Bristol-Myers Squibb’s ORENCIA (abatacept) Receives FDA Approval for Treatment of Active Psoriatic Arthritis (PsA) in Adults

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ORENCIA demonstrated symptom improvement in two randomized, double-blind, placebo-controlled trials that included adult PsA patients with active musculoskeletal symptoms

ORENCIA now approved in three autoimmune diseases

PRINCETON, N.J.--(BUSINESS WIRE)---Bristol-Myers Squibb Company (NYSE:BMY) announced today the U.S. Food and Drug Administration (FDA) has approved ORENCIA for the treatment of adults with active Psoriatic Arthritis (PsA)\(^1\), a chronic\(^2\), inflammatory disease that can affect both the skin and musculoskeletal system.\(^3\) ORENCIA is approved and available in both intravenous and subcutaneous (SC) injection formulations.\(^1\) ORENCIA should not be administered concomitantly with TNF antagonists, and is not recommended for use concomitantly with other biologic Rheumatoid Arthritis (RA) therapy, such as anakinra.\(^1\) This approval marks the third autoimmune disease indication for ORENCIA.\(^1\)

“This approval underscores the efficacy of ORENCIA in adult patients with active Psoriatic Arthritis, who have been in need of new treatments,” said Brian J. Gavin, Vice President, ORENCIA Development Lead at Bristol-Myers Squibb. “Helping to advance clinical understanding of autoimmune conditions is a key focus of our immunoscience research, and we’re proud to introduce ORENCIA, a selective T-cell co-stimulation modulator, as an additional treatment option for PsA.”

The co-stimulation blockade of ORENCIA inhibits T-cell activation and the resulting cascade of events that contribute to inflammation. T-cell activation is involved in the pathogenesis of PsA.\(^4\)

Psoriatic Arthritis can cause joint pain, stiffness and reduced range of motion\(^3\), potentially affecting the ability to do everyday activities, such as getting dressed and tying shoes.\(^3,5\) In PsA, the immune system attacks healthy joints and skin.\(^6\)

“This Psoriatic Arthritis takes a toll on patients and families over time,” said Randy Beranek, president and CEO, National Psoriasis Foundation. “We welcome the introduction of an additional treatment option for adults with active Psoriatic Arthritis, because we believe advancements, along with further research, education and support services, are critical to helping improve the lives of those impacted.”

The approval was based on results from two randomized, double-blind, placebo-controlled trials in which ORENCIA improved (or reduced) disease activity in both TNF-naive and exposed patients with high disease activity, high tender and swollen joints, and a disease duration of more than seven years.\(^1,4,8\)

ORENCIA PsA IV and SC Studies Demonstrated Improved Disease Response

The efficacy of ORENCIA was assessed in two randomized, double-blind, placebo-controlled studies (Studies PsA-I and PsA-II) in 594 adult patients with disease duration more than seven years. Patients had active Psoriatic Arthritis (≥ 3 swollen joints and ≥ 3 tender joints) despite prior treatment with DMARD therapy and had one qualifying psoriatic skin lesion of at least 2 cm in diameter. In PsA-I and PsA-II, 37% and 61% of patients, respectively, were treated with TNF inhibitors (TNFi) previously.\(^1\) The primary endpoint for both PsA-I and PsA-II was the proportion of patients achieving ACR 20 response at Week 24 (Day 169).\(^1\)

In PsA-I, a dose-ranging study, 170 patients received study drug IV at Days 1, 15, 29, and then every 28 days thereafter in a double-blind manner for 24 weeks, followed by open-label ORENCIA every 28 days. Patients were randomized to receive placebo or ORENCIA 3 mg/kg, 10 mg/kg (weight range-based dosing: 500 mg for patients weighing less than 60 kg, 750 mg for patients weighing 60 to 100 kg, and 1000 mg for patients weighing greater than 100 kg), or two doses of 30 mg/kg followed by weight range-based dosing of 10 mg/kg without escape for 24 weeks. Patients were allowed to receive stable doses of concomitant methotrexate, low dose corticosteroids (equivalent to ≤ 10 mg of prednisone) and/or NSAIDs during the trial. At enrollment, approximately 60% of patients were receiving methotrexate.\(^1\)
In PsA-II, 424 patients were randomized 1:1 to receive weekly doses of SC placebo or ORENCIA 125 mg SC without a loading dose for 24 weeks, followed by open-label ORENCIA 125 mg SC weekly. Patients were allowed to receive stable doses of concomitant methotrexate, sulfasalazine, leflunomide, hydroxychloroquine, low dose corticosteroids (equivalent to ≤ 10 mg of prednisone) and/or NSAIDs during the trial. At randomization, 60.4% of patients were receiving methotrexate.¹

A higher proportion of patients treated with ORENCIA 10 mg/kg IV or 125 mg SC achieved an ACR20 response at Week 24 compared to placebo, 47.5% versus 19.0% and 39.4% versus 22.3% (p< 0.05), respectively.² Responses were seen regardless of prior anti-TNFα treatment and regardless of concomitant non-biologic DMARD treatment.¹ Improvements in enthesis and dactylitis were seen with ORENCIA treatment at Week 24 in both IV and SC.¹

There was a higher proportion of ORENCIA IV patients with at least a 0.30 decrease from baseline in Health Assessment Questionnaire-Disability Index (HAQ-DI) score at Week 24, with an estimated difference for ORENCIA 10 mg/kg (weight range-based dosing as described above) (45.0%) vs. placebo (19.0%) of 26.1 (95% confidence interval: 6.8, 45.5).¹ The proportion of ORENCIA SC patients with at least a 0.35 decrease from baseline in HAQ-DI on ORENCIA was 31%, as compared to 24% on placebo (estimated difference: 7%; 95% confidence interval: -1%, 16%).³ There was a higher adjusted mean change from baseline in HAQ-DI on ORENCIA SC (-0.33) vs. placebo (-0.20) at Week 24, with an estimated difference of -0.13 (95% confidence interval: -0.25, -0.01).³

The safety profile of ORENCIA was comparable between studies PsA-I and PsA-II and consistent with the safety profile in RA. The most serious adverse reactions reported in studies of adult RA patients were serious infections (3% ORENCIA vs 1.9% placebo) and malignancies (1.3% ORENCIA vs 1.1% placebo). Headache, upper respiratory tract infection, nasopharyngitis, and nausea were the most commonly reported adverse events (≥ 10%) in the adult RA clinical studies. In PsA-II, the most common adverse reactions (≥ 5%) were nasopharyngitis, upper respiratory tract infection, and bronchitis.

“It can be difficult to treat active Psoriatic Arthritis patients because the disease course is unpredictable, and patients are often treated with a variety of medications such as classic DMARDs and TNFs over time.⁴ Furthermore, once they have been treated, it may be more difficult to obtain an adequate efficacy response,” said Philip Mease, M.D., Clinical Professor at the University of Washington School of Medicine and Director of the Rheumatology Clinical Research Division of Swedish Medical Center. “The data that formed the basis of this approval demonstrate that ORENCIA offers an additional treatment option for patients with active Psoriatic Arthritis who have already tried a TNF inhibitor, as well as those who have not.”

**About Psoriatic Arthritis**

Psoriatic arthritis (PsA) is a chronic², inflammatory disease that can affect both the skin and musculoskeletal system.³ PsA can cause joint pain, stiffness and reduced range of motion.³ Most commonly affecting the distal joints (those closest to the nail) of the fingers or toes, as well as the wrists, knees, ankles and lower back, the disease usually appears between the ages of 30 to 50, but can begin as early as childhood.³ Men and women are equally at risk.³ Early recognition, diagnosis and treatment of Psoriatic Arthritis are critical to helping relieve pain and inflammation.³

**Indication and Important Safety Information for ORENCIA® (abatacept)**

**Indication and Usage**

**Adult Rheumatoid Arthritis (RA):** ORENCIA® (abatacept) is indicated for reducing signs and symptoms, inducing major clinical response, inhibiting the progression of structural damage, and improving physical function in adult patients with moderately to severely active RA. ORENCIA may be used as monotherapy or concomitantly with disease-modifying anti-rheumatic drugs (DMARDs) other than tumor necrosis factor (TNF) antagonists.

**Juvenile Idiopathic Arthritis (JIA):** ORENCIA® (abatacept) is indicated for reducing signs and symptoms in patients 2 years of age and older with moderately to severely active polyarticular JIA. ORENCIA may be used as monotherapy or concomitantly with methotrexate (MTX).

**Adult Psoriatic Arthritis (PsA):** ORENCIA® (abatacept) is indicated for the treatment of adult patients with active PsA.

**Important Limitations of Use:** ORENCIA should not be administered concomitantly with TNF antagonists, and is not recommended for use concomitantly with other biologic RA therapy, such as anakinra.

**Important Safety Information for ORENCIA® (abatacept)**

**Concomitant Use with TNF Antagonists:** Concurrent therapy with ORENCIA and a TNF antagonist is not recommended. In controlled clinical trials, adult RA patients receiving concomitant intravenous ORENCIA and TNF antagonist therapy experienced more infections (63%) and serious infections (4.4%) compared to patients treated with only TNF antagonists (43% and 0.8%, respectively), without an important enhancement of efficacy.

**Hypersensitivity:** Anaphylaxis or anaphylactoid reactions can occur during or after an infusion and can be life-threatening. There were 2 cases (<0.1%; n=2688) of anaphylaxis or anaphylactoid reactions in clinical trials with adult RA patients treated with intravenous ORENCIA. Other reactions potentially associated with drug hypersensitivity, such as hypotension, urticaria, and dyspnea, each occurred in <0.9% of patients. There was one case of a hypersensitivity reaction with ORENCIA in JIA clinical trials (0.5%; n=190). In postmarketing experience, a case of fatal anaphylaxis following the first infusion of ORENCIA was reported. Appropriate medical support measures for treating hypersensitivity reactions should be available for immediate use. If an anaphylactic or other serious allergic reaction occurs, administration of ORENCIA should be stopped immediately and permanently discontinued, with appropriate therapy instituted.

**Infections:** Serious infections, including sepsis and pneumonia, have been reported in patients receiving ORENCIA. Some of these infections have been fatal. Many of the serious infections have occurred in patients on concomitant
Immunosuppressive therapy which, in addition to their underlying disease, could further predispose them to infection. Caution should be exercised in patients with a history of infection or underlying conditions which may predispose them to infections. Treatment with ORENCIA should be discontinued if a patient develops a serious infection. Patients should be screened for tuberculosis and viral hepatitis in accordance with published guidelines, and if positive, treated according to standard medical practice prior to therapy with ORENCIA.

**Immunizations:** Live vaccines should not be given concurrently with ORENCIA or within 3 months of its discontinuation. The efficacy of vaccination in patients receiving ORENCIA is not known. ORENCIA may blunt the effectiveness of some immunizations. It is recommended that JIA patients be brought up to date with all immunizations in agreement with current immunization guidelines prior to initiating therapy with ORENCIA.

**Use in Patients with Chronic Obstructive Pulmonary Disease (COPD):** Adult COPD patients treated with ORENCIA developed adverse events more frequently than those treated with placebo, including COPD exacerbations, cough, rhonchi, and dyspnea. In adult RA studies, 97% of COPD patients treated with ORENCIA developed adverse reactions versus 88% treated with placebo and respiratory disorders occurred more frequently in patients treated with ORENCIA compared to those on placebo (43% vs 24%, respectively), including COPD exacerbation, cough, rhonchi, and dyspnea. A greater percentage of adult RA patients treated with ORENCIA developed a serious adverse event compared to those on placebo (27% vs 6%), including COPD exacerbation [3 of 37 patients (8%)] and pneumonia [1 of 37 patients (3%)]. Use of ORENCIA in patients with RA and COPD should be undertaken with caution, and such patients monitored for worsening of their respiratory status.

**Blood Glucose Testing:** ORENCIA for intravenous administration contains maltose, which may result in falsely elevated blood glucose readings on the day of infusion when using blood glucose monitors with test strips utilizing glucose dehydrogenase pyrroloquinoline quinone (GDH-PQQ). Consider using monitors and advising patients to use monitors that do not react with maltose, such as those based on glucose dehydrogenase nicotaine adenine dinucleotide (GDH-NAD), glucose oxidase or glucose hexokinase test methods. ORENCIA for subcutaneous (SC) administration does not contain maltose; therefore, patients do not need to alter their glucose monitoring.

**Pregnancy:** There are no adequate and well-controlled studies of ORENCIA use in pregnant women and the data with ORENCIA use in pregnant women are insufficient to inform on drug-associated risk. A pregnancy registry has been established to monitor pregnancy outcomes in women exposed to ORENCIA during pregnancy. Healthcare professionals are encouraged to register patients by calling 1-877-311-8972.

**Lactation:** There is no information regarding the presence of abatacept in human milk, the effects on the breastfed infant, or the effects on milk production. However, abatacept was present in the milk of lactating rats dosed with abatacept.

**Most Serious Adverse Reactions:** Serious infections (3% ORENCIA vs 1.9% placebo) and malignancies (1.3% ORENCIA vs 1.1% placebo).

**Malignancies:** The overall frequency of malignancies was similar between adult RA patients treated with ORENCIA or placebo. However, more cases of lung cancer were observed in RA patients treated with ORENCIA (0.2%) than those on placebo (0%). A higher rate of lymphoma was seen compared to the general population; however, patients with RA, particularly those with highly active disease, are at a higher risk for the development of lymphoma. The potential role of ORENCIA in the development of malignancies in humans is unknown.

**Most Frequent Adverse Events (≥10%):** Headache, upper respiratory tract infection, nasopharyngitis, and nausea were the most commonly reported adverse events the adult RA clinical studies. Other events reported in ≥5% of JIA patients were diarrhea, cough, pyrexia, and abdominal pain. In general, the adverse events in JIA and adult PsA patients were similar in frequency and type to those seen in adult RA patients.

**Note concerning ORENCIA administration options:** Intravenous dosing has not been studied in patients younger than 6 years of age. The safety and efficacy of ORENCIA Clickject™ Autoinjector for subcutaneous injection has not been studied in patients under 18 years of age.

Please click here to see the Full Prescribing Information.

**About Bristol-Myers Squibb Immunoscience**

With a robust pipeline of immunomodulatory therapies, Bristol-Myers Squibb is committed to the discovery and development of transformational medicines for patients suffering from immune-mediated disease. As we learn more about the immune system in diseases with substantial unmet medical needs, the potential for new therapies that modulate the immune system continues to drive our research efforts.

**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 and Facebook.

**Bristol-Myers Squibb Forward-Looking Statement**

This press release contains "forward-looking statements" as that term is defined in the Private Securities Litigation Reform Act of 1995 regarding the research, development and commercialization of pharmaceutical products. Such forward-looking statements are based on current expectations and involve inherent risks and uncertainties, including factors that could delay, divert or change any of them, and could cause actual outcomes and results to differ materially from current expectations. No forward-looking statement can be guaranteed. Forward-looking statements in this press release should be evaluated together with the many uncertainties that affect Bristol-Myers Squibb's business, particularly those identified in the cautionary factors discussion in Bristol-Myers Squibb's Annual Report on Form 10-K for the year ended December 31, 2016 in our Quarterly Reports on Form 10-Q and our Current Reports on Form 8-K. Bristol-Myers Squibb undertakes no
obligation to publicly update any forward-looking statement, whether as a result of new information, future events or otherwise.

References


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