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MHLW Approves New Indication for ARGATROBAN Injection

Osaka, Japan – January 9, 2019 – Sawai Pharmaceutical Co., Ltd. (Sawai, Head office: Osaka, Japan, President: Mitsuo Sawai) today received approval of partial change applications by the Ministry of Health, Labour and Welfare (MHLW) for ARGATROBAN Injection 10 mg [SAWAI]*. This approval expands the indication of ARGATROBAN Injection 10 mg [SAWAI] to include the same uses as their brand equivalents.

* Brand products: Novastan® HI Injection 10 mg / 2 mL and Slonnon® HI Injection 10 mg / 2 mL

“Indications and Usage” and “Dosage and Administration” after approvals are described below (New approval is underlined);

Indications and Usage

1. Improvement of neurological symptoms (motor paralysis) and activities of daily living (walking, standing, maintaining a sitting position, diet) associated with the following diseases:
   ・Acute cerebral thrombosis within 48 hours after the onset of symptoms (excluding lacunar type)
2. Improvement of ulcers of the extremities, pain at rest, and cold sensation associated with chronic arterial occlusion (Buerger's disease and arteriosclerosis obliterans)
3. Prevention of blood coagulation in extracorporeal circuit in the following patients (during haemodialysis)
   ・Patients with congenital antithrombin III deficiency
   ・Patients with decreased antithrombin III
   (When antithrombin III decreased to less than 70% within the normal range, and heparin sodium or heparin calcium did not improve clotting (residual blood) in the extracorporeal circulation.)
   ・<u>Patients with heparin-induced thrombocytopenia (HIT) type II</u>
4. <u>Prevention of blood coagulation undergoing percutaneous coronary intervention in patients with heparin-induced thrombocytopenia (HIT) type II (including cases at risk of developing)</u>
5. <u>Prophylaxis of thrombosis in patients with heparin-induced thrombocytopenia (HIT) type II</u>

Dosage and Administration

1. Improvement of neurologic symptoms (motor paralysis) and activities of daily living (walking, standing, maintaining a sitting position, diet) associated with the following diseases:
   ・Acute cerebral thrombosis within 48 hours after the onset of symptoms (excluding lacunar type)
   In general, for adults, 6 ampules (60 mg as argatroban hydrate) diluted with fluid are

administered by continuous intravenous injection once daily over a period of 24 hours for the first 2 days. One ampule (10 mg as argatroban hydrate) diluted with an appropriate volume of fluid is administered by intravenous injection twice a day for the next 5 days, in the morning and evening, over a period of 3 hours. The dosage may be adjusted according to the patient's age and symptoms.

2. Improvement of ulcers of the extremities, pain at rest, and cold sensation in patients with chronic arterial occlusion (Buerger's disease and arteriosclerosis obliterans)
   In general, for adults, 1 ampule (10 mg as argatroban hydrate) diluted with an appropriate volume of fluid is administered by intravenous injection twice a day over a few hours. The dosage may be adjusted according to the patient's age and symptoms.
3. Prevention of blood coagulation in extracorporeal circuit in the following patients (during haemodialysis)
   ・Patients with congenital antithrombin III deficiency
   ・Patients with decreased antithrombin III
   (When antithrombin III decreased to less than 70% within the normal range, and heparin sodium or heparin calcium did not improve clotting (residual blood) in the extracorporeal circulation.)
   ・Patients with heparin-induced thrombocytopenia (HIT) type II
   In general, for adults, 1 ampule (10 mg as argatroban hydrate) is administered into the circuit at the beginning of extracorporeal circulation, followed by 2.5 ampules (25 mg as argatroban hydrate) administered every hour after extracorporeal circuit start. The dosage may be adjusted for individual patients based on prolongation of coagulation time, blood clot in the circuit (residual blood), dialysis efficiency, and hemostasis at the end of dialysis. The standard dosage is 0.5 to 4 ampules (5 to 40 mg as argatroban hydrate) per hour.
4. Prevention of blood coagulation undergoing percutaneous coronary intervention in patients with heparin-induced thrombocytopenia (HIT) type II (including cases at risk of developing)
   In general, for adults, 0.1 mg/kg as argatroban hydrate diluted with an appropriate volume of fluid is administered (can be administrated undiluted) intravenously over a period of 3 to 5 minutes, and 6 μg/kg/minute as argatroban hydrate is administered by continuous intravenous infusion for 4 hours after surgery. If continuous anticoagulation is required, the dosage should be reduced to 0.7 μg/kg/minute. This dosage of continuous intravenous infusion is just an approximatestandard; the dosage may be adjusted appropriately under coagulation monitoring.
5. Prophylaxis of thrombosis in patients with heparin-induced thrombocytopenia (HIT) type II
   In general, for adults, 0.7 μg/kg/minute as argatroban hydrate diluted with an appropriate volume of fluid is administered (can be administrated undiluted) by intravenous injection followed continuous infusion. Start at a low dosage in patients with hepatic function disorder or at risk of bleeding. In addition, the dosage may be adjusted based on the activated partial thromboplastin time (aPTT), and determined for individual patients.

About Sawai

Founded in 1929, Sawai Pharmaceutical Co., Ltd. has grown into one of the leading generics companies in Japan. Guided by its corporate philosophy, “Always Putting Patients First,” Sawai markets more than 700 high-quality generic products and reliably delivers them to patients throughout Japan. In 2017, Sawai acquired US-based Upsher-Smith Laboratories, LLC marking its first step in overseas expansion to become a globally recognized generic pharmaceutical company. For more information, visit: https://www.sawai.co.jp/en/.

The product announced in this press release is not approved by the Food & Drug Administration for sale and distribution in the United States.

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