UCB News

UCB receives CHMP positive opinion for Cimzia® in severe active axial spondyloarthritis

- CHMP adopts positive opinion for Cimzia® (certolizumab pegol) in adult patients with severe active axial spondyloarthritis (axSpA) comprising ankylosing spondylitis (AS) and axSpA without radiographic evidence of AS (nr-axSpA)
- Positive opinion is supported by data from the first Phase 3 study to include people living with ankylosing spondylitis and axSpA without radiographic evidence of AS
- European Commission decision expected in Q4 2013
- Approval would represent the second European indication for Cimzia®

Brussels, Belgium – 20 September 2013: UCB today announced that the European Medicines Agency's (EMA's) Committee for Medicinal Products for Human Use (CHMP) has adopted a positive opinion recommending extending the European Union marketing authorization for the use of Cimzia® (certolizumab pegol) in the treatment of adult patients with severe active axial spondyloarthritis (axSpA).

AxSpA is a form of spondyloarthritis that affects mainly the spine and sacroiliac joints, and comprises both ankylosing spondylitis (AS) and axSpA without X ray evidence of AS (non-radiographic axSpA [nr-axSpA]) sub-groups.[1] An approval for adult patients living with severe active axial spondyloarthritis would represent the second indication for Cimzia® in countries of the European Union. In general, the European Commission follows the recommendations of the CHMP and usually delivers its final decision within two months of the CHMP recommendation.

"The CHMP positive opinion is an important milestone since people living with severe active axSpA in Europe may soon have a new treatment option whether or not they have X ray evidence of structural damage to their sacroiliac joints," said Professor Dr. Iris Loew-Friedrich, Chief Medical Officer and Executive Vice President, UCB. "This is particularly important for patients living with axial spondyloarthritis without radiographic evidence of AS, whose symptoms may be just as debilitating as those with AS but for whom treatment options are currently limited."

The positive opinion for severe active axSpA comprising AS and axSpA without radiographic evidence of AS follows the EMA's review of data from the RAPID™-axSpA study which was the first randomized, controlled, Phase 3 study of an anti-TNF to enroll both AS and axSpA without radiographic evidence of AS patients.[2] The study is an on-going, Phase 3, multicenter, randomized, double-blind, placebo-controlled trial that was designed to evaluate the efficacy and safety of certolizumab pegol in patients with active axSpA.[3]

The primary endpoint of the RAPIDTM-axSpA study was ASAS20 at week 12, and was achieved with clinical and statistically significant improvements in ASAS20 responses in both dosing arms (200 mg every 2 weeks and 400 mg every 4 weeks) vs. placebo ($p \leq 0.004$).[2] The safety profile for axial spondyloarthritis patients treated with certolizumab pegol was consistent with the safety profile of certolizumab pegol reported in rheumatoid arthritis trials.[2]
In the European Union, certolizumab pegol is approved in combination with methotrexate (MTX) for the treatment of moderate to severe active rheumatoid arthritis in adult patients inadequately responsive to disease-modifying anti-rheumatic drugs, including MTX. Certolizumab pegol can be given as monotherapy in case of intolerance to MTX or when continued treatment with MTX is inappropriate.[4]

The EMA is currently reviewing another filing for certolizumab pegol in the treatment of adult patients with active psoriatic arthritis. In the US, both PsA and axSpA filings are currently under review by the US Food and Drug Administration (FDA).

Notes to editors

About RAPID™-axSpA study[3]
The RAPIDTM-axSpA study is an ongoing Phase 3, multicenter, randomized, double-blind, placebo-controlled study designed to evaluate the efficacy and safety of certolizumab pegol in patients with active axSpA. Patients (n=325) were randomized 1:1:1 to placebo, or 400 mg certolizumab pegol at week 0, 2 and 4 loading dose followed by either 200 mg certolizumab pegol every two weeks or 400 mg certolizumab pegol every four weeks. Patients enrolled in the study must have active disease and failed at least one non-steroidal anti-inflammatory drug (NSAID). Within the placebo arm, patients who failed to achieve an ASAS20 response at weeks 14 and 16 were re-randomized at week 16 to receive certolizumab pegol 200 mg every 2 weeks or 400 mg every 4 weeks, following the loading dose.

About axSpA [5,6,7,8]
Spondyloarthritis (SpA) can affect the spine, peripheral joints, ligaments, tendons and other extraarticular tissues such as the eyes, skin and gut. SpA can be divided into peripheral and axial spondyloarthritis (axSpA), depending on the location of the predominant features. While axSpA mostly affects the spine and sacroiliac joints, peripheral SpA predominantly affects the peripheral joints. axSpA can be further divided into ankylosing spondylitis (AS) and axSpA without radiographic evidence of AS.

Ankylosing Spondylitis
Ankylosing Spondylitis, or AS, is a chronic inflammatory rheumatic disease of the spine and is the most well-recognized subset of axSpA. The symptoms of AS can vary, but most people experience back pain and stiffness due to inflammation which can proceed to fusion of the sacroiliac joints. The condition usually begins between 15 and 35 years of age, with prevalence estimated to be 0.1-1.1% of the population. AS is more common in men than in women. Ankylosing spondylitis has a genetic component and is associated with the HLA-B27 gene.

axSpA without radiographic evidence of AS
Patients with no definitive sacroiliitis on conventional radiographs but similar clinical features to AS patients and showing either sacroiliitis on MRI or who are HLA-B27 positive may be classified as having axSpA without X ray evidence of AS (nr-axSpA).

About CIMZIA®
Cimzia® is the only Fc-free, PEGylated anti-TNF (Tumor Necrosis Factor). Cimzia® has a high affinity for human TNF-alpha, selectively neutralizing the pathophysiological effects of TNF-alpha. Over the past decade, TNF-alpha has emerged as a major target of basic research and clinical investigation. This cytokine plays a key role in mediating pathological inflammation, and excess TNF-alpha production has been directly implicated in a wide variety of diseases. Cimzia® in combination with MTX is approved in the EU for the treatment of moderate to severe active RA in adult patients inadequately responsive to disease-modifying antirheumatic drugs (DMARDs) including MTX. Cimzia® can be given as monotherapy in case of intolerance to MTX or when continued treatment with MTX is inappropriate. UCB is also developing Cimzia® in other autoimmune disease indications. Cimzia® is a registered trademark of UCB PHARMA S.A.

Cimzia® (certolizumab pegol) EU/EEA Important Safety Information
Cimzia® was studied in 4,049 patients with RA in controlled and open label trials for up to 92 months. The commonly reported adverse reactions (1-10%) in clinical trials with Cimzia® and post-marketing were viral infections (includes herpes, papillomavirus, influenza), bacterial infections (including abscess), rash, headache (including migraine), asthaenia, leukopaenia (including lymphopaenia, neutropaenia), 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, herpes zoster, lymphoma, leukaemia, solid organ tumours, angioneurotic oedema, cardiomyopathies (includes heart failure),

ischemic coronary artery disorders, pancytopaenia, 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% of patients discontinued taking Cimzia® due to adverse events vs. 2.7% for placebo.

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 or moderate to severe heart failure.

Serious infections including sepsis, tuberculosis and opportunistic infections have been reported in patients receiving Cimzia.® Some of these events have been fatal. Monitor patients closely for signs and symptoms of infections including tuberculosis before, during and after treatment with Cimzia.® Treatment with Cimzia® must not be initiated in patients with a clinically important active infection. If an infection develops, monitor carefully and stop Cimzia® if infection becomes serious. 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.® Patients should be instructed to seek medical advice if signs/symptoms (e.g. persistent cough, wasting/weight loss, low grade fever, listlessness) suggestive of tuberculosis occur during or after therapy 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 clinical symptoms and/or radiographic evidence of demyelinating disease; of formation of autoantibodies and uncommonly of the development of a lupus-like 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 hematologic system, including medically significant cytopaenia, have been infrequently 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 12th August 2013.

http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Product_Information/human/001037/WC500069763.pdf

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About UCB

UCB, Brussels, Belgium (www.ucb.com) is a global biopharmaceutical company focused on the discovery and development of innovative medicines and solutions to transform the lives of people living with severe diseases of the immune system or of the central nervous system. With 9000 people in approximately 40 countries, the company generated revenue of EUR 3.4 billion in 2012. UCB is listed on Euronext Brussels (symbol: UCB).

Forward looking statements

This press release contains forward-looking statements based on current plans, estimates and beliefs of management. All statements, other than statements of historical fact, are statements that could be deemed forward-looking statements, including estimates of revenues, operating margins, capital expenditures, cash, other financial information, expected legal, political, regulatory or clinical results and other such estimates and results. By their nature, such forward-looking statements are not guarantees of future performance and are subject to risks, uncertainties and assumptions which could cause actual results to differ materially from those that may be implied by such forward-looking statements contained in this press release. Important factors that could result in such differences include: changes in general economic, business and competitive conditions, the inability to obtain necessary regulatory approvals or to obtain them on acceptable terms, costs associated with research and development, changes in the prospects for products in the pipeline or under development by UCB, effects of future judicial decisions or governmental investigations, product liability claims, challenges to patent protection for products or product candidates, changes in laws or regulations, exchange rate fluctuations, changes or uncertainties in tax laws or the administration of such laws and hiring and retention of its employees. UCB is providing this information as of the date of this press release and expressly disclaims any duty to update any information contained in this press release, either to confirm the actual results or to report a change in its expectations.

There is no guarantee that new product candidates in the pipeline will progress to product approval or that new indications for existing products will be developed and approved. Products or potential products which are the subject of partnerships, joint ventures or licensing collaborations may be subject to differences between the partners. Also, UCB or others could discover safety, side effects or manufacturing problems with its products after they are marketed.

Moreover, sales may be impacted by international and domestic trends toward managed care and health care cost containment and the reimbursement policies imposed by third-party payers as well as legislation affecting biopharmaceutical pricing and reimbursement.