SDM
WFH SHARED DECISION MAKING TOOL

# BISPECIFIC ANTIBODY THERAPY

## BISPECIFIC ANTIBODY THERAPY

***What are bispecific antibody therapies?***

Bispecific antibody therapies belong to the non-factor replacement therapy class and are used to treat hemophilia A.

Antibodies are Y-shaped proteins that can selectively bind to other proteins. Bispecific antibodies can bind to two different proteins at the same time. In hemophilia A, the antibody acts as a bridge between two important proteins in the body, factor IXa (9a) and factor X (10), which helps the blood clot more efficiently: this mimics the function of the missing factor VIII (8), and therefore, these therapies are also referred to as factor VIII(a)-mimetics.

***What are the different types of bispecific antibody therapy?***

One bispecific antibody therapy, emicizumab (HEMLIBRA), a factor VIIIa mimetic, has been approved for the treatment of hemophilia A.[1] Mim8 is another factor VIIIa mimetic in phase 3 clinical trials.[2]

***How is the mechanism of action of bispecific antibodies different from other treatments for hemophilia?***

The main treatment types for hemophilia are clotting factor replacement therapy (standard half-life (SHL) and extended half-life (EHL)), bispecific antibodies, re-balancing agents, and gene therapy. All these treatments help the blood clot more efficiently, but they all work in different ways.

Clotting factor replacement therapy provides a short-term increase in factor levels by injecting the needed clotting factor protein directly into the blood of a person with hemophilia.

Bispecific antibodies are Y-shaped proteins that act as a bridge between factor IXa and factor X, which helps the blood to clot more efficiently. This antibody bridge mimics the function of the missing activated factor VIII (i.e., factor VIIIa-mimetic).

**Bispecific Antibody Therapy**

Rebalancing therapies restore the disrupted balance between the levels of anticoagulation (i.e., anti-clotting) factors and clotting factors in the blood, thereby improving blood clotting.

Gene therapy introduces a working copy of the missing clotting factor gene. Once the gene is introduced, the body can produce the missing protein and maintain adequate clotting factor levels, on its own, for an extended time.

## TREATMENT WITH BISPECIFIC ANTIBODY THERAPIES

| | |
|---|---|
| ***Who is eligible to use bispecific antibodies?*** | Bispecific antibodies work by mimicking the effects of activated factor VIII and are therefore only available for people with hemophilia A. Emicizumab is approved for use in people with factor VIII inhibitors and people without inhibitors who have severe disease (FVIII activity <1%) or moderate disease (FVIII activity between 1 and 5%) with severe bleeding phenotype.[1,2] Emicizumab can be used in all age groups (newborn and older). |
| ***How are prophylactic bispecific antibody therapies administered?*** | Bispecific antibody therapies are administered by subcutaneous injection directly under the skin; there is no need to find a vein. The injection takes approximately one minute and can be done at home or at a clinic. |
| ***What is the treatment frequency for prophylaxis with bispecific antibody therapies?*** | Prophylactic treatment with bispecific antibody therapies (specifically emicizumab) is administered every 1, 2, or 4 weeks depending on your personal preference.[1] There is an initial loading dose period (4 weeks) with weekly treatment. |
| ***Can bispecific antibody therapies be used in combination with other hemophilia treatments?*** | In some cases, additional therapies (clotting factor replacement therapies or bypassing agents) may be required, especially during traumatic breakthrough bleeding or surgical procedures. This should be discussed with your healthcare team. |

## EFFICACY OF BISPECIFIC ANTIBODY THERAPIES

| | |
|---|---|
| ***How will clotting factor levels be affected?*** | Bispecific antibodies will not change the clotting factor levels. Studies show that the effect of factor VIIIa-mimetic therapies is similar to having mild hemophilia. |
| ***How will bispecific antibody therapies affect my annual bleed rate?*** | Any form of regular prophylactic treatment is likely to reduce your annual bleed rate. Clinical trials for emicizumab reported a median annual bleed rate of 1.5 for patients taking 1.5 mg/kg every week and 1.3 for patients taking 3 mg/kg every two weeks; 55.6% and 60% patients reported zero bleeds.[1] |

## SAFETY OF BISPECIFIC ANTIBODY THERAPIES

| | |
|---|---|
| ***What are the possible side effects of bispecific antibody therapies?*** | The most common side effects reported for emicizumab include injection site reactions, headache, and joint pain (arthralgia), which occurred in about 1 in 10 patients. |
| ***Are there any known serious side effects or long-term risks?*** | No major safety concerns with emicizumab have been detected when used in hemophilia A without inhibitors. However, in people with inhibitors, there is a risk of severe and potentially life-threatening thromboembolic events (blood clots in the veins or arteries) when used in combination with an activated prothrombin complex concentrate.[1] |

## MONITORING AND FOLLOW-UP AFTER BISPECIFIC ANTIBODY THERAPY TREATMENT

| | |
|---|---|
| ***How often will you need follow up and monitoring with bispecific antibody therapies?*** | As with all hemophilia treatment classes, regular monitoring by your health care team is recommended. Clinical review should be conducted annually and as needed. |
| ***What will happen in the event of a bleed, injury, or surgery?*** | In the event of a bleed, injury, or planned surgical procedure, additional treatments may be required. This should be discussed with your healthcare team. |

1 Information H-FP. Hemlibra Prescribing Information [online]. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/761083s015lbl.pdf. Accessed 05/13/2023.
2 ClinicalTrials.gov. Ongoing Phase 3 Studies for Mim8: NCT05053139, NCT05306418, NCT05685238, and NCT05878938 [online].

Last reviewed: July 2023
This is a living document that will be updated as new evidence becomes available.