

## Patient - Hemlibra and Surgeries and Procedures

This letter contains information you requested on surgeries and procedures performed in people with hemophilia A during treatment with 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

**Inhibitors:** In hemophilia A, inhibitors are antibodies against infused factor VIII (factor 8 or FVIII) clotting proteins. These antibodies make the infused factor VIII products not effective.

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

**Thrombotic events:** Blood clots that form in blood vessels.

### 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.<sup>1</sup>

### What were the HAVEN trials that studied Hemlibra?

Four Phase 3 trials studied how safe and how well Hemlibra worked to prevent bleeds in people with hemophilia A with or without FVIII inhibitors.<sup>1</sup>

- The HAVEN 1, 3, and 4 trials enrolled adult and adolescents, 12 years or older, with hemophilia A with or without FVIII inhibitors.<sup>1</sup>
- The HAVEN 2 trial enrolled children less than 12 years (or 12-17 years if they weighed <40 kg or 88 lbs) with hemophilia A with FVIII inhibitors.<sup>1</sup>

### Were surgeries or procedures performed in people treated with Hemlibra in the HAVEN clinical trials?

The HAVEN trials were not intended to study the outcomes of surgeries in people taking Hemlibra.<sup>2</sup> People could not enroll in the trials if they had a planned major surgery. Certain elective minor procedures were permitted and unplanned surgeries occurred during the HAVEN studies. These surgeries were managed by the treating doctor.

## How many surgeries occurred in the HAVEN trials in people taking Hemlibra?




A total of 233 surgeries were performed in 126 people treated with Hemlibra.<sup>2</sup>



- 215 minor surgeries and procedures were performed in 115 people
- 18 major surgeries were performed in 18 people

## What minor surgeries were performed in people taking Hemlibra in the HAVEN trials and how were they managed?



Most minor surgeries (66%, or 141 out of 215) were managed without preventive clotting factor.<sup>2</sup>

- Most of these (91%, or 128 out of 141) had no treated bleeds after the surgery.

<p>62 dental procedures</p> 	<ul style="list-style-type: none"><li>• No preventive clotting factor was used in 40 dental procedures<ul style="list-style-type: none"><li>○ 27 out of 40 had no bleeds after surgery</li><li>○ 13 out of 40 had bleeds that occurred after surgery. 9 bleeds were treated with clotting factor and 4 bleeds were not treated</li></ul></li><li>• 22 dental procedures were performed with preventive clotting factor<ul style="list-style-type: none"><li>○ 11 bleeds occurred after surgery, 5 were treated with clotting factor, and 6 were not treated</li></ul></li></ul>
<p>36 venous access device or port procedures</p> 	<ul style="list-style-type: none"><li>• No preventive clotting factor was used in 27 procedures<ul style="list-style-type: none"><li>○ 25 out of 27 had no bleeds after surgery</li><li>○ 2 out of 27 had bleeds that occurred after surgery. 1 was treated with clotting factor and 1 was not treated</li></ul></li><li>• 9 procedures were performed with preventive clotting factor<ul style="list-style-type: none"><li>○ 2 bleeds occurred after surgery and were treated with clotting factor</li></ul></li></ul>
<p>30 endoscopic procedures</p> 	<ul style="list-style-type: none"><li>• An endoscopic procedure is one in which an instrument is introduced into the body to give a view of its internal parts</li><li>• No preventive clotting factor was used in 17 procedures<ul style="list-style-type: none"><li>○ No bleeds occurred after surgery in any of the 17 cases</li></ul></li><li>• 13 procedures were performed with preventive clotting factor; 1 bleed occurred after surgery and did not require treatment</li></ul>

<p>25 joint procedures</p> 	<ul style="list-style-type: none"> <li>• No preventive clotting factor was used in 12 joint procedures <ul style="list-style-type: none"> <li>○ 11 out of 12 had no bleeds after surgery</li> <li>○ 1 out of 12 had bleeding that occurred after surgery and was treated with clotting factor</li> </ul> </li> <li>• 13 procedures performed with preventive clotting factor; 1 bleed occurred after surgery and did not require treatment</li> </ul>
<p>62 other surgeries and procedures</p> 	<ul style="list-style-type: none"> <li>• No preventive clotting factor was used in 45 procedures <ul style="list-style-type: none"> <li>○ 41 out of 45 had no bleeds after surgery</li> <li>○ 4 out of 45 had bleeds that occurred after surgery. 2 bleeds were treated with clotting factor and 2 bleeds were not treated</li> </ul> </li> <li>• 17 procedures performed with preventive clotting factor <ul style="list-style-type: none"> <li>○ 4 bleeds occurred after surgery and 2 were treated with clotting factor and 2 were not treated</li> </ul> </li> </ul>

## What major surgeries were performed in people taking Hemlibra in the HAVEN trials and how were they managed?

	<p>The most common type of major surgeries were joint surgeries, including joint arthroplasties and synovectomies.<sup>2</sup></p> <ul style="list-style-type: none"> <li>• Joint arthroplasties are joint replacements or joint reconstruction surgeries. <ul style="list-style-type: none"> <li>○ 5 major joint arthroplasties were performed on ankles, hips, and knees</li> </ul> </li> <li>• Synovectomies are surgeries performed to remove inflamed synovial tissue, which is a layer that lines the joints or tendons <ul style="list-style-type: none"> <li>○ 4 major synovectomies were performed</li> </ul> </li> </ul>
	<p>Some other types of major surgeries included (not a complete list):</p> <ul style="list-style-type: none"> <li>• Open reduction of fracture (procedure performed to help correct a fracture)</li> <li>• Muscle suture (procedure to stitch together a muscle wound)</li> </ul>

Preventive clotting factor was used for 15 out of the 18 major surgeries (83%).<sup>2</sup> Of these 15 cases, 12 had no bleeds after the surgery. In the 3 cases with bleeding after surgery:

- One bleed occurred after surgery and was treated with clotting factor.
- Two bleeds that occurred after surgery were not treated.

In the 3 major surgeries that used no preventive clotting factor, no bleeds occurred after surgeries.

### **What are safety results from the surgeries performed in the HAVEN trials?**

No deaths occurred as a result of any surgery performed in people with hemophilia A with or without FVIII inhibitors.<sup>2</sup> No blood clots (thrombotic events) occurred as a result of any surgery.

### **Have other surgeries been reported in people taking Hemlibra?**

STASEY was a Phase 3b study that evaluated Hemlibra prophylaxis in adults and adolescents, 12 years or older, with hemophilia A with FVIII inhibitors.<sup>3</sup> There were 56 minor surgeries and 22 major unplanned surgeries.

- Majority of the minor surgeries (32 out of 56) were managed without additional preventative coagulation factor.
- Minor surgeries included dental procedures, skin-related procedures, tumor removal, repairing of fistula (an unusual opening in body parts), laser eye surgery, removal of hematoma (collection of blood), hernia-related, sutures or stitches, and removal of cysts.
- Of the 22 major surgeries, 18 were managed with preventative coagulation factor. Seven of the surgeries had bleeds that required treatment, 6 had bleeds that didn't require treatment, and 9 had no bleeds after the surgery.
- Major surgeries included joint arthroplasties (replacements or reconstructions), hemorrhoid operations, imaging test to look at the arteries of the heart, abdominal and colon-related surgeries.

Outside of the HAVEN trials and STASEY, there have been reports of surgeries in people taking Hemlibra prophylaxis. Some of the surgeries and procedures described include an emergency appendectomy, hernia repair, circumcision, vasectomy, urethroplasty (repair of the urethra), endoscopy (a procedure to put a scope to examine internal parts of the body), dental procedures such as tooth extractions and dental crown placement, ear tube removal, hip replacements, knee replacements, inserting or removing venous access devices or ports, and procedures involved digestive system.<sup>4-18</sup>

### **Talk to your treating doctor if a surgery or procedure is needed and you are taking Hemlibra prophylaxis.**

Talk to your treating doctor and develop a plan for any surgeries or procedures that may be performed if you are taking Hemlibra prophylaxis.

### **Hemlibra Surgeries and Procedures References**

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