February 21, 2020

Bristol-Myers Squibb K.K.
Ono Pharmaceutical Co., Ltd.

BMSKK and ONO Receive Approval of Orencia® for I.V. Infusion, Orencia® Syringe for S.C. Injection and Orencia® Auto-injector for S.C. Injection, a Selective T-cell Co-Stimulation Modulator in Japan, to Include the Description of Prevention of Structural Damage of Joints in Current Indication of Rheumatoid Arthritis

Bristol-Myers Squibb K.K. (Head office: Shinjuku, Tokyo; Representative Director and President: Jean-Christophe Barland) and Ono Pharmaceutical Co., Ltd. (Headquarters: Osaka, Japan; President, Representative Director, Gyo Sagara) announced today that the Companies have received an approval of "Orencia® (generic name: abatacept; genetic recombinant) for Intravenous Infusion 250mg," "Orencia® for Subcutaneous Injection 125mg Syringe 1mL" and "Orencia® for Subcutaneous Injection 125mg Auto-injector 1 mL" ("Orencia"), a selective T-cell co-stimulation modulator, to include the description of "prevention of the structural damage of the joints" in the currently approved indication of rheumatoid arthritis for a partial change in approved items of the manufacturing and marketing approval in Japan.

This approval is based on the results from a multicenter, randomized, double-blind, placebo-controlled, post-marketing clinical trial (IM101-338 study) conducted to meet the conditional approval for the indication of rheumatoid arthritis (which have had inadequate response to conventional treatment only) approved in July 2010 in Japan, as well as a Phase 3b, multicenter, randomized, investigator-blinded, active-controlled clinical trial (IM101-235 study) conducted outside Japan.

In IM101-338 study, the efficacy and safety of Orencia in combination therapy with methotrexate were evaluated compared to methotrexate alone. The combination therapy of Orencia and methotrexate demonstrated a statistically significant difference in the primary endpoint, a change from baseline in modified Total Sharp Score (mTSS) at 24-weeks post-treatment, versus methotrexate alone.

No new safety concerns were shown in the analysis of the safety in both studies, except for identified risks of Orencia.

Outline of Orencia® for Intravenous Infusion 250 mg, Orencia® for Subcutaneous Injection 125mg Syringe 1mL and Orencia® for Subcutaneous Injection 125mg Auto-injector 1 mL

Product name	1. Orencia® for Intravenous Infusion 250 mg 2. Orencia® for Subcutaneous Injection 125mg Syringe 1mL/Auto-injector 1 mL
Generic name	Abatacept (genetic recombination)
Indications	1. Following diseases shown insufficient effect with existing treatments: Rheumatoid arthritis (including prevention of the structural damage of the joints) Active polyarticular juvenile idiopathic arthritis 2. Rheumatoid arthritis shown insufficient effect with existing treatments (including prevention of the structural damage of the joints)

<table>
<tr><td>Dosage and Administration</td><td>1. Rheumatoid arthritis
Usually, for adults, abatacept should be administered as an intravenous infusion as per the doses below. Following the initial administration, it should be administered at 2 and 4 weeks after the first infusion and every 4 weeks thereafter.
<table><tr><th>Body weight</th><th>Dose</th><th>No. of vials</th></tr><tr><td>< 60kg</td><td>500mg</td><td>2 vials</td></tr><tr><td>60kg-100kg</td><td>750mg</td><td>3 vials</td></tr><tr><td>> 100kg</td><td>1g</td><td>4 vials</td></tr></table>
Active polyarticular juvenile idiopathic arthritis (JIA)
Usually, abatacept should be administered at 10 mg/kg (body weight). Following the initial administration, it should be administered at 2 and 4 weeks after the first infusion and every 4 weeks thereafter.
However, it should be infused intravenously at 750 mg where the body weight ranges between ≥75 kg and ≤100 kg, and at 1 g with body weight of >100 kg.
2. Usually, for adults, inject intravenously abatacept as a loading dose on the first day of treatment, followed by subcutaneous injection of 125 mg of abatacept on the same day. After that, inject 125 mg of abatacept subcutaneously once a week. It is allowed to begin the course with subcutaneous injection at 125 mg of abatacept once a week.</td></tr>
<tr><td>Manufacturer/ Distributor:</td><td>1. Manufactured and marketed by Bristol-Myers Squibb K.K.
2. Manufactured and marketed (imported) by Bristol-Myers Squibb K.K.</td></tr>
<tr><td>Distributor</td><td>1. Co-promoted by Ono Pharmaceutical Co., Ltd.
2. Distributed by Ono Pharmaceutical Co., Ltd.</td></tr>
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Note: The underlined parts show the revised ones according to this approval.

About Rheumatoid Arthritis

Rheumatoid arthritis (RA) is an inflammatory autoimmune disease characterized by inflammation of joint synovium, causing swelling and pain of many joints. It is estimated that there are approximately 600,000 to 1,000,000 patients diagnosed with RA in Japan. This disease causes inflammation typically in small joints of the fingers, wrists and toes. If the disease progresses, bones and cartilage are gradually destructed. If larger joints such as hips, knees and elbows are destructed, this causes joint deformity and difficulty in movement of the body. These symptoms significantly reduce activities of daily living (ADL), and also significantly affect quality of life (QOL).

About Orencia

Orencia is a genetically recombinant soluble fusion protein that consists of the extracellular domain of cytotoxic T-lymphocyte-antigen-4 (CTLA-4) linked to the Fc portion of human IgG1. Orencia is a biologic product that suppresses activation of T-cells by binding specifically with CD80 and CD86 on the surface of the antigen-presenting cells and improves signs and symptoms, physical functions, and health-related quality of life in patients with rheumatoid arthritis.

In Japan, Orencia Intravenous Infusion received manufacturing and marketing approval for the treatment of rheumatoid arthritis with inadequate response to existing therapies in July 2010, followed by approval for the subcutaneous syringe formulation in June 2013 and for the subcutaneous auto-injector formulation in February 2016. Orencia Intravenous Infusion was approved for the treatment of active polyarticular juvenile idiopathic arthritis in February 2018.

Orencia was first approved in the US in December 2005 as a treatment for rheumatoid arthritis, and is now approved in more than 50 countries worldwide.

About the Bristol-Myers Squibb and Ono Pharmaceutical Collaboration

Bristol-Myers Squibb (BMS) and Ono concluded a co-commercialization agreement for Orencia on September 21, 2011, and have initiated co-promotion activities from June 4, 2013. The product has been developed by both companies.

About Bristol-Myers Squibb

Bristol-Myers Squibb is a global biopharmaceutical company whose mission is to discover, develop and deliver innovative medicines that help patients prevail over serious diseases. For more information about Bristol-Myers Squibb, visit us at BMS.com or follow us on LinkedIn, Twitter, YouTube, Facebook and Instagram.

About Ono Pharmaceutical Co., Ltd.

Ono Pharmaceutical Co., Ltd., headquartered in Osaka, is an R&D-oriented pharmaceutical company committed to creating innovative medicines in specific areas. ONO focuses on the oncology, immunology, neurology and specialty research with high medical needs as priority areas toward discovery and development of innovative new drugs. For further information, please visit the company's website at www.ono.co.jp/eng.

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