September 21, 2018

EA Pharma Co., Ltd.
Mochida Pharmaceutical Co., Ltd.

Marketing and Manufacturing Approval of Chronic Constipation Treatment "MOVICOL®" Obtained in Japan

EA Pharma Co., Ltd. (President, Yuji Matsue; Headquarters, Tokyo, Japan) (hereinafter "EA Pharma") and Mochida Pharmaceutical Co., Ltd. (President, Naoyuki Mochida; Headquarters, Tokyo, Japan) (hereinafter "Mochida") announced today that EA Pharma has obtained the marketing and manufacturing approval of chronic constipation treatment "MOVICOL®" (Development code AJG555, hereinafter "MOVICOL®"), which EA Pharma and Mochida have jointly developed for the Japanese market.

MOVICOL® increases the moisture in the intestinal tract by osmolality of its main ingredient polyethylene glycol, which increases fecal moisture, softens feces, increases fecal volume and physiologically activates the peristaltic movement of the colon to promote bowel movement.

The product has been mainly marketed in Europe and other markets, under the brand name *MOVICOL*, and widely used for treatment of chronic constipation in pediatric and adult patients. The guidelines of NICE (National Institute for Health and Care Excellence) UK recommend the use of polyethylene glycol preparations for treatment of pediatric chronic constipation, and so do the guidelines of World Gastroenterology Organisation for treatment in adults.

In Japan, in consideration of the situation that use of polyethylene glycol preparations for chronic constipation was not approved, Japanese Society for Pediatric Gastroenterology, Hepatology and Nutrition submitted the letter of request for development of polyethylene glycol preparations for pediatrics to the Evaluation Committee on Unapproved or Off-Labeled Drugs with High Medical Needs[1)]. In April's meeting in 2015, the Committee concluded that there were high unmet medical needs for polyethylene glycol preparations for chronic constipation. Upon request from the Ministry of Health, Labour and Welfare, Ajinomoto Pharmaceuticals Co., Ltd. (now EA Pharma) in-licensed MOVICOL® from Norgine B.V. (Headquarters, the Netherlands), and EA Pharma and Mochida jointly developed the product for orally available treatment of chronic constipation in pediatric and adult patients in Japan.

The above marketing and manufacturing approval was based on two phase III clinical trials conducted in Japan. The phase III clinical trial in adults consisted of a confirmatory period of placebo-controlled double-blind study and a consecutive arminidtration period of open-label long-term administration study. In the confirmatory period, 156 patients of the age 15 years or above with chronic constipation with spontaneous bowel movement[2)] frequency less than 3 times a week in average for at least 6 months were given orally 2 to 6 sachets daily of placebo or MOVICOL® depending on symptoms for 2 weeks. As a result, the spontaneous bowel movement frequency (the primary endpoint) statistically significantly increased in the MOVICOL® group as compared with the placebo group. In the subsequent 52-week consecutive administration period, the spontaneous bowel movement frequency was steadily maintained in most cases.

In the phase III clinical trial (a baseline-controlled open-label study) in pediatric patients, 39 patients of the age between 2-14 years with spontaneous bowel movement frequency less than 2 times a week in average for at least 2 months were given orally MOVICOL® 1-4 sachets for patients with the age between 2-6 years, 2-4 sachets for those between 7-11 years and 2-6 sachets for those between 12-14 years daily depending on symptoms for 12 weeks. As a result, the spontaneous bowel movement frequency (the primary endpoint) statistically significantly increased as compared with the baseline.
The major side effects in the above trials were mild diarrhea and abdominal pain. No serious side effects were observed.

The prevalence of constipation is high in women in the young and both men and women in the elderly, and the symptoms can become severe particularly in pediatric patients. The symptoms of constipation are reduced bowel movements, feeling of incomplete evacuation, hard stools and others. When the symptoms become chronic, many patients suffer from a decline of QOL (Quality of Life).

EA Pharma and Mochida have respectively distributed “GOOFICE® 5 mg Tablet”, bile acid transporter inhibitor for chronic constipation treatment, under the same brand name since its launch in Japan in April 2018. Likewise, EA Pharma and Mochida distribute MOVICOL® respectively under the same brand name after inclusion of MOVICOL® in the National Health Insurance drug price list. With the new treatment MOVICOL®, EA Pharma and Mochida strive to increase treatment options for patients with chronic constipation with various disease histories to contribute to fulfillment of varied needs of patients with chronic constipation, their families and healthcare providers to increase their benefits.

1) The Evaluation Committee on Unapproved or Off-Labeled Drugs with High Medical Needs
   This committee was organized in the Ministry of Health, Labour and Welfare to evaluate the medical needs of the drugs and indications that are not approved in Japan (“unapproved or off-labeled drugs”) and the appropriateness of filing the public knowledge-based application and requirement of additional studies for filing the marketing and manufacturing application to promote development of unapproved or off-labeled drugs by pharmaceutical companies.
2) Defecation without use of laxative, enema or manual disimpaction

End

Media Inquires	
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More Information

1. "MOVICOL®" Product Outline

Brand name	MOVICOL®
Nonproprietary name	macrogol 4000, sodium chloride, sodium bicarbonate, potassium chloride
Marketing and manufacturing approval date	September 21, 2018
Manufacturer and distributor	EA Pharma Co., Ltd.
Distributor	Mochida Pharmaceutical Co., Ltd.
Indication	Chronic constipation (excluding structural disease-induced constipation)
Dosage and administration	Dissolve this medicine in water and drink. For children of the age between 2 and 6 years, normally 1 sachet should be orally given at once per day for the initial dose. Then, the dose can be increased or decreased depending on symptoms, orally given 1-3 times per day. The maximum daily dose is 4 sachets (up to 2 sachets at once). At least a 2-day interval is needed for every dose escalation, and the dose should not be increased exceeding1 sachet per day. For children of the age between 7 and 11 years, normally 2 sachets should be orally given at once per day for the initial dose. Then, the dose can be increased or decreased depending on symptoms, orally given 1-3 times per day. The maximum daily dose is 4 sachets (up to 2 sachets at once). At least a 2-day interval is needed for every dose escalation, and the dose should not be increased exceeding 1 sachet per day. For adults and children of the age 12 years and above, normally 2 sachets should be orally given at once per day for the initial dose. Then, the dose can be increased or decreased depending on symptoms, orally given 1-3 times per day. The maximum daily dose is 6 sachets (up to 4 sachets at once). At least a 2-day interval is needed for every dose escalation, and the dose should not be increased exceeding 2 sachets per day.

2. About "GOOFICE® 5 mg Tablet"

"GOOFICE® 5 mg Tablet", which EA Pharma in-licensed from Albireo AB (Headquarters, Sweden), is an orally available chronic constipation* treatment having a novel mechanism of action. "GOOFICE® 5 mg Tablet" inhibits the bile acid transporter that regulates reabsorption of bile acids thereby increasing the flow of bile acids to the colon, which is expected to enhance colonic motility. EA Pharma and Mochida have a joint development and marketing agreement for "GOOFICE® 5 mg Tablet". After EA Pharma obtained the marketing and manufacturing approval on January 19, 2018, EA Pharma and Mochida started distribution of "GOOFICE® 5 mg Tablet" respectively under the same brand name on April 19, 2018 in Japan. EA Pharma also has a co-promotion agreement with Eisai Co., Ltd. EA Pharma and Eisai Co., Ltd. jointly provide the proper use information of "GOOFICE® 5 mg Tablet".

*Excluding mechanical disorder-induced constipation

3. About EA Pharma Co., Ltd.

EA Pharma Co., Ltd., a subsidiary of Eisai Co., Ltd. for gastrointestinal disease area, was established in April 2016 by integration of the gastrointestinal business unit with more than 60 years history of the Eisai Group and the gastrointestinal business unit of the Ajinomoto Group having amino acid as its business core. EA Pharma is a gastrointestinal specialty pharma with a full value chain covering R&D, logistics and sales & marketing.

For more information on EA Pharma Co., Ltd., please see https://www.eapharma.co.jp/en/

4. About Mochida Pharmaceutical Co., Ltd.

Mochida Pharmaceutical Co., Ltd. has been committed to research and development of innovative pharmaceutical products since its establishment thereby providing distinctive medicines to the medical field. Currently, the core pharmaceutical business focuses resources on the targeted areas of cardiovascular medicine, obstetrics and gynecology, dermatology, psychiatry and gastroenterology, while also providing medicine for intractable disease as well as generics including biosimilars, to meet medical needs.

For more information on Mochida Pharmaceutical Co., Ltd., please see
http://www.mochida.co.jp/english/

*「MOVICOL」 is a registered trademark of the Norgine group.
(In this document, *MOVICOL* means the product marketed in non-Japan countries.)