Patient – Hemlibra and Treating Breakthrough Bleeds in Hemophilia A Without Inhibitors

This letter contains information you requested on treating breakthrough bleeds in people with hemophilia A without factor VIII (factor 8 or FVIII) inhibitors who take Hemlibra® (emicizumab-kxwh) prophylaxis. This letter includes studies with the strongest and most relevant data.

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

Activated prothrombin complex concentrates (aPCC): A bypassing agent also known as FEIBA® that contains active and inactive clotting factors.

Bypassing agent: This is a type of treatment developed for people with inhibitors. Bypassing agents go around or "bypass" the factors that are blocked by the inhibitor to help the body form a clot.

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 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.

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.

Thrombotic events: Blood clots that form in blood vessels.

Thrombotic microangiopathy (TMA): Thrombotic microangiopathy is a potentially life-threatening condition in which blood clots form in small blood vessels that may result in damage to the kidneys and/or other organs.

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 week.

What clinical trials studied Hemlibra in people with hemophilia A without FVIII inhibitors?

HAVEN 3 studied how safe and well Hemlibra prophylaxis worked to prevent bleeds in adults and adolescents with hemophilia A without FVIII inhibitors.[2] HAVEN 3 only enrolled people without inhibitors. Another study, HAVEN 4, enrolled adults and adolescents with or without FVIII inhibitors.[3]

- The HAVEN 3 study enrolled 152 people with hemophilia A without inhibitors. [2]
- The HAVEN 4 study enrolled 41 people with or without inhibitors.[3] Only 5 people had inhibitors, and the other 36 people did not have inhibitors.

Most of the information below will be from the HAVEN 3 study because the people who participated in this trial all had hemophilia A without FVIII inhibitors.

How should I treat breakthrough bleeds when using Hemlibra prophylaxis?

- Hemlibra increases the potential for your blood to clot.[1]
- Hemlibra cannot be used as a treatment for breakthrough bleeds. If you use Hemlibra prophylaxis, you need to have a second therapy available, like a FVIII product, to treat breakthrough bleeds.
- Talk to your doctor to develop a plan for managing breakthrough bleeds.
- Carefully follow your doctor's instruction regarding when to use infused FVIII, and the exact dose and schedule you should use to treat bleeds.
- Serious side effects of thrombotic microangiopathy and blood clots (thrombotic events) have happened in people who used aPCC (FEIBA®) to treat bleeds while on Hemlibra.
    - aPCC (FEIBA®) is a medicine that is used by some people with hemophilia A with factor VIII inhibitors, because they cannot use infused factor VIII therapy.
- It is recommended you keep track in a diary or journal the bleeds that happen and the treatment, doses, and when the doses were given to treat each bleed.

What was the experience in HAVEN 3 with using infused FVIII to treat breakthrough bleeds in people taking Hemlibra prophylaxis?

During the HAVEN 3 study, there were 215 treatment events with FVIII products in people taking Hemlibra.[2] Of these treatment events, 80% were treated with FVIII doses less than 50 IU/kg. Most treatment events (81%) lasted for less than 1 day. No serious side effects were related to the combined use of Hemlibra and FVIII.

After the main readout of the study above, 1 person in HAVEN 3 had an acute coronary artery syndrome, a condition resulting from reduced blood flow to the heart.[4] No aPCC (FEIBA®) was used in this case. The event happened around the time of a surgical procedure, and this person had a history of a heart condition. This person continued Hemlibra treatment in the study.

What serious side effects occurred when aPCC (FEIBA®) was used with Hemlibra in the clinical studies for hemophilia A with inhibitors?

Serious side effects of TMA and blood clots (thrombotic events) happened when on average a cumulative amount of >100 U/kg/24 hours of aPCC (FEIBA®) was given for 24 hours or more to people using Hemlibra prophylaxis.[1] These events happened in people with FVIII inhibitors in the HAVEN 1 study.

- aPCC (FEIBA®) is a bypassing agent used in people with hemophilia A with FVIII inhibitors, who do not respond to FVIII therapy.

During HAVEN 3, did people taking Hemlibra use short-acting or long-acting FVIII products to treat bleeds?

During HAVEN 3, people taking Hemlibra prophylaxis used FVIII products for a variety of reasons such as treating a bleed or before a surgical procedure.[2]

Among people taking Hemlibra who used FVIII products, most used short-acting FVIII, about 86% used short-acting FVIII product and about 13% used long-acting (also called extended half-life) FVIII products.[5] A few people used both short-acting and long-acting FVIII products during the study[5]

In HAVEN 3 how much infused FVIII was used to treat a bleed in people using Hemlibra?

Infused FVIII used to treat breakthrough bleeds was compared in 48 people who took FVIII prophylaxis before they switched to Hemlibra prophylaxis in HAVEN 3.[6] Overall, people used

less FVIII to treat bleeds when taking Hemlibra. This is because people had fewer bleeds when taking Hemlibra than when they took FVIII prophylaxis. The treatment of each breakthrough bleed was similar on Hemlibra and FVIII prophylaxis. While taking Hemlibra prophylaxis, most people used 1 – 4 infusions of FVIII to treat a bleed, and the median amount of FVIII that people used to treat a bleed was 50 units/kg.

Patient – Hemlibra and Treating Breakthrough Bleeds in Hemophilia A Without Inhibitors References

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