

March 23, 2021

Ono and Seikagaku Announce a Manufacturing and Marketing Approval in Japan for JOYCLU® 30mg Intra-articular Injection, a Joint Function Improvement Agent, for the Indication of Osteoarthritis (Knee Joint and Hip Joint)

Ono Pharmaceutical Co., Ltd. (Osaka, Japan; “Ono”) and Seikagaku Corporation (Tokyo, Japan; “Seikagaku”) announced today that Seikagaku has obtained from the Ministry of Health, Labour and Welfare (MHLW) a manufacturing and marketing approval in Japan for JOYCLU® 30mg Intra-articular Injection (generic name: diclofenac etalhyaluronate sodium; development code: ONO-5704/SI-613; “JOYCLU”) for the indication of osteoarthritis (knee joint and hip joint).

The approval is based on the results of three Phase III clinical studies*1 conducted with ONO-5704/SI-613 in Japan. In the confirmatory study in patients with knee osteoarthritis, ONO-5704/SI-613 group demonstrated a statistically significant improvement in WOMAC pain scores (a knee pain evaluation index, 100 mm VAS scale) over twelve weeks after the initial injection (three injections every four weeks), the primary endpoint of the study, compared to an inactive placebo group. Further, the safety profile of ONO-5704/SI-613 has shown no clinically significant concerns in the study.

JOYCLU is a formulation in which hyaluronic acid and diclofenac (an anti-inflammatory drug) are chemically bound using Seikagaku’s own proprietary technology. It is designed to release diclofenac by hydrolysis in the joint. Improvement of symptoms of osteoarthritis (knee joint and hip joint) is expected by the administration of JOYCLU into the joint cavity once every four weeks. Further, since JOYCLU is administered directly into the joint cavity as an injectable treatment, systemic exposure to diclofenac is low, and the risk of systemic adverse drug reaction is thought to be low. JOYCLU is the first joint function improvement agent in Japan indicated for the treatment of osteoarthritis of the hip joint.

Ono and Seikagaku aim to contribute to improvement of quality of life (QOL) in patients by providing a new treatment option for osteoarthritis (knee joint and hip joint).

Seikagaku will manufacture and market JOYCLU, and Ono will be responsible for distribution. We will announce the launch date of JOYCLU following the National Health Insurance drug price listing. There is no change in the forecast of consolidated financial results for the fiscal year ending March 31, 2021 for either Ono or Seikagaku in connection with this matter.

- *1: 1) Confirmatory study in patients with knee osteoarthritis
 2) Clinical study in patients with osteoarthritis (four joint sites: shoulder, elbow, hip, and ankle)
 3) Long-term study in patients with osteoarthritis, primarily for safety evaluation (five joint sites: knee, shoulder, elbow, hip, and ankle)

Overview of JOYCLU

Product name	JOYCLU® 30mg Intra-articular Injection
Generic name	Diclofenac etalhyaluronate sodium
Indications	Osteoarthritis (knee joint and hip joint)
Dosage and administration	Ordinarily, one syringe (containing 30 mg of diclofenac etalhyaluronate sodium) is administered into the joint cavity in an adult patient once every four weeks.
Manufacturing and marketing	Seikagaku Corporation
Distributor	Ono Pharmaceutical Co., Ltd.
Date of manufacturing and marketing approval	March 23, 2021

About Osteoarthritis

Osteoarthritis is a disease caused by articular cartilage damage, leading to inflammation and pain, which results in deterioration of QOL. Osteoarthritis of the knee is caused by factors such as aging, and osteoarthritis of the hip is caused by congenital and other factors. The number of symptomatic patients with knee osteoarthritis in Japan is estimated to be about 7.8 million. The disease is particularly common in women and is reported to affect approximately 70% of women in their 70s.^{*2} Also, based on X-ray diagnosis, the prevalence rate of osteoarthritis of the hip is reported to be in the range of 1.0 - 4.3% of the population, 0.0 - 2.0% in men and 2.0 - 7.5% in women.^{*3}

*2: Yoshimura N et al., *J Bone Miner Metab*, 2009;27:620-8

*3: *Clinical Practice Guideline on the Management of Osteoarthritis of the Hip* (2016). 2nd Edition. Tokyo: Nankodo Co., Ltd.; 2016: 10-13.

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