September 25th, 2023

Kissei Pharmaceutical Co., Ltd.
(Code 4547, Tokyo Stock Exchange Prime Market)
Maruishi Pharmaceutical Co., Ltd.

KORSUVA® IV Injection Syringe 17.5μg, 25.0μg and 35.0μg Granted Marketing Authorization Approval in Japan for Treatment of Pruritus in Patients Undergoing Hemodialysis

Kissei Pharmaceutical Co., Ltd. (Head Office: Matsumoto, Nagano, Japan; Chairman and CEO: Mutsuo Kanzawa; "Kissei") and Maruishi Pharmaceutical Co., Ltd. (Head Office: Tsurumi, Osaka, Representative Director and President: Katsuhito Inoue; "Maruishi") today announced that Maruishi has received manufacturing and marketing approval from the Ministry of Health, Labour and Welfare for KORSUVA® IV Injection Syringe 17.5μg, 25.0μg, and 35.0μg (generic name: difelikefalin acetate, development code: MR13A9 " KORSUVA®") for the treatment of pruritus in patients undergoing hemodialysis.

KORSUVA® is a kappa opioid receptor agonist originated and developed by Cara Therapeutics, Inc. (Head Office: USA, President and CEO：Christopher Posner; "Cara") and is the first intravenous formulation product in the world approved for the treatment of moderate-to-severe pruritus associated with chronic kidney disease in patients undergoing hemodialysis. It was approved by the U.S. Food and Drug Administration in August 2021 and by the European Commission in April 2022.

In April 2013, Maruishi acquired the rights for the development and commercialization for acute pain and uremic pruritus in Japan, and since March 2017, Maruishi and Kissei have been jointly developing KORSUVA® for the indication of uremic pruritus in Japan. After KORSUVA® achieved favorable results in the Phase III clinical trial in Japan[1], a manufacturing and marketing approval application was submitted in September 2022[2]. KORSUVA® will be manufactured by Maruishi and marketed by Kissei in Japan.

KORSUVA® is provided as a pre-filled syringe formulation to facilitate convenience in the medical environment. Kissei and Maruishi will prepare for the smooth launch of KORSUVA® to expand treatment options for uremic pruritus and to improve the QOL (Quality of Life) of patients undergoing hemodialysis.

1. News Release on January 7, 2022
   Positive Topline Results from Japanese Phase III Clinical Study (double-blind period) of Difelikefalin (MR13A9) in Hemodialysis Patients with Pruritus

2. News Release on September 28, 2022
   Difelikefalin New Drug Application Submitted in Japan for Treatment of Pruritus in Hemodialysis Patients

For more details, please visit https://www.kissei.co.jp/ or https://www.maruishi-pharm.co.jp/.

《 Reference 》

Product Summary of KORSUVA® IV Injection Syringe

<table>
<tr><td>Brand Name</td><td>KORSUVA® IV Injection Syringe 17.5μg
KORSUVA® IV Injection Syringe 25.0μg
KORSUVA® IV Injection Syringe 35.0μg</td></tr>
<tr><td>Generic Name</td><td>Difelikefalin acetate</td></tr>
<tr><td>Indications</td><td>Treatment of pruritus in hemodialysis patients (for use only when conventional treatments are not sufficiently effective)</td></tr>
<tr><td>Dosage and Administration</td><td>The usual dosage for adults is administered as difelikefalin three times per week by intravenous bolus injection into the venous line of the dialysis circuit at the end of each hemodialysis treatment, as shown in the table below.

<table><tr><th>Dry weight</th><th>Dosage</th></tr><tr><td>Less than 45 kg</td><td>17.5 μg</td></tr><tr><td>Over 45 kg less than 65 kg</td><td>25.0 μg</td></tr><tr><td>Over 65 kg less than 85 kg</td><td>35.0 μg</td></tr><tr><td>Over 85 kg</td><td>42.5 μg</td></tr></table></td></tr>
<tr><td>Formulation</td><td>IV Injection Syringe</td></tr>
<tr><td>Manufacturing and Marketing Authorization Holder</td><td>Maruishi Pharmaceutical Co., Ltd.</td></tr>
<tr><td>Distributer</td><td>Kissei Pharmaceutical Co., Ltd.</td></tr>
<tr><td>Date of Marketing Approval in Japan</td><td>September 25, 2023</td></tr>
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About uremic pruritus in dialysis patients

Uremic pruritus is a common itching condition in spite of the absence of obvious skin lesion, which occurs in many patients with end-stage renal disease undergoing hemodialysis.

It is reported that long-lasting and intense distressing itching in these patients make their QOL very low and have negative impacts on psychological and physical health such as poor sleep quality, depression, and an increased risk of death.

It is considered that endogenous opioids are related to pruritus as one of the expression mechanisms of pruritus in dialysis patients. Difelikefalin acetate selectively activates kappa opioid receptor which is one of the subtypes of opioid receptors, and is indicated to suppress pruritus.

About Kissei Pharmaceutical Co., Ltd.

Kissei is a Japanese pharmaceutical company based on the management philosophy “contributing to society through high-quality, innovative pharmaceutical products” and “serving society through our employees.” As a strong R&D-oriented corporation, it concentrates on providing innovative pharmaceuticals to patients worldwide in the focus fields of urology, nephrology/dialysis, gynecology and rare/intractable diseases.

For more details about Kissei Pharmaceutical Co., Ltd., please visit https://www.kissei.co.jp/.

About Maruishi Pharmaceutical Co., Ltd.

Maruishi is a specialty pharma that has a strong presence in the perioperative and infection control area and is known as a leading producer of Japanese Pharmacopoeia drugs. Making use of the technology, knowledge, and know-how that have been cultivated over 130 years of history, Maruishi continues to contribute to the healthcare and improvement of QOL of the patients.

For more details about Maruishi Pharmaceutical Co., Ltd., please visit https://www.maruishi-pharm.co.jp/.

About Cara Therapeutics, Inc.

Cara Therapeutics (Nasdaq: CARA) is a commercial-stage biopharmaceutical company leading a new treatment paradigm to improve the lives of patients suffering from pruritus.

For more information, visit https://www.caratherapeutics.com/ and follow the company on X (Twitter), LinkedIn and Instagram.