Published on BMS Newsroom (https://news.bms.com) on 07/29/2011

U.S. Food and Drug Administration Approves Subcutaneous Formulation of ORENCIA® (abatacept), a Proven Non-Anti-TNF Biologic for Adults with Moderate to Severe Rheumatoid Arthritis

Release Date: Friday, July 29, 2011 8:12 pm EDT

Terms: R&D News

Dateline City: PRINCETON, N.J.

- First biologic available in both subcutaneous (SC) and intravenous (IV) formulations for the treatment of rheumatoid arthritis
- Subcutaneous ORENCIA demonstrated similar efficacy (non-inferior for American College of Rheumatology [ACR] 20 responses at 6 months) to the intravenous formulation and a consistent safety profile at 6 months
- The overall frequency of injection site reactions was 2.6% (19/736) and 2.5% (18/721) for the ORENCIA SC group and the ORENCIA IV group (SC placebo), respectively
- The overall immunogenicity frequency to ORENCIA was 1.1% (8/725) and 2.3% (16/710) for the subcutaneous and intravenous groups, respectively
- High patient retention rates (94%) were seen with the subcutaneous and intravenous formulations at 6 months

PRINCETON, N.J.--(BUSINESS WIRE)--Bristol-Myers Squibb Company (NYSE: BMY) today announced that the U.S. Food and Drug Administration (FDA) has approved a subcutaneous (SC) formulation of ORENCIA® (abatacept) for the treatment of adults with moderate to severe rheumatoid arthritis (RA). ORENCIA 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 rheumatoid arthritis. ORENCIA may be used as monotherapy or concomitantly with disease-modifying antirheumatic drugs (DMARDs) other than tumor necrosis factor (TNF) antagonists. ORENCIA should not be administered concomitantly with TNF antagonists. ORENCIA is not recommended for use concomitantly with other biologic RA therapy, such as anakinra.

ORENCIA is the first and only biologic for the treatment of RA available in self-injectable (SC) and also an intravenous (IV) infusion formulation. Since the majority of RA patients initiating therapy with a biologic receive their treatment by SC injection, the approval of ORENCIA SC offers physicians a choice for more of their patients.

The new self-injectable formulation is a fixed 125 mg dose administered weekly through an injection under the skin following a single IV loading dose of approximately 10 mg/kg. Patients who are unable to receive an infusion may initiate weekly injections of subcutaneous ORENCIA without an intravenous loading dose. Patients transitioning from ORENCIA intravenous therapy to subcutaneous administration should administer the first subcutaneous dose instead of the next scheduled intravenous dose.

ORENCIA SC demonstrated similar efficacy (non-inferior for ACR 20 responses at 6 months) and safety to ORENCIA IV in a large non-inferiority trial. Concurrent therapy with ORENCIA and a biologic DMARD is not recommended. In controlled clinical trials, patients receiving concomitant 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. In the cumulative clinical trial program for IV, serious infections were 3% in ORENCIA® (abatacept) vs. 1.9% in placebo while malignancies were 1.3% in ORENCIA vs. 1.1% in placebo.

"Physicians now have a new option of a non anti-TNF, with a different mechanism of action, when administering a biologic in a
subcutaneous formulation,” said Mark C. Genovese, M.D., professor of medicine and co-chief, Division of Immunology and Rheumatology, Stanford University Medical Center and lead investigator of the registrational study supporting the approval. “The ORENCIA subcutaneous formulation demonstrated efficacy and safety consistent with the IV formulation. This choice is important for both patients and physicians when managing moderate to severe RA.”

The ORENCIA SC development program is composed of four clinical trials which studied nearly 2,000 patients. The Phase 3 comparative trial studied 1,457 patients, making it the single largest Phase 3 registrational trial of biologics in RA patients. The other three studies primarily evaluated safety and immunogenicity in three clinical scenarios: patients receiving ORENCIA as a monotherapy, patients withdrawn from and re-introduced to ORENCIA SC therapy and patients switching from ORENCIA IV to ORENCIA SC therapy.

“The continued development of ORENCIA exemplifies our company’s focus on areas of serious diseases and biologics drug development.”

ACQUIRE (Abatacept Comparison of Subcutaneous vs. Intravenous in Inadequate Responders to Methotrexate), the Phase 3 registrational trial, was a randomized, double-blind, double-dummy, multinational study. The primary endpoint of ACQUIRE was to determine non-inferiority of ORENCIA SC plus methotrexate (MTX) to ORENCIA IV plus MTX by difference in ACR 20 response at 6 months. The study included 1,457 patients with moderately to severely active RA, most of whom had an inadequate response to MTX. Patients were randomized to weekly injections of a 1 mL solution containing a 125 mg dose of ORENCIA SC plus MTX, following a single IV loading dose (approximately 10 mg/kg) on Day 1, or ORENCIA IV (approximately 10 mg/kg) plus MTX on Days 1, 15, 29 and every 4 weeks thereafter, for 6 months.

Comparable ACR 20 response rates of 76% (95% confidence interval [CI]: -4.2, 4.8 [based on prespecified margin for non-inferiority of -7.5%]) for the SC group were seen in both groups of patients receiving SC injections plus MTX or IV infusions plus MTX at month 6. ACR 50 and ACR 70 responses were comparable between ORENCIA SC and IV as were improvements in all patient-reported outcomes studied – pain, physical function and global assessment of disease activity for ORENCIA SC and IV at 6 months. High retention rates were seen at month 6: 94% of patients receiving SC injections plus MTX and 94% of patients receiving ORENCIA IV plus MTX remained in the study.

The safety experience and immunogenicity for ORENCIA SC was consistent with the profile for IV therapy. Local subcutaneous injection-site reactions occurred in 2.6% of patients receiving ORENCIA SC plus MTX and 2.5% of patients receiving SC placebo plus MTX. All injection-site reactions (including hematoma, pruritus and erythema) were mild (83%) to moderate (17%) and none necessitated drug discontinuation. Immunogenicity was observed in 1.1% and 2.3% of ORENCIA® (abatacept) SC plus MTX and ORENCIA IV plus MTX patients, respectively. There was no correlation of immunogenicity with effects on pharmacokinetics, efficacy or safety.

The most common adverse events reported in greater than 5% of patients in either the SC or IV ORENCIA groups were headache, nasopharyngitis, upper respiratory tract infection, diarrhea and nausea. Serious adverse events occurred in 4.2% of patients in the ORENCIA SC plus MTX group and 4.9% of patients in the ORENCIA IV plus MTX group. Of those, serious infections occurred in 0.7% of patients in the ORENCIA SC plus MTX group versus 1.4% of patients in the ORENCIA IV plus MTX group while malignancies occurred in 0.4% of patients in the ORENCIA SC plus MTX group versus 0.7% of patients in the ORENCIA IV plus MTX group.

ORENCIA SC will be commercially available in the U.S. in September 2011. Physicians and patients interested in finding out about the education and support that is available should call 1-800-ORENCIA, or visit www.ORENCIA.com for more information.

About ORENCIA

ORENCIA SC and IV 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 rheumatoid arthritis. ORENCIA may be used as monotherapy or concomitantly with disease-modifying antirheumatic drugs (DMARDs) other than tumor necrosis factor (TNF) antagonists.

ORENCIA IV is indicated for reducing signs and symptoms in pediatric patients 6 years of age and older with moderately to severely active polyarticular juvenile idiopathic arthritis. ORENCIA IV may be used as monotherapy or concomitantly with methotrexate (MTX). ORENCIA SC has not been studied in pediatric patients. ORENCIA should not be administered concomitantly with TNF antagonists.

ORENCIA is not recommended for use concomitantly with other biologic rheumatoid arthritis (RA) therapy, such as anakinra.

ORENCIA is the first and only biologic therapy for moderate to severe rheumatoid arthritis available in subcutaneous injection or intravenous infusion formulations. ORENCIA is intended for use under the guidance of a physician or healthcare practitioner.

ORENCIA IV was approved for patients initiating therapy with a biologic in 2005. Since launch, more than 71,000 patients in the US have been prescribed ORENCIA IV. In clinical trials, ORENCIA IV has been shown to stop the progression of joint damage and has demonstrated efficacy and an established safety profile. Clinical trials for ORENCIA® (abatacept) SC and IV have collected over 15,000 patient years of safety data.

Important Safety Information About ORENCIA

Concomitant Use with TNF Antagonists: Concurrent therapy with ORENCIA and a biologic DMARD is not recommended. In controlled clinical trials, adult patients receiving concomitant 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: Less than 1% of adult patients treated with ORENCIA experienced hypersensitivity reactions, including some cases of anaphylaxis or anaphylactoid reactions. Other events potentially associated with drug hypersensitivity, such as hypotension, urticaria, and dyspnea, each occurred in less than 0.9% of patients treated with ORENCIA, and generally occurred within 24 hours of infusion. Appropriate medical support measures for treating hypersensitivity reactions should be available for immediate use in the event of a reaction.

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 immuno-suppressive 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 as it may blunt the effectiveness of some immunizations.

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 (97% vs 88%, respectively). Respiratory disorders occurred more frequently in patients treated with ORENCIA compared to those on placebo (43% vs 24%, respectively), including COPD exacerbations, cough, rhonchi, and dyspnea. A greater percentage of 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 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 nicotine adenine dinucleotide (GDH-NAD), glucose oxidase or glucose hexokinase test methods. ORENCIA® (abatacept) for subcutaneous administration does not contain maltose; therefore, patients do not need to alter their glucose monitoring.

Pregnant and Nursing Mothers: ORENCIA should be used during pregnancy only if clearly needed. The risk for development of autoimmune diseases in humans exposed in utero to abatacept has not been determined. Nursing mothers should be informed of the risk/benefit of continued breast feeding or discontinuation of the drug. A pregnancy registry has been established to monitor fetal outcomes. Healthcare professionals are encouraged to register pregnant patients exposed to ORENCIA by calling 1-877-311-8972.

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 patients treated with ORENCIA or placebo. However, more cases of lung cancer were observed in 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 in the adult RA clinical studies. Click here for Full Prescribing Information, or visit www.ORENCIA.com or www.bms.com.

About Rheumatoid Arthritis

Rheumatoid arthritis (RA) is a systemic, chronic, autoimmune disease characterized by inflammation in the lining of joints (or synovium), causing joint damage with chronic pain, stiffness, swelling and fatigue. RA causes limited range of motion and decreased joint function. The condition is more common in women than in men, who account for 75% of patients diagnosed with RA.

ORENCIA is one treatment option indicated in adult patients with moderately to severely active RA. ORENCIA may be used as a monotherapy or concomitantly with DMARDs other than TNF antagonists. ORENCIA is not recommended for use concomitantly with other biologic RA therapy, such as anakinra.

About Bristol-Myers Squibb

Bristol-Myers Squibb is a global biopharmaceutical company committed to discovering, developing and delivering innovative medicines that help patients prevail over serious diseases. For more information about Bristol-Myers Squibb, visit www.bms.com, or follow us on Twitter at http://twitter.com/bmsnews.

ORENCIA is a registered trademark of Bristol-Myers Squibb.

This press release contains “forward-looking statements” as that term is defined in the Private Securities Litigation Reform Act of 1995 regarding product development. 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. Among other risks, there can be no guarantee that the subcutaneous formulation of ORENCIA® (abatacept) will become a commercially successful product. 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, 2010, 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.

**Language:**
English

**Contact:**
Bristol-Myers Squibb
Media:
Ken Dominski, 609-252-5251
ken.dominski@bms.com
or
Investors:
John Elicker, 609-252-4611
john.elicker@bms.com

**Ticker Slug:**
*Ticker: BMY*
*Exchange: NYSE*