Innovation all for the patients

CHUGAI

Roche A member of the Roche group

Anti-Coagulation Factor IXa/X Humanized Bispecific Monoclonal Antibody HEMLIBRA® Subcutaneous Injection Approved in Japan

-- For People with Hemophilia A with Factor VIII Inhibitors --

TOKYO, March 23, 2018 -- Chugai Pharmaceutical Co., Ltd. (TOKYO: 4519) announced today that the Ministry of Health, Labour and Welfare has approved its coagulation factor VIII substitute / anti-coagulation factor IXa/X humanized bispecific monoclonal antibody, "HEMLIBRA® Subcutaneous Injection 30mg, 60mg, 90mg, 105mg, 150mg" [generic name: emicizumab (genetical recombination)] for routine prophylaxis to prevent or reduce the frequency of bleeding episodes in patients with congenital factor VIII deficiency (hemophilia A) with factor VIII inhibitors.

"With this approval, I'm very thrilled that the day that HEMLIBRA will be available to people with hemophilia A in Japan is approaching," said Chugai's President and CEO, Tatsuro Kosaka. "HEMLIBRA is a first-in-class antibody developed with Chugai's proprietary antibody engineering technologies, aiming to tackle unmet medical needs. We believe that the drug will bring innovation to people with hemophilia A and their family with its clinical aspects as well as by allowing a once-weekly subcutaneous injection."

This approval is based on two pivotal clinical studies for people with hemophilia A with inhibitors: the results of HAVEN 1 study (NCT02622321) for adolescents and adults, and the interim analysis of HAVEN 2 study (NCT02795767) in children.

HEMLIBRA is a bispecific monoclonal antibody, which was developed using Chugai's proprietary antibody engineering technologies. The drug is designed to bind factor IXa and factor X. In doing so, HEMLIBRA provides the cofactor function of factor VIII in people with hemophilia A, who either lack or have impaired coagulation function of factor VIII[1, 2]. In November 2017, the drug (US product name: HEMLIBRA®; Genentech) was approved by the U.S. Food and Drug Administration and was marketed for "routine prophylaxis to prevent or reduce the frequency of bleeding episodes in adult and pediatric patients with hemophilia A (congenital factor VIII deficiency) with factor VIII inhibitors." In Europe, it obtained regulatory approval from the European Commission for routine prophylaxis of bleeding episodes in people with hemophilia A with factor VIII inhibitors in February 2018 (EU product name: HEMLIBRA®; Roche).

Hemophilia is an inherited, serious bleeding disorder where a person's blood does not clot properly, leading to uncontrolled bleeding which can occur spontaneously. Hemophilia consists of hemophilia A and hemophilia B, caused by the lack of factor VIII and factor IX, respectively. In Japan, it is reported that about 5,000 people are hemophilia A and about 1,000 people are hemophilia B[3]. The current standard treatment for hemophilia A is factor VIII replacement therapy and 25–30% of people with severe hemophilia A develop 'inhibitors' to factor VIII replacement therapies[4]. Inhibitors are antibodies that attack and destroy the replaced factor VIII, because it is

CHUGAI PHARMACEUTICAL CO., LTD. Corporate Communications Dept.
1-1, Nihonbashi-Muromachi 2-chome, Chuo-ku Tokyo, 103-8324 Japan
Media Relations Group TEL: +81-(0)3-3273-0881 E-mail: pr@chugai-pharm.co.jp
Investor Relations Group TEL: +81-(0)3-3273-0554 E-mail: ir@chugai-pharm.co.jp

recognized as a foreign substance. Once people acquire inhibitors, it is expected to be difficult for them to administer factor VIII replacement therapies.

Conditions for approval

・A risk management plan should be created and appropriately implemented.
・Because the number of participants in Japanese clinical trials was very limited, post-marketing drug use surveillance of all patients receiving HEMLIBRA treatment should be conducted until data for a certain number of patients have been accumulated, in order to understand background information on people using HEMLIBRA as well as to collect safety and efficacy data on HEMLIBRA promptly, and take necessary measures for the appropriate use of HEMLIBRA.
・Early phase post-marketing vigilance should be conducted.

All-case registration surveillance

The all-case registration surveillance is scheduled to collect the data of approximately 100 people who receive HEMLIBRA. The data will be reviewed to determine whether a new surveillance or further safety measures should be conducted. Results of the surveillance will be reported to the regulatory authorities, and the data shall be announced at future scientific meetings.

Note: The description of DOSAGE AND ADMINISTRATION in the Japanese package insert
The following description is noted as <Precautions related to DOSAGE AND ADMINISTRATION>
“HEMLIBRA should be used in routine prophylaxis to prevent or reduce the frequency of bleeding episodes and should not be used for on-demand hemostatic treatment.”

About the results of HAVEN 1 study and HAVEN 2 study

Press release issued on June 26, 2017
https://www.chugai-pharm.co.jp/english/news/detail/20170626140000.html

References

1. Kitazawa, et al. Nature Medicine 2012; 18(10): 1570
2. Sampei, et al. PLoS ONE 2013; 8: e57479
3. WFH Annual Global Survey 2016.:
http://www1.wfh.org/publications/files/pdf-1690.pdf
4. Gomez K, et al. Key issues in inhibitor management in patients with haemophilia. Blood Transfus. 2014; 12: s319–s329.