



UCB announces approval of Cimzia® in China

- After receiving priority review in 2018, CIMZIA® (certolizumab pegol) is now approved in China for the treatment of Moderate-to-Severe Rheumatoid Arthritis
- CIMZIA approval in China reinforces UCB's ongoing commitment to supporting patient value across China and to offering Chinese patients innovative medicines to help manage their disease

Brussels (Belgium), July 22, 2019 – 07:00 (CET): Belgium-based global bio-pharmaceutical company UCB today announced it has received an Import Drug License (IDL) from the National Medical Product Administration (NMPA), enabling people living with moderate-to-severe rheumatoid arthritis to access CIMZIA® (certolizumab pegol) in China. This approval provides the first biologic therapy in UCB's portfolio in China, allowing the company to transition its agile biopharmaceutical model into this important patient population.

The NMPA granted priority review for the approval of CIMZIA to treat moderate-to-severe RA in 2018, based on the therapeutic advantage seen with the therapy. The submission was based on Phase 3 clinical trial results, RAPID-C and RAPID-C open-label extension (OLE), which demonstrated efficacy and safety for the approved indication in China. In the 24-week RAPID C study, Cimzia in combination with methotrexate showed a rapid onset of response, sustained effects in reducing the signs and symptoms of rheumatoid arthritis and improving physical function compared with methotrexate alone with an acceptable safety profile in Chinese patients with rheumatoid arthritis and an inadequate response to methotrexate.ⁱ UCB also included in the submission specific pregnancy and lactation information, based on findings from two first-of-their-kind studies in women of childbearing age, CRIB and CRADLE, together with pregnancy outcomes data.

The results of the RAPID-C and RAPID-C OLE trials demonstrate the potential value of CIMZIA for Chinese patients.ⁱⁱ In addition, due to its unique Fc-free molecular structure, CIMZIA is the only anti-TNF that has evidence from clinical studies from conception to late pregnancy and lactation.ⁱⁱⁱ

Rheumatoid arthritis is three times more common in women than men. For women patients who have family plans, treatment planning is a key concern. The approval of Cimzia provides an exciting new choice for those affected by rheumatoid arthritis in China, and especially for women of childbearing age," said Professor Li Zhanguo from Peking University People's Hospital, Former President of Asia Pacific league of Associations for Rheumatology, Former Chair of Chinese Rheumatology Association.

“UCB has a long heritage in rheumatology, with many years of clinical experience with CIMZIA in moderate-to-severe rheumatoid arthritis, and we are delighted to be bringing a new treatment option to Chinese patients living with this challenging chronic rheumatic condition. This approval is also important for Chinese women who need treatment options to manage their RA without compromising their plans for pregnancy and breastfeeding,” said Emmanuel Caeymaex, Executive Vice President, Immunology Patient Value Unit, UCB. “As a company, UCB is fully dedicated to delivering innovative medicines by connecting our science and research to the needs of patients suffering from severe immunological conditions.”

There are an estimated 5 million patients living with rheumatoid arthritis in China, with an age-adjusted prevalence of 0.28% (95% CI 0.19%, 0.41%), indicating a need for effective treatment options.^{iv}

UCB will ensure accelerated patient access to Cimzia® through a pioneering partnership with Cinkate, a well-established Chinese pharmaceutical company in rheumatology. The leading digital solutions from Cinkate will help the alliance to gain patient insights and maximize Physician-Patient interaction for better disease management.

UCB has been present in China since 1996 and has a strong commitment to making our novel medicines available to support patients living with severe diseases in the country. UCB’s innovative neurology drugs Neupro and Vimpat were approved in China in 2018. Additionally, in 2014, UCB inaugurated a new state of the art 13,000 m² manufacturing site in Zhuhai, which strengthened the company’s footprint in the country.

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.

About CIMZIA® in Fertility, Pregnancy and Lactation in the EU/EEA

Women of childbearing potential

The use of adequate contraception should be considered for women of childbearing potential. For women planning pregnancy, continued contraception may be considered for 5 months after the last CIMZIA dose due to its elimination rate, but the need for treatment of the woman should also be taken into account (see below).

Pregnancy

Data from more than 500 prospectively collected pregnancies exposed to CIMZIA with known pregnancy outcomes, including more than 400 pregnancies exposed during the first trimester, does not indicate a malformative effect of CIMZIA. However, the available clinical experience is too limited to, with a reasonable certainty, conclude that there is no increased risk associated with CIMZIA administration during pregnancy.

Animal studies using a rodent anti-rat TNF α did not reveal evidence of impaired fertility or harm to the foetus. However, these are insufficient with respect to human reproductive toxicity. Due to its inhibition of TNF α , CIMZIA administered during pregnancy could affect normal immune response in the newborn.

CIMZIA should only be used during pregnancy if clinically needed. Non-clinical studies suggest low or negligible level of placental transfer of a homologue Fab-fragment of certolizumab pegol (no Fc region).

In a clinical study 16 women were treated with certolizumab pegol (200 mg every 2 weeks or 400 mg every 4 weeks) during pregnancy. Certolizumab pegol plasma concentrations measured in 14 infants at birth were Below the Limit of Quantification (BLQ) in 13 samples; one was 0.042 μ g/ml with an infant/mother plasma ratio at birth of 0.09%. At Week 4 and Week 8, all infant concentrations were BLQ. The clinical significance of low levels certolizumab pegol for infants is unknown. It is recommended to wait a minimum of 5 months following the mother's last CIMZIA administration during pregnancy before administration of live or live-attenuated vaccines (e.g. BCG vaccine), unless the benefit of the vaccination clearly outweighs the theoretical risk of administration of live or live-attenuated vaccines to the infants.

Breastfeeding

In a clinical study in 17 lactating women treated with CIMZIA, minimal transfer of certolizumab pegol from plasma to breast milk was observed. The percentage of the maternal certolizumab pegol dose reaching an infant during a 24 hour period was estimated to 0.04% to 0.30%. In addition, since certolizumab pegol is a protein that is degraded in the gastrointestinal tract after oral administration, the absolute bioavailability is expected to be very low in a breastfed infant. Consequently, CIMZIA can be used during breastfeeding.

Important Safety Information about CIMZIA® in the EU/EEA

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%) in clinical trials with Cimzia® and post-marketing were viral infections (includes herpeszoster, 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 (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% 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 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. 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® until the infection is controlled. 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, including multiple sclerosis; 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 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.

Cimzia® was studied in 325 patients with active axial spondyloarthritis (axSpA) and in 409 patients with psoriatic arthritis (PsA) for up to 4 years. 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 18 months. The safety profile of Cimzia® 400 mg every 2 weeks and Cimzia® 200 mg every 2 weeks were generally similar.

Please consult the full prescribing information in relation to other side effects, full safety and prescribing information. European SmPC date of revision March 2019.

https://www.ema.europa.eu/documents/product-information/cimzia-epar-product-information_en.pdf

CIMZIA® is a registered trademark of the UCB Group of Companies.

For further information:

Corporate Communications

France Nivelles,
Global Communications,
UCB
T +32.2.559.9178,
france.nivelles@ucb.com

Laurent Schots,
Media Relations, UCB
T +32.2.559.92.64,
laurent.schots@ucb.com

Investor Relations

Antje Witte,
Investor Relations, UCB

T +32.2.559.94.14,
antje.witte@ucb.com

Isabelle Ghellynck
T +32.2.559.9588
Isabelle.Ghellynck@ucb.com

Immunology Communications

Andrea Christopher,
Immunology Communications,
UCB

T +1.404.483.7329
andrea.christopher@ucb.com

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 in immunology and neurology. With approximately 7 500 people operating in 40 countries, the company generated revenue of € 4.6 billion in 2018. UCB is listed on Euronext Brussels (symbol: UCB). Follow us on Twitter: @UCB_news

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.

Additionally, information contained in this document shall not constitute an offer to sell or the solicitation of an offer to buy any securities, nor shall there be any offer, solicitation or sale of securities in any jurisdiction in which such offer, solicitation or sale would be unlawful prior to the registration or qualification under the securities laws of such jurisdiction. UCB is providing this information as of the date of this document 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.

iL. Bi, Y. Li, L. He, H. Xu, Z. Jiang, Y. Wang, X. Li, W. Wei, J. Gu, G. Wang, Z. Zhang, B. Zhou, Y. Liu, Z. Wu, H. Liu, D. He, Z. Lv, Z. Li, X. Zuo, L. Dong, H. Wu, H. Zhang, H. Chen, C. Bao, Z. Zhang, M. Zhang, H. Song, Y. Zheng, L. Jiang, X. Liu, M. Boehnlein, J. Dunkel, J. Shao, K. Harris, Z. Li. *Clin Exp Rheumatol*. 2019; 37(2):227-234. Epub 2018 Aug 29.

ⁱⁱBi L, Li Y, He L, Xu H, Gu J, Wang G, Zhang Z, Liu Y, Boehnlein M, Dunkel J, Shao J, Harris K, Li Z. Rapid Onset of Response Observed with Certolizumab Pegol in Rheumatoid Arthritis Patients with Inadequate Response to Methotrexate: Efficacy and Safety Results of a Randomized, Double-Blind, Placebo-Controlled Phase 3 Study [abstract]. *Arthritis Rheumatol*. 2017; 69 (suppl 10)

ⁱⁱⁱRAPID-C OLE. Clinical Study Report. Data on File. UCB. 2018.

ⁱⁱⁱ Mariette X, Forger F, Abraham B, et al. *Ann Rheum Dis* Published Online First: 13 October 2017. doi:10.1136/annrheumdis-2017-212196

ⁱⁱⁱ Clowse ME, Förger F, Hawng C, et al. Minimal to no transfer of certolizumab pegol into breast milk: results from CRADLE, a prospective, postmarketing, multicentre, pharmacokinetic study. *Ann Rheum Dis*. 2017;0:1–7.

^{iv} Ru Li, Jian Sun, Li-Min Ren, Hong-Yu Wang, Wen-Hong Liu, Xue-Wu Zhang, Shi Chen, Rong Mu, Jing He, Yi Zhao, Li Long, Yan-Ying Liu, Xia Liu, Xiao-Lan Lu, Yu-Hui Li, Shi-Yao Wang, Si-Si Pan, Chun Li, Hong-Yuan Wang and Zhan-Guo Li. Epidemiology of eight common rheumatic diseases in China: a large-scale cross-sectional survey in Beijing. *Rheumatology* 2012;51:721-729.