# Patient – Hemlibra Use in Hemophilia A Without Inhibitors

This letter contains information you requested on the use of Hemlibra® (emicizumab-kxwh) to treat people with hemophilia A without factor VIII (factor 8 or FVIII) inhibitors. This letter includes studies with the strongest and most relevant data from clinical trials.

This information is provided only for educational purposes and not for use in treatment decisions. You should talk with your healthcare provider for specific information and advice about your condition, your individual situation, healthcare coverage, and any current or potential treatments.

## Glossary

**Inhibitors:** In hemophilia A, inhibitors are antibodies against infused FVIII clotting proteins. These antibodies make the infused FVIII products not effective.

**Loading dose and maintenance dose:** A loading dose is a higher dose given at the beginning of treatment to make sure that the amount of drug in the body reaches a therapeutic level before dropping down to a lower maintenance dose that will keep the amount of drug in the body at the therapeutic level.

**Median:** The median is the middle number in a sorted list of numbers (example, 28 is the median of 5, 20, 28, 89, 100).

**On-demand:** On-demand refers to a treatment that is given as needed. For example, when bleeding occurs.

**Prophylaxis:** Also known as "prophy", it is a treatment given on a regular schedule to prevent bleeds.

**Spontaneous bleed:** A spontaneous bleed is a bleed that happens without an obvious cause.

**Subcutaneous injection:** Injection that is given under the skin in the subcutaneous space (in the fatty layer between the skin and muscle). The medicine is then absorbed into the small vessels of the subcutaneous space and goes into the blood where it works.

**Target joint:** A target joint is a joint that has frequent and recurrent bleeds resulting in joint damage.

**Treated bleed:** A treated bleed is any bleed that requires treatment with infused clotting factor.

## What is Hemlibra?

Hemlibra is a medicine that is approved by the Food and Drug Administration (FDA) for prophylaxis in adults and children with hemophilia A, with or without FVIII inhibitors.[1]

Hemlibra is given as a loading dose of 3 mg/kg by subcutaneous injection once weekly for the first 4 weeks, followed by a maintenance dose of either 1.5 mg/kg once weekly, or 3 mg/kg once every 2 weeks, or 6 mg/kg once every 4 weeks.[1]

## What is HAVEN 3 and what are the results in people with severe hemophilia A without inhibitors?

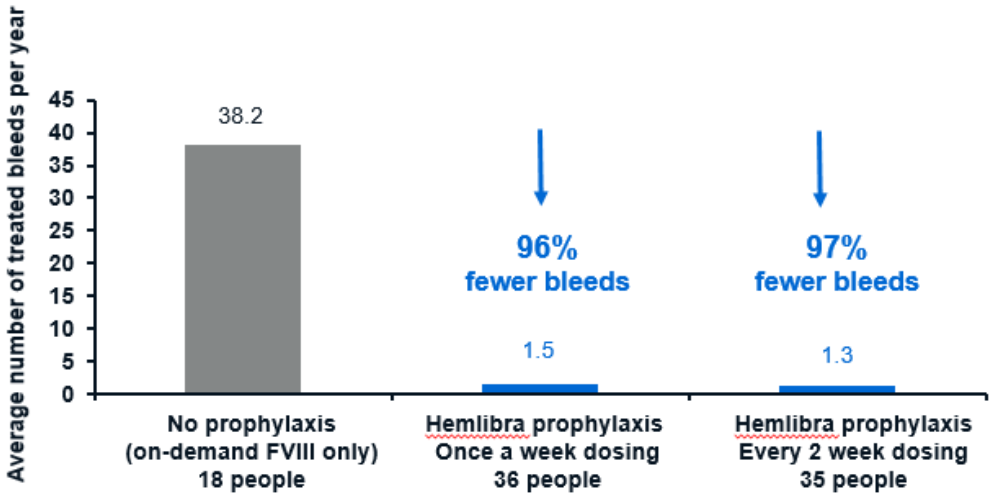
HAVEN 3 was a clinical trial that studied how safe and how well Hemlibra worked to prevent bleeds in 152 people (all males), 12 years or older with severe hemophilia A without inhibitors.[2] The effects of 2 different doses of Hemlibra were compared with no prophylaxis after at least 6 months on the study. People who used on-demand FVIII treatment before entering HAVEN 3 were randomly assigned to 1 of 3 treatments:

- **Hemlibra once a week**: 3 mg/kg once a week for 4 weeks, then 1.5 mg/kg once weekly
- **Hemlibra every 2 weeks**: 3 mg/kg once a week for 4 weeks, then 3 mg/kg every 2 weeks
- **No prophylaxis**: only on-demand FVIII to treat bleeds (did not use prophylaxis)

### *What was the effect of Hemlibra on bleeding in HAVEN 3?*

People who took Hemlibra prophylaxis had substantially fewer treated bleeds compared with people who took no prophylaxis (Figure 1).[2]

**Figure 1: Treated Bleed Results in HAVEN 3[2]**




Most people treated with Hemlibra prophylaxis (56% of those treated once a week and 60% of those treated once every 2 weeks) did not have any treated bleeds, whereas all people in the on-demand FVIII group (no prophylaxis) had at least one treated bleed. In addition, Hemlibra reduced the number of all bleeds (whether the bleed was treated or not), treated spontaneous bleeds, treated joint bleeds, and treated target joint bleeds compared with the on-demand group.[2]

### *Did Hemlibra prophylaxis prevent more bleeds than prophylaxis with infused FVIII?*

A "before and after study" compared the number of treated bleeds that happened in 48 people when they used FVIII prophylaxis, then entered HAVEN 3 and switched to Hemlibra once a week.[2]

After this group of 48 people switched from FVIII prophylaxis to Hemlibra prophylaxis, 68% fewer treated bleeds happened.[2] The average number of treated bleeds per year was 2 on Hemlibra prophylaxis compared to 5 on FVIII prophylaxis. On FVIII prophylaxis, 40% did not have treated bleeds, and on Hemlibra, 54% did not have treated bleeds.[2]

## What is HAVEN 4 and what are the results in people with severe hemophilia A without inhibitors?

HAVEN 4 studied how safe and how well Hemlibra worked to prevent bleeds in 41 people (12 years or older) with severe hemophilia A with or without inhibitors, after at least 6 months on the study.[3] Hemlibra was given as 3 mg/kg once a week for 4 weeks, then 6 mg/kg every 4 weeks. Most people who entered this study (36 people, or 88%) had hemophilia A without inhibitors.

### *What was the effect of Hemlibra dosed every 4 weeks on bleeding in HAVEN 4?*

Among the 41 people in the study, there were a total of 51 treated bleeds. Most of the treated bleeds (75%) were due to an injury or trauma; 25% were spontaneous bleeds.

Most people (56%) did not have treated bleeds while taking Hemlibra every 4 weeks, 29% did not have any bleeds (treated or not), and 71% did not have any treated joint bleeds.[3]

## What side effects were seen with Hemlibra in the HAVEN 3 and HAVEN 4 studies?

The most frequent side effects reported were redness, tenderness, warmth, and itching where Hemlibra injection was given.[2,3]

In HAVEN 3, 1 person stopped taking Hemlibra because of side effects that were mild in severity, including inability to sleep, hair loss, nightmare, feeling tired, depressed mood, headache, and itching.[2] In HAVEN 4, no one stopped taking Hemlibra because of side effects.[3]

## What is HAVEN 6 and what are the results in people with moderate and mild hemophilia A without inhibitors?

HAVEN 6 is a clinical trial conducted to evaluate the safety and effectiveness of Hemlibra to prevent bleeds in people with moderate and mild hemophilia A without FVIII inhibitors.[4]

In this trial, Hemlibra was given at a dose of 3 mg/kg once a week for 4 weeks, followed by patients' choice of maintenance dosing: 1.5 mg/kg once a week, 3 mg/kg twice a week, or 6 mg/kg every 4 weeks.

Results are available from 72 people treated with Hemlibra who were evaluated for a median of 56 weeks.

- 21 people had mild and 51 people had moderate hemophilia A without inhibitors
- 67% of people taking Hemlibra prophylaxis had no bleeds that needed infused FVIII
- 89% of people taking Hemlibra prophylaxis had no joint bleeds that needed infused FVIII

The most common side effects were headache and local injection site reactions; both in 17% of patients. There were 248 side effects in 72 patients. Fifteen patients reported a side effect that was considered related to Hemlibra; most common being local injection site reactions. Side effects did not cause any changes or discontinuation of treatment in any patient.

## What is HAVEN 7 and what are the interim (early) results in infants <12 months old with hemophilia A without inhibitors?

HAVEN 7 is an ongoing study evaluating the use of Hemlibra in infants less than 12 months old who had severe hemophilia A without FVIII inhibitors.[5] Interim analysis from the study in 54 infants (all males) are available.

Infants are started with a loading dose of 3 mg/kg once weekly for the first 4 weeks. Following the loading dose, maintenance dose of 3 mg/kg once every 2 weeks is given for 48 weeks. After 48 weeks, parents/caregivers may choose for their child to continue with the same dose or change to 1.5 mg/kg weekly or 6 mg/kg every 4 weeks for a 7 year long-term follow-up.

### *What was the effect of Hemlibra on bleeding in the interim (early) analysis in HAVEN 7?*

Results from the interim analysis showed that approximately 78% of patients had zero treated bleeds and 98% had zero treated muscle bleeds.[5] All treated bleeds were caused by injuries and none of the infants were treated for a spontaneous bleed. Overall, approximately 43% of infants had zero bleeds (treated or not). No incidences of brain hemorrhage occurred.

### *How safe was Hemlibra in the interim (early) analysis in HAVEN 7?*

In the interim analysis, 314 side effects were reported in 54 infants; approximately 93% of patients reported a side effect.[5] The only side effect that was deemed by the investigators to be related to Hemlibra was injection site reactions, which occurred in 17% of infants. Approximately 15% of infants had a serious side effect that included injuries and infections. There were no deaths and no serious side effects of blood clots and thrombotic microangiopathy. None of the side effects led to treatment discontinuation or dose change.

## Hemlibra Use in Hemophilia A without Inhibitors References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2. Mahlangu J, Oldenburg J, Paz-Patel I, et al. Emicizumab prophylaxis in patients who have hemophilia A without inhibitors [supplementary appendix appears online]. N Engl J Med 2018;379:811-822. https://www.nejm.org/doi/pdf/10.1056/NEJMoa1803550

3. Pipe S, Shima M, Lehle M, et al. Efficacy, safety, and pharmacokinetics of emicizumab prophylaxis given every 4 weeks in people with haemophilia A (HAVEN 4): a multicentre, open-label, non-randomised phase 3 study. Lancet. E-pub Date: July 2019. DOI # https://doi.org/10.1016/S2352-3026(19)30054-7.

4. Hermans C, Negrier C, Lehle M, et al. Emicizumab Prophylaxis for the Treatment of People with Moderate or Mild Hemophilia A without Factor VIII Inhibitors: Results from the Primary Analysis of the HAVEN 6 Study. Presented at the International Society on Thrombosis and Haemostasis in London, UK; July 9-13, 2022. ISTH Oral presentation #OC 30.5. https://www.isth.org/

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