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Chugai Obtains Regulatory Approval for “Piasky 340mg” for Paroxysmal Nocturnal Hemoglobinuria in Japan

- Providing convenience of once every 4 week subcutaneous administration for treatment-naïve patients, or for patients switching to this drug from other C5 inhibitors, with paroxysmal nocturnal hemoglobinuria (PNH), a designated intractable disease
- This approval for not only naïve PNH but also including patients switching from previously approved C5 inhibitors, is the first in the world
- Second approved drug that applies Chugai’s proprietary recycling antibody technology and also the fifth Chugai originated global product
- Approval based mainly on the global phase III clinical studies (COMMODORE2 and COMMODORE1) in patients with PNH

TOKYO, March 26, 2024 -- Chugai Pharmaceutical Co., Ltd. (TOKYO: 4519) announced today that it has obtained regulatory approval from the Ministry of Health, Labour and Welfare (MHLW) for Piasky® for Injection 340 mg (generic name: crovalimab (genetical recombination)) (hereafter, Piasky), a pH-dependent binding humanized anti-complement (C5) monoclonal antibody for the treatment of paroxysmal nocturnal hemoglobinuria (PNH). Piasky was approved in China in February this year for the treatment of adults and adolescents (12 years of age and above) with PNH who have not been previously treated with complement inhibitors. Japan is the first country in the world to obtain approval without restrictions on switching from existing C5 inhibitors, and without restrictions of age in patients over body weight of 40kg. It is currently under review for PNH by other regulatory authorities, including in the United States, Europe, and Taiwan.

“We are very pleased that Piasky, a Chugai originated drug, has now been approved in Japan, and that we will be able to offer a new treatment option for PNH, a designated intractable disease. By applying Chugai's proprietary antibody technology, Piasky has been made available to be administered subcutaneously once every four weeks and in low doses. Since treatment for PNH continues over a long period of time, we believe that improving the convenience by offering subcutaneous administration will reduce the burden on patients and caregivers and minimize interruptions to their day-to-day lives. In addition, the drug can be administered based on body weight regardless of age, which is expected to contribute to the treatment of a wide range of patients” said Chugai’s President and CEO, Dr. Osamu Okuda.

This approval was based mainly on the results of the COMMODORE 2 study in patients with PNH who were naïve to C5 inhibitors and the COMMODORE 1 study in patients with PNH who switched to crovalimab from previously approved C5 inhibitors. Both are global phase III studies in collaboration with Roche, and Japan is also participating.

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Piasky uses Chugai's Recycling Antibody® technology. Unlike conventional antibodies that bind to an antigen only once, crovalimab has been engineered to bind to the antigen repeatedly, enabling low dose subcutaneous administration every four weeks. This is the second approval for a drug using the recycling antibody technology following Enspryng® for the treatment of neuromyelitis optica spectrum disorder (NMOSD).

[Approval Information]
Product name: PIASKY® for Injection 340 mg
Generic name: crovalimab (genetical recombination)
Indications: Paroxysmal nocturnal hemoglobinuria
Dosage and administration:
The usual Day 1 dose is 1000 or 1500 mg of crovalimab (genetical recombination) once by intravenous infusion, and subsequently, 340 mg is subcutaneously administered once on Days 2, 8, 15, and 22, and 680 or 1020 mg is subcutaneously administered once every 4 weeks from Day 29 onward, taking the patient's body weight into account.

[Reference Information]
New Data Presented at EHA Show Chugai's Subcutaneously Administered Crovalimab Achieved Disease Control and was Well-Tolerated in People with Paroxysmal Nocturnal Hemoglobinuria (PNH) (Press release June 12, 2023)
https://www.chugai-pharm.co.jp/english/news/detail/20230612170001_992.html

About Piasky
Pisaky is an anti-C5 recycling antibody created with Chugai's Recycling Antibody® technology. Recycling antibodies are designed to achieve pH-dependent antigen binding so that a single antibody molecule can bind with the antigen multiple times, enabling a longer efficacy compared with a conventional antibody. Crovalimab is designed to target C5, a key component of the complement system, and is expected to control complement activity. It is also expected to reduce the treatment burden for patients and their caregivers through subcutaneous administration. Since crovalimab binds to complement C5 at a different site from existing antibody drugs, it can be an effective treatment option for patients with a specific C5 gene mutation reported in Asia (appears in approximately 3.2% of Japanese patients with PNH), which causes existing antibody drugs not to bind to C5.[1,2]
Piasky has been approved in China in February 2024, for the treatment of adults and adolescents (12 years of age and above) with PNH who have not been previously treated with complement inhibitors, as Chugai's fifth global drug. Also, it is under review by other regulatory authorities, including in the US, EU, and Taiwan. In addition, clinical trials are ongoing for atypical hemolytic uremic syndrome (aHUS), and Roche is conducting trials for sickle cell disease (SCD) and lupus nephritis overseas.

About paroxysmal nocturnal hemoglobinuria
Paroxysmal nocturnal hemoglobinuria (PNH) is an acquired hematopoietic stem cell disorder characterized by intravascular hemolysis due to complement activation. It is caused by the clonal expansion of hematopoietic stem cells, driven by acquired mutations in the *PIG-A* gene.[3] While symptoms may vary in each individual, there are typically two types. One is symptoms attributed to the characteristic hemolysis in

PNH, such as hemoglobinuria and thrombosis. The other is hematopoietic failures similar to those associated with aplastic anemia. PNH may cause complications, including chronic kidney disease and pulmonary hypertension. In Japan, PNH is a rare disease that is listed as one of the designated intractable diseases (designated intractable disease 62). 1,035 individuals have been granted the medical care recipient certificate for PNH as of the end of FY2022.[4]

Source:

1. Fukuzawa T, et al. Long lasting neutralisation of C5 by SKY59, a novel recycling antibody, is a potential therapy for complement-mediated diseases. 2017; Sci Rep 7, 1080.
2. Nishimura J et al. Genetic variants in C5 and poor response to eculizumab. N Engl J Med. 2014 Feb 13;370(7):632-9.
3. Working group for the development of the reference guide revision of diagnostic criteria and practice for paroxysmal nocturnal hemoglobinuria (PNH). Referenced Guide to Paroxysmal Nocturnal Hemoglobinuria Treatment Revised FY2022. (in Japanese only)
4. Portal Site of Official Statistics of Japan website (https://www.e-stat.go.jp/). Report on Public Health Administration and Services FY2022, Accessed March 2024. (in Japanese only)

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