UCB News

CIMZIA® is the First and Only Biologic Approved in Europe with the Option for a Reduced Maintenance Dose for Patients Across the Full Axial Spondyloarthritis Spectrum

- European label extended to include a dose reduction option for the treatment of adult patients with axial spondyloarthritis (axSpA), including non-radiographic and radiographic axSpA, who are in sustained remission after one year of CIMZIA® (certolizumab pegol) treatment,[1] underpinned by results of the Phase 3b C-OPTIMISE study[2]
- C-OPTIMISE showed that, once axSpA patients are in sustained remission, it is possible to benefit from a reduced CIMZIA dosing regimen without compromising clinical efficacy[2]

Brussels, Belgium – 5 August 2020 – UCB today announced that the European Medicines Agency (EMA) has approved a label extension for CIMZIA® (certolizumab pegol) for use in adult patients with axial spondyloarthritis (axSpA) at a reduced maintenance dose of 200 mg every four weeks (Q4W), once sustained remission is achieved after one year of CIMZIA 200 mg every two weeks (Q2W) or 400 mg Q4W.[1] The approval makes CIMZIA the only biologic in Europe with a dose reduction option in its label for patients in the broad axSpA population.[1]

Clinical remission is recommended as a major treatment target in the Assessment of SpondyloArthritis international Society (ASAS)/European League Against Rheumatism (EULAR) recommendations for axSpA and treat-to-target recommendations for spondyloarthritis.[3,4] Additionally, strategies for the maintenance of remission are necessary to prevent future deterioration in disease status.[5]

Maintenance dose reduction supports the long-term management of patients with axSpA, when sustained disease remission has been achieved.[2] This approach offers an additional option that preserves the clinical benefits to patients of remaining on treatment, while responding to specific patient needs, and can optimise the cost of their therapy.[2] The extension of CIMZIA's label in Europe[1] addresses an under-recognised unmet need[6,7] by providing the first validated dose reduction strategy for patients across the broad axSpA spectrum who have achieved sustained remission.

"AxSpA patients typically experience symptom onset in their mid-twenties and may therefore be concerned about lifelong continuation of therapy. The CIMZIA label extension now offers healthcare providers a validated dose reduction strategy that can meet the needs of patients. Furthermore, the option to reduce the maintenance dose may provide cost reductions, benefiting the wider healthcare system," said Robert Landewé, MD, PhD, Amsterdam Rheumatology & Clinical Immunology Center, and lead author of the C-OPTIMISE study.

"C-OPTIMISE is the first and only randomised controlled trial to compare both maintenance dose continuation and dose reduction versus placebo in a broad axSpA population. Taken with previous clinical evidence showing that early treatment of axSpA with CIMZIA provides improved clinical outcomes, axSpA patients have a treatment option that can help address their symptoms at every stage of their disease: from initiation of biologic therapy, to remission and maintenance. Our clinical study package in axSpA showed that r-axSpA and nr-axSpA are part of the same disease entity. If treated early, remission is a realistic target and patients can have the flexibility to reduce their dose once they have achieved sustained remission," said Emmanuel Caeymaex, Executive Vice President Immunology Solutions and Head of US, UCB.

The EMA label extension is based on data from the Phase 3b C-OPTIMISE trial in adults with early active axSpA.[2] At week 48 of the induction period, 43.9 percent (323/736) of patients achieved sustained remission (Ankylosing Spondylitis Disease Activity Score (ASDAS) <1.3 at weeks 32 or 36 and 48). Of those patients, 313 were randomised to full maintenance dose (CIMZIA 200 mg Q2W), reduced maintenance dose (CIMZIA 200 mg Q4W), or placebo.[2] At week 96, 84 percent, 79 percent and 20 percent of patients receiving the full maintenance dose, reduced maintenance dose, or placebo, respectively, remained flare-free.[2] Of patients who flared in the reduced maintenance dose arm, 60 percent regained remission after 12 weeks of treatment with the full maintenance dose of CIMZIA.[2]

There were no differences in responses between radiographic axSpA (r-axSpA) and non-radiographic axSpA (nr-axSpA) patients in both the induction and maintenance periods.[2] No new safety signals with CIMZIA were observed over the course of the study compared to previous studies.[1,2] In patients who achieve sustained

remission, dose reduction is an option, but treatment should not be withdrawn, because of the high risk of flare.[2]

About Non-Radiographic Axial Spondyloarthritis (nr-axSpA) and Radiographic Axial Spondyloarthritis (r-axSpA)
Non-radiographic axSpA (nr-axSpA) and radiographic axSpA (r-axSpA, also known as ankylosing spondylitis or AS) comprise the axial spondyloarthritis, or axSpA, spectrum of disease, which typically starts in patients in their mid-twenties. Nr-axSpA and r-axSpA share similar symptomology and disease burden. In r-axSpA, there is a definitive structural damage in the sacroiliac joints detectable by x-ray. In nr-axSpA, there is no definitive radiographic sacroiliitis, though magnetic resonance imaging (MRI) testing often shows evidence of active sacroiliitis, visible as inflammation in the sacroiliac joints. Historically, nr-axSpA has not been well-recognised due to a lack of understanding of the disease history, progression, and prognosis, resulting in substantial diagnostic delay. As a result, nr-axSpA is often misdiagnosed and undertreated.

Axial spondyloarthritis is estimated to affect up to 1.4 percent of adults.[8,9] Roughly two thirds of nr-axSpA patients are women.[10] Yet, axSpA is often overlooked in women, with 89 percent being initially misdiagnosed, leading to a significantly longer time to diagnosis in women compared to men, on average more than two years. Underdiagnosis or misdiagnosis can have long-term consequences for patients with axSpA.[11]

About the C-OPTIMISE Study[2]
C-OPTIMISE was a two-part, multicentre Phase 3b trial in adults with early active axSpA (radiographic and non-radiographic). During the 48-week open-label induction period, patients received CIMZIA 200 mg every 2 weeks (Q2W) with loading dose of CIMZIA 400 mg at weeks 0, 2 and 4. At week 48, patients in sustained remission (Ankylosing Spondylitis Disease Activity Score (ASDAS) <1.3 at weeks 32 or 36 and 48) were randomised to CIMZIA 200 mg Q2W (full maintenance dose), CIMZIA 200 mg every 4 weeks (Q4W; reduced maintenance dose) or placebo (withdrawal) for an additional 48 weeks. The primary endpoint was the proportion of patients remaining flare-free (flare: ASDAS ≥2.1 at two consecutive visits or ASDAS >3.5 at any time point) during the maintenance period.

C-OPTIMISE is the first and only randomised, interventional, placebo-controlled study in the full axSpA spectrum with three arms (full dose, reduced dose and placebo) that provides strong evidence on the dosing options for healthcare professionals to manage axSpA patients that have achieved sustained remission with CIMZIA treatment.

About CIMZIA® in the EU/EEA
In the EU, CIMZIA® in combination with methotrexate (MTX) is indicated for the treatment of moderate to severe active RA in adult patients inadequately responsive to disease-modifying anti-rheumatic drugs (DMARDs) including MTX.

CIMZIA can be given as monotherapy in case of intolerance to MTX or when continued treatment with MTX is inappropriate. CIMZIA in combination with MTX is also indicated for the treatment of severe, active and progressive RA in adults not previously treated with MTX or other DMARDs.

CIMZIA has been shown to reduce the rate of progression of joint damage as measured by X-ray and to improve physical function, when given in combination with MTX.

CIMZIA, in combination with MTX, is also indicated for the treatment of active psoriatic arthritis in adults when the response to previous DMARD therapy has been inadequate. CIMZIA can be given as monotherapy in case of intolerance to MTX or when continued treatment with MTX is inappropriate.

CIMZIA is also indicated in the EU for the treatment of adult patients with severe active axial spondyloarthritis (axSpA), comprising:

- Ankylosing spondylitis (AS) – adults with severe active AS who have had an inadequate response to, or are intolerant to non-steroidal anti-inflammatory drugs (NSAIDs).
- Axial spondyloarthritis (axSpA) without radiographic evidence of AS – adults with severe active axSpA without radiographic evidence of AS but with objective signs of inflammation by elevated C-reactive

protein (CRP) and/or Magnetic Resonance Imaging (MRI) who have had an inadequate response to, or are intolerant to NSAIDs.

CIMZIA is also indicated for the treatment of moderate to severe plaque psoriasis in adults who are candidates for systemic therapy.

Cimzia® (certolizumab pegol) EU/EEA* Important Safety Information

Cimzia® was studied in 4,049 patients with rheumatoid arthritis (RA) in controlled and open label trials for up to 92 months. The commonly reported adverse reactions (1-10 percent) in clinical trials with Cimzia® and post-marketing were viral infections (includes herpes zoster, papillomavirus, influenza), bacterial infections (including abscess), rash, headache (including migraine), asthenia, leukopenia (including lymphopenia, neutropenia), eosinophilic disorder, pain (any sites), pyrexia, sensory abnormalities, hypertension, pruritus (any sites), hepatitis (including hepatic enzyme increase), injection site reactions, and nausea. Serious adverse reactions include sepsis, opportunistic infections, tuberculosis (including miliary, disseminated and extrapulmonary), herpes zoster, lymphoma, leukaemia, solid organ tumours, angioneurotic oedema, cardiomyopathies (includes heart failure), ischemic coronary artery disorders, pancytopenia, hypercoagulation (including thrombophlebitis, pulmonary embolism), cerebrovascular accident, vasculitis, hepatitis/hepatopathy (includes cirrhosis), and renal impairment/nephropathy (includes nephritis). In RA controlled clinical trials, 4.4 percent of patients discontinued taking Cimzia® due to adverse events vs. 2.7 percent for placebo.

Cimzia® was initially studied in 325 patients with active axial spondyloarthritis (including ankylosing spondylitis and non-radiographic axial spondyloarthritis) in the AS001 clinical study for up to 4 years, which includes a 24-week placebo-controlled phase followed by a 24-week dose-blind period and a 156-week open-label treatment period. Cimzia® was subsequently studied in 317 patients with non-radiographic axial spondyloarthritis in a placebo-controlled study for 52 weeks (AS0006). Cimzia® was also studied in patients with axial spondyloarthritis (including ankylosing spondylitis and non-radiographic axial spondyloarthritis) in a clinical study for up to 96 weeks, which included a 48-week open-label run-in phase (N=736) followed by a 48-week placebo-controlled phase (N=313) for patients in sustained remission (C-OPTIMISE). In all 3 studies, the safety profile for these patients was consistent with the safety profile in rheumatoid arthritis and previous experience with Cimzia®.

Cimzia® was studied in 409 patients with psoriatic arthritis (PsA) in a clinical study for up to 4 years which included a 24-week placebo-controlled phase followed by a 24-week dose-blind period and a 168-week open-label treatment period.

The safety profile for axSpA and PsA patients treated with Cimzia® was consistent with the safety profile in RA and previous experience with Cimzia®.

Cimzia® was studied in 1112 patients with psoriasis in controlled and open-label studies for up to 3 years. In the Phase III program, the initial and maintenance periods were followed by a 96-week open-label treatment period. The long-term safety profile of Cimzia® 400 mg every 2 weeks and Cimzia® 200 mg every 2 weeks was generally similar and consistent with previous experience with Cimzia.

Cimzia® is contraindicated in patients with hypersensitivity to the active substance or any of the excipients, active tuberculosis or other severe infections such as sepsis or opportunistic infections, and moderate to severe heart failure.

Serious infections including sepsis, tuberculosis and opportunistic infections (e.g. histoplasmosis, nocardia, candidiasis) have been reported in patients receiving Cimzia®. Some of these events have been fatal. Before initiation of therapy with Cimzia®, all patients must be evaluated for both active and inactive (latent) tuberculosis infection. If active tuberculosis is diagnosed prior to or during treatment, Cimzia® therapy must not be initiated and must be discontinued. If latent tuberculosis is diagnosed, appropriate anti-tuberculosis therapy must be started before initiating treatment with Cimzia®.

Reactivation of hepatitis B has occurred in patients receiving a TNF-antagonist including Cimzia® who are chronic carriers of the virus (i.e. surface antigen positive). Some cases have had a fatal outcome. Patients

should be tested for HBV infection before initiating treatment with Cimzia®. Carriers of HBV who require treatment with Cimzia® should be closely monitored and in the case of HBV reactivation Cimzia® should be stopped and effective anti-viral therapy with appropriate supportive treatment should be initiated.

TNF antagonists including Cimzia® may increase the risk of new onset or exacerbation of GL-P-CZ-axSpA-1900034 Important Safety Information Cimzia Revised April 2020 * EU/EEA means European Union/European Economic Area clinical symptoms and/or radiographic evidence of demyelinating disease including multiple sclerosis; of formation of autoantibodies and uncommonly of the development of a lupuslike syndrome; of severe hypersensitivity reactions. If a patient develops any of these adverse reactions, Cimzia® should be discontinued and appropriate therapy instituted.

With the current knowledge, a possible risk for the development of lymphomas, leukaemia or other malignancies in patients treated with a TNF antagonist cannot be excluded. Rare cases of neurological disorders, including seizure disorder, neuritis and peripheral neuropathy, have been reported in patients treated with Cimzia®.

Adverse reactions of the haematologic system, including medically significant cytopenia, have been reported with Cimzia®. Advise all patients to seek immediate medical attention if they develop signs and symptoms suggestive of blood dyscrasias or infection (e.g., persistent fever, bruising, bleeding, pallor) while on Cimzia®. Consider discontinuation of Cimzia® therapy in patients with confirmed significant haematological abnormalities.

The use of Cimzia® in combination with anakinra or abatacept is not recommended due to a potential increased risk of serious infections. As no data are available, Cimzia® should not be administered concurrently with live vaccines. The 14-day half-life of Cimzia® should be taken into consideration if a surgical procedure is planned. A patient who requires surgery while on Cimzia® should be closely monitored for infections.

Please consult the full prescribing information in relation to other side effects, full safety and prescribing information.
European SmPC date of revision July 2020.
https://www.ema.europa.eu/en/documents/product-information/cimzia-epar-product-information_en.pdf

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