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Whom It May Concern

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Kyorin Pharmaceutical Receives Marketing Approval for the Interstitial cystitis “Zymso® Intravesical Solution 50%”

TOKYO, Japan (January 22, 2021) —Kyorin Pharmaceutical Co., Ltd. (Head office: Chiyoda-ku, Tokyo, President: Shigeru Ogihara, hereinafter "KYORIN "), a wholly owned subsidiary of KYORIN Holdings, Inc., received approval from the Ministry of Health, Labour and Welfare (hereinafter “MHLW”) as of January 22, 2021 to market the Interstitial cystitis “Zymso® Intravesical Solution 50%” (hereinafter “Zymso ”) in Japan.

Zymso is an intravesical infusion containing 50% (w / w) of dimethyl sulfoxide, and its phase III clinical trial (multicenter, randomized, double-blind, placebo-controlled, parallel-group study) in 96 Japanese patients with interstitial cystitis was conducted, and its efficacy and safety were evaluated and approved.

As a result of the review by The Evaluation Committee on Unapproved or Off-labeled Drugs with High Medical Needs set by MHLW, Intravesical instillation therapy of dimethyl sulfoxide was judged to meet the "standards for medical need". After that, MHLW widely recruited the development company and KYORIN expressed its development intentions and developed the drug in Japan. In September 2017, Zymso was designated as an orphan drug by MHLW.

KYORIN adds Zymso to its product lineup in the urology field which is a priority therapeutic area for KYORIN. KYORIN further contributes to the treatment and QOL improvement for patients with interstitial cystitis as a therapeutic drug that meets unmet medical needs.

Further details, including the timing of release and projected sales, will be announced in a timely manner after Zymso is listed on the National Health Insurance drug price list.

(Product Information)

Brand name : Zymso® Intravesical Solution 50%
Generic name : Dimethyl Sulfoxide
Indications : Improvement of symptoms of interstitial cystitis (Hunner type) (chronic pelvic pain, pressure and discomfort associated with the bladder, lower urinary tract symptoms such as increased urgency or pollakiuria)

Dosage and Administration:

The usual dosage for adults is 50 mL of 50% (w / w) dimethyl sulfoxide solution per vial (27g as dimethyl sulfoxide) instilled into the bladder 6 times at 2-week intervals. After intravesical injection, hold it in the bladder for at least 15 minutes before draining it.

[Reference for interstitial cystitis]

■ About interstitial cystitis disease, pathophysiology and epidemiology

Interstitial cystitis is a disease that presents with frequent, increased, urgent urination and bladder pain. Among them, bladder pain that occurs when the bladder is full is a characteristic symptom, but in some cases, remarkable frequent urination without bladder pain is main complaint. Persistent symptoms greatly interfere with the patient's daily life and lead to a significant decrease in QOL. It mainly affects middle-aged and older women, but it is not uncommon for younger people and male to develop it. Although the exact number of patients in Japan is unknown, a survey in 2013 reported that the number of patients under treatment in Japan was about 4,500, making it one of the orphan diseases.

In the Clinical Guideline for Interstitial Cystitis/Bladder Pain Syndrome issued in 2019 (hereinafter “Clinical Guideline for IC / BPS”), only the Hunner type was defined as interstitial cystitis. The pathological findings of the Hunner type are defect of the urothelium, infiltration of inflammatory cells in the submucosa of the bladder, and small vascular growth, which are different from those of the non-Hunner type. In addition, increase of inflammation-related molecules on the inner wall of the bladder was observed only in the Hunner type, and whole genome analysis showed that only the Hunner type had obvious inflammatory findings in the inner wall of the bladder.

■ About treatment method of interstitial cystitis

Clinical Guideline for IC / BPS includes conservative treatment, drug treatment, intravesical instillation therapy, and endoscopic treatment etc. for interstitial cystitis, but there is no established treatment as recommended grade A (highly recommended). In addition, at present, the only treatment method covered by health insurance in Japan is bladder hydrodistension, therefore treatment option under health insurance is limited.

(Background materials)

Yamada Y, Nomiya A, Niimi A, Igawa Y, Ito T, Tomoe H, et al. A survey on clinical practice of interstitial cystitis in Japan. *Transl Androl Urol.* 2015; 4(5): 486-90.

Clinical Guideline for Interstitial Cystitis/Bladder Pain Syndrome 2019 edited by Society of Interstitial Cystitis of Japan / The Japanese Urological Association