Patient – Side Effects with Hemlibra

This letter contains information you requested on side effects of Hemlibra® (emicizumab-kxwh). 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.

Inhibitors: In hemophilia A, inhibitors are antibodies against infused factor VIII (factor 8 or 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.

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): 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 weeks.[1]

Hemlibra increases the potential for your blood to clot. Carefully follow your doctor's instructions about when to use an on-demand bypassing agent or FVIII, and the exact dose and schedule you should use to treat bleeds.

Which studies looked at side effects of Hemlibra in people with hemophilia A?

Phase 3 studies have looked at how safe Hemlibra was in people with hemophilia A with or without FVIII inhibitors.[1]

- HAVEN 1, HAVEN 3, and HAVEN 4 enrolled adults and adolescents 12 years or older.
- HAVEN 2 enrolled children less than 12 years old.

Hemlibra was given as a loading dose of 3 mg/kg by subcutaneous injection once weekly for the first 4 weeks, followed by maintenance dosing:

- In HAVEN 1, the Hemlibra maintenance dose was 1.5 mg/kg once weekly.
- In HAVEN 2, the Hemlibra maintenance dose was either 1.5 mg/kg once weekly, or 3 mg/kg every 2 weeks, or 6 mg/kg every 4 weeks.
- In HAVEN 3, the Hemlibra maintenance dose was either 1.5 mg/kg/week or 3 mg/kg every 2 weeks.
- In HAVEN 4, the Hemlibra maintenance dose was 6 mg/kg every 4 weeks.

From the HAVEN studies, as well as an earlier small dose-finding study, information on side effects was collected from a total of 391 people with hemophilia A who took Hemlibra.

What were the most common side effects in people who got Hemlibra?

The most common side effects in people who got Hemlibra were redness, tenderness, warmth, or itching where the injection was given, also known as injection site reaction. Headache and joint discomfort were also common.[1] Table 1 shows side effects that happened in at least 5% of the people who took Hemlibra in the studies.

Table 1: Most Common Adverse Reactions (Side Effects)[1]

	Percent of People (Total 391 people)
Injection site reaction	22%
Joint discomfort	15%
Headache	15%
Diarrhea	6%
Fever	6%

How many thrombotic events (blood clots) and TMA events happened with Hemlibra and aPCC (FEIBA®) in the studies?

Blood clots happened in 0.5% of people (2 out of 391) and TMA in 0.8% of people (3 out of 391).[1] These events happened in the HAVEN 1 study.

- In each case, the blood clot or TMA happened when on average a cumulative amount of over 100 units/kg per 24 hours of aPCC (FEIBA®) was given for 24 hours or more while on Hemlibra.[1,2] Each of these 5 cases improved after aPCC (FEIBA®) was stopped.
- Neither blood clot needed blood thinning medicine. One of the 2 people with a blood clot restarted Hemlibra.[1,2]
- Of the 3 people with TMA, 1 person restarted Hemlibra. A death happened in 1 of these people because of rectal bleeding, unrelated to Hemlibra.[1,2]

What are signs and symptoms of blood clots and TMA?

Some signs and symptoms of blood clots and TMA are listed in Table 2. These are not all the possible signs or symptoms that could happen.[1] Tell your doctor right away or go to the nearest emergency department if you have any of these signs and symptoms.[1]

Table 2: Signs and Symptoms of TMA and Blood Clots[1]

	Description	Signs and Symptoms	
TMA (thrombotic microangiopathy)	A condition involving injury to and blood clots in small vessels that may cause harm to the kidneys, brain and other organs	• confusion • weakness • swelling of the arms and legs • yellowing of the skin • yellowing of the eyes	• stomach or back pain • nausea • vomiting • feeling sick • decreased urination
Blood clot (thrombotic event)	Blood clots can form in the blood vessels in your arm, leg, lung, or head	• swelling in your arm or leg • pain or redness in the arm or leg • shortness of breath • abnormal or difficulty breathing	• fast heart beat • coughing up blood • feeling faint • headache • numbness in the face • eye pain or swelling • trouble seeing

Side Effects with Hemlibra References

1. Hemlibra® [package insert]. Genentech, Inc.; South San Francisco, CA. October 2018.
2. Oldenburg J, Mahlangu JN, Kim B, et al. Emicizumab prophylaxis in hemophilia A with inhibitors [supplementary appendix appears online]. N Engl J Med 2017;377:809-818. https://www.ncbi.nlm.nih.gov/pubmed/28691557