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Eisai Co., Ltd.

EISAI ENTERS INTO LICENSING AGREEMENT WITH MEDAC CONCERNING ANTI-RHEUMATIC AGENT METHOTREXATE SUBCUTANEOUS INJECTION IN JAPAN

Eisai Co., Ltd. (Headquarters: Tokyo, CEO: Haruo Naito, "Eisai") announced today that it has entered into a license agreement with medac Gesellschaft für klinische Spezialpräparate mbH (Headquarters: Wedel, Germany, "Medac") for the commercialization of its anti-rheumatic agent methotrexate (MTX) subcutaneous injection (pre-filled syringe) in Japan. Medac is marketing this product mainly in Europe and the United States.

Under the agreement, Eisai will obtain exclusive rights to market MTX subcutaneous injection in Japan. Medac will submit a manufacturing and marketing authorization application for the product after conducting a clinical study in Japan. Once approved, Eisai will distribute the product. In accordance with the agreement, Eisai will pay Medac an upfront payment as well as developmental and sales milestone payments.

MTX is used as the first-line option for the treatment of rheumatic arthritis. However, it is known that its bioavailability shows significant interindividual variability in oral administration.[1] MTX subcutaneous injection which Eisai is in-licensing from Medac, is administered once a week via subcutaneous injection and enables a high bioavailability to be maintained. Furthermore, MTX subcutaneous injection has been reported to have a lower intensity of some gastrointestinal side effects than the oral drug.[2,3]

It is reported that there are approximately 700,000 - 800,000 rheumatoid arthritis patients in Japan.[4] Eisai markets the anti-rheumatic agents HUMIRA® and Careram® in Japan, and has a wealth of clinical data and experience in the field of rheumatoid arthritis. With the addition of MTX subcutaneous injection as the first choice for rheumatoid arthritis treatment to these existing products, it will be possible to make a major contribution to the patients in wider treatment stages for rheumatoid arthritis including the initial treatment.

By providing MTX subcutaneous injection as a new option for use in drug therapy for rheumatoid arthritis, Eisai will make further contributions to address the diversified needs of, and increase the benefits provided to, rheumatoid arthritis patients and their families.

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[Notes to editors]

1. About Methotrexate Subcutaneous Injection

Methotrexate (MTX) is positioned as the anchor drug for rheumatoid arthritis treatment.[5] For rheumatoid arthritis, it is believed that MTX regulates cell growth by inhibiting folate metabolism in lymphocytes and other cells, and also has an anti-inflammatory mechanism through the promotion of adenosine synthesis in vascular endothelial cells and other cells in synovial membranes. The subcutaneous formulation is administered once a week via subcutaneous injection, which enables a high bioavailability to be maintained. Furthermore, MTX subcutaneous injection has been reported to have a lower intensity of some gastrointestinal side effects than the oral drug.[2,3]

2. About Medac

Medac is a pharmaceutical company located in Wedel, Germany (suburbs of Hamburg), specialized in the treatment and diagnosis of oncological, urological and autoimmune diseases since 1970, and we are very much aware of the particular requirements of these fields. We take responsibility for our actions and all our expertise is geared to the provision of qualitatively perfect and reliable products for patients, doctors, laboratory personnel and hospitals.
For more information about Medac, please visit https://www.medac.de (available in German only)

[1] Lebbe C, et al. *Ann Rheum Dis* 1994; 53(7) 475-477

[2] Rutkowska-Sak L, et al. *Reumatologia* 2009; 47 (4) 207-211

[3] Cipriani P, et al. *Clin Ther* 2014; 36(3) 427-435

[4] Report from Study Committee on Rheumatoid Arthritis and Allergy
http://www.mhlw.go.jp/stf/houdou/2r9852000001nfao-att/2r9852000001nfdx.pdf

[5] Japan College of Rheumatology, Clinical practice guideline of methotrexate for patients with rheumatoid arthritis: 2016 update version