that affect factor levels (standard half-life (SHL) and extended half-life (EHL)

Variables	Impacts on factor levels
Most important	
• Frequency of dosing[a]	• Doubling frequency of infusions (without changing the dose/infusion) provides on average 5 half-lives of additional coverage
• Half-life/clearance[b]	• Doubling half-life provides on average 5 half-lives of additional coverage
Least Important	
• Dose	• Doubling dose provides 1 half-life of additional coverage
• Recovery	• Doubling recovery provides 1 half-life of additional coverage

Prophylaxis can be given using either clotting factor replacement therapy (SHL or EHL) or non-factor replacement therapy

SHL replacement therapy

- Standard half-life (SHL) CFC can be used as prophylactic therapy for people with Hemophilia A and B
- Frequent infusions required:
  - 3-4 times per week for FVIII
  - 2-3 times per week for FIX
- Difficult to achieve factor trough levels much higher than 1 IU/dL (1%)
- Leads to need for central venous access devices (CVAD) in many children
- Can lead to reduced adherence in older children/adults

EHL replacement therapy

- EHL CFC are used as prophylaxis therapy for Hemophilia A and B
- EHL FVIII show modest improved half-lives (1.4-1.6-fold longer) vs SHL FVIII
- EHL FIX show greatly improved half-lives (3-5-fold longer) vs SHL FIX
- Allows for
  - Less frequent infusions (in most patients once weekly for HB; twice / wk for Hemophilia A), and/or
  - More effective prophylaxis: higher level of prevention of bleeds while maintaining similar dosing schedules

Non-factor replacement therapy

- Emicizumab is used as a prophylactic treatment for hemophilia A only
- Emicizumab is the only non-factor replacement therapy licensed at time of this publication
- Administered subcutaneously once weekly (or as infrequently as once every 2 or 4 weeks in some cases)
- Non-factor products may allow for less burdensome prophylaxis, which may improve adherence and lead to increased uptake of prophylaxis among patients not currently on prophylaxis (including those with moderate hemophilia), permitting them increased participation in social and sports activities

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For more information on the WFH Guidelines for the Management of Hemophilia, visit www.WFH.org/TGResourceHub