



## **CIMZIA® (certolizumab pegol) label update marks major advance for women of childbearing age with chronic inflammatory disease in the U.S.**

- U.S. Food and Drug Administration (FDA) approves label change for UCB's CIMZIA® (certolizumab pegol)
- Data added to the label includes first-of-their-kind pharmacokinetic studies demonstrating negligible to low transfer of CIMZIA through placenta and minimal transfer to breast milk from mother to infant<sup>1,2</sup>

**Brussels, Belgium – 22 March, 7:00 CEST** – UCB announced today that the U.S. Food and Drug Administration (FDA) approved a label update that includes pharmacokinetic data showing negligible to low transfer of CIMZIA® (certolizumab pegol) through placenta and minimal transfer to breast milk from mother to infant. These data provide essential information to healthcare providers to inform the care of women with chronic inflammatory disease, including rheumatoid arthritis (RA), ankylosing spondylitis (AS), psoriatic arthritis (PsA) and Crohn's disease (CD), throughout their reproductive health journey.

Chronic inflammatory diseases such as RA, AS, PsA and CD often affect women of childbearing age.<sup>3</sup> Approximately 17% of patients with these chronic inflammatory diseases in the U.S. are women aged 18-45.<sup>4</sup> Research in RA and CD patients has shown that the consequences of active disease during pregnancy can have serious implications for both mother and infant, including an increased risk of miscarriage,<sup>5</sup> difficulties in the third trimester and birth, an increased risk of preterm delivery, and the infant being small for gestational age.<sup>6,4</sup>

“It is well recognized that women with chronic inflammatory disease face uncertainty during motherhood, given the lack of information on treatment during pregnancy and breastfeeding. Many women with chronic inflammatory disease discontinue their biologic treatment during pregnancy, often when they need disease control the most,” said CRADLE lead study author Megan E. B. Clowse, MD, MPH, Duke University Medical Center. “These data for CIMZIA provide important information to empower women and healthcare providers making decisions about treatment during pregnancy and breastfeeding.”

“Recognition and public support for the unique family planning needs of women with chronic inflammatory disease is crucial for this underserved population. The label change for CIMZIA is important for women and their treating physicians to make informed decisions to manage their condition along their pregnancy journey. During this significant time in their lives, we're proud to offer support and important treatment information to women and their physicians as they plan for pregnancy and adequate disease management,” said Emmanuel Caeymaex, Head of Immunology and Executive Vice President, Immunology Patient Value Unit, UCB. “UCB is executing on its Patient Value Strategy to connect the unmet needs of patients with innovative science. This new label update reaffirms UCB's commitment to providing cutting edge research, developing medicines that treat serious, chronic diseases and supporting underserved patient populations with unmet needs, like women of childbearing age.”

Limited data from the ongoing pregnancy registry on use of CIMZIA in pregnant women are not sufficient to inform a risk of major birth defects or other adverse pregnancy outcomes.

Some women with rheumatic chronic inflammatory disease experience persistent moderate-to-high disease activity during pregnancy. These women are faced with difficult questions regarding the

impact of active disease flares on themselves and their babies, and need more information on therapeutic intervention.<sup>7-12</sup> Given the fact that postpartum disease flares occur in 50-90% of women with chronic inflammatory diseases, women who are considering breastfeeding, along with their treating physicians, face a conflict between the risks of maternal medications and the health benefits of breastfeeding for mother and infant.<sup>2,7</sup>

UCB has been leading the way in studying how biologic drugs impact women of childbearing age. Two key areas of focus are the transfer of a biologic drug through the placenta to the fetus and via the mother's breast milk to the infant. Anti-TNF lactation data historically has been based on case reports without any controlled studies. However, UCB is changing the way this research is conducted. The findings from two first-of-their-kind studies have strong implications for this patient population as they consider pregnancy. Based on results from the landmark CRIB study, there is negligible to low placental transfer evident from mother to child during pregnancy. Data from CRADLE, the prospective pharmacokinetic trial measuring the presence of an anti-TNF in breast milk, found minimal transfer of CIMZIA during lactation. UCB developed the CRADLE study with input from the FDA, including the agency's Division of Pediatric and Maternal Health.

The approval of the CIMZIA label update is based on data from the post-marketing pharmacokinetic CRIB and CRADLE studies. The studies included women with RA, PsA, AS and CD.

### **About the CRIB Study<sup>1</sup>**

CRIB was a pharmacokinetic study assessing the potential level of placental transfer of certolizumab pegol (CZP) from pregnant women to their infants. The study followed sixteen women ( $\geq 30$  weeks gestation) who were already receiving CZP at approved doses.

The study found that CZP levels were below the lower limit of quantification (LLOQ = 0.032 micrograms/mL) in 13 out of 15 infant blood samples at birth, and in all samples at weeks four and eight. One infant had a minimal CZP level of 0.042ug/mL, which was 0.09% of the mother's plasma concentration at birth. In a second infant, delivered by emergency Caesarean section, the concentration was 0.485 mcg/mL, which was 4.49% of the mother's plasma concentration at birth. At Week 4 and Week 8, all 15 infants had no measurable concentrations. No anti-CZP antibodies were detected in mothers, umbilical cords, or infants. Among 16 exposed infants, one serious adverse reaction was reported in a neonate who was treated empirically with intravenous antibiotics due to an increased white blood cell count; blood cultures were negative. These data indicate negligible to low placental transfer of CZP from mothers to infants, suggesting minimal in-utero fetal exposure during the third trimester.

### **About the CRADLE Study<sup>2</sup>**

The primary objectives of the CRADLE pharmacokinetic study were to determine the concentration of CZP in human breast milk and the average daily infant dose, an estimation of the daily dose of maternal CZP ingested by the breastfeeding infant.

Among 137 breast milk samples from 17 mothers, 56% had no measurable CZP; the remaining samples showed minimal levels of CZP. The median of the estimated average daily infant doses was 0.0035 mg/kg/day (range: 0 to 0.01 mg/kg/day). The percentage of the maternal dose (200 mg CIMZIA dosed once every 2 weeks), that reaches an infant ranged from 0.56% to 4.25% based on samples with measurable certolizumab pegol concentration.

In CRADLE, no serious adverse reactions were noted in the 17 infants in the study. Adverse events in mothers exposed to CZP were consistent with the known safety profile of CZP.<sup>2</sup>

### **About CIMZIA® in the US**

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.

CIMZIA® is indicated for the treatment of adults with moderately to severely active rheumatoid arthritis, adults with active psoriatic arthritis (PsA), and adults with active ankylosing spondylitis (AS).

In addition, it is indicated for reducing signs and symptoms of Crohn's disease and maintaining clinical response in adult patients with moderately to severely active disease who have had an inadequate response to conventional therapy. See important safety information including risk of serious bacterial, viral and fungal infections and tuberculosis below.

### **Important Safety Information about CIMZIA® in the US**

#### **Risk of Serious Infections and Malignancy**

**Patients treated with CIMZIA® are at an increased risk for developing serious infections that may lead to hospitalization or death. Most patients who developed these infections were taking concomitant immunosuppressants such as methotrexate or corticosteroids. CIMZIA® should be discontinued if a patient develops a serious infection or sepsis. Reported infections include:**

- **Active tuberculosis, including reactivation of latent tuberculosis. Patients with tuberculosis have frequently presented with disseminated or extrapulmonary disease. Patients should be tested for latent tuberculosis before CIMZIA® use and during therapy. Treatment for latent infection should be initiated prior to CIMZIA® use.**
- **Invasive fungal infections, including histoplasmosis, coccidioidomycosis, candidiasis, aspergillosis, blastomycosis, and pneumocystosis. Patients with histoplasmosis or other invasive fungal infections may present with disseminated, rather than localized disease. Antigen and antibody testing for histoplasmosis may be negative in some patients with active infection. Empiric anti-fungal therapy should be considered in patients at risk for invasive fungal infections who develop severe systemic illness.**
- **Bacterial, viral and other infections due to opportunistic pathogens, including Legionella and Listeria.**

**The risks and benefits of treatment with CIMZIA® should be carefully considered prior to initiating therapy in patients with chronic or recurrent infection. Patients should be closely monitored for the development of signs and symptoms of infection during and after treatment with CIMZIA®, including the possible development of tuberculosis in patients who tested negative for latent tuberculosis infection prior to initiating therapy.**

**Lymphoma and other malignancies, some fatal, have been reported in children and adolescent patients treated with TNF blockers, of which CIMZIA® is a member. CIMZIA® is not indicated for use in pediatric patients.**

Patients treated with CIMZIA® are at an increased risk for developing serious infections involving various organ systems and sites that may lead to hospitalization or death. Opportunistic infections

due to bacterial, mycobacterial, invasive fungal, viral, parasitic, or other opportunistic pathogens including aspergillosis, blastomycosis, candidiasis, coccidioidomycosis, histoplasmosis, legionellosis, listeriosis, pneumocystosis and tuberculosis have been reported with TNF blockers. Patients have frequently presented with disseminated rather than localized disease.

Treatment with CIMZIA® should not be initiated in patients with an active infection, including clinically important localized infections. CIMZIA® should be discontinued if a patient develops a serious infection or sepsis. Patients greater than 65 years of age, patients with co-morbid conditions, and/or patients taking concomitant immunosuppressants (e.g., corticosteroids or methotrexate) may be at a greater risk of infection. Patients who develop a new infection during treatment with CIMZIA® should be closely monitored, undergo a prompt and complete diagnostic workup appropriate for immunocompromised patients, and appropriate antimicrobial therapy should be initiated. Appropriate empiric antifungal therapy should also be considered while a diagnostic workup is performed for patients who develop a serious systemic illness and reside or travel in regions where mycoses are endemic.

## Malignancies

During controlled and open-labeled portions of CIMZIA® studies of Crohn's disease and other diseases, malignancies (excluding non-melanoma skin cancer) were observed at a rate of 0.5 per 100 patient-years among 4,650 CIMZIA®-treated patients versus a rate of 0.6 per 100 patient-years among 1,319 placebo-treated patients. In studies of CIMZIA® for Crohn's disease and other investigational uses, there was one case of lymphoma among 2,657 CIMZIA®-treated patients and one case of Hodgkin's lymphoma among 1,319 placebo-treated patients. In CIMZIA® RA clinical trials (placebo-controlled and open label), a total of three cases of lymphoma were observed among 2,367 patients. This is approximately 2-fold higher than expected in the general population. Patients with RA, particularly those with highly active disease, are at a higher risk for the development of lymphoma. The potential role of TNF blocker therapy in the development of malignancies is not known.

Malignancies, some fatal, have been reported among children, adolescents, and young adults who received treatment with TNF-blocking agents (initiation of therapy ≤18 years of age), of which CIMZIA® is a member. Approximately half of the cases were lymphoma (including Hodgkin's and non-Hodgkin's lymphoma), while the other cases represented a variety of different malignancies and included rare malignancies associated with immunosuppression and malignancies not usually observed in children and adolescents. Most of the patients were receiving concomitant immunosuppressants.

Cases of acute and chronic leukemia have been reported with TNF-blocker use. Even in the absence of TNF-blocker therapy, patients with RA may be at a higher risk (approximately 2-fold) than the general population for developing leukemia.

Postmarketing cases of hepatosplenic T-cell lymphoma (HSTCL), a rare type of T-cell lymphoma that has a very aggressive disease course and is usually fatal, have been reported in patients treated with TNF blockers, including CIMZIA®. The majority of reported TNF blocker cases occurred in adolescent and young adult males with Crohn's disease or ulcerative colitis. Almost all of these patients had received treatment with the immunosuppressants azathioprine and/or 6-mercaptopurine (6-MP) concomitantly with a TNF blocker at or prior to diagnosis. Carefully assess the risks and benefits of treatment with CIMZIA®, especially in these patient types.

Melanoma and Merkel cell carcinoma have been reported in patients treated with TNF-antagonists, including CIMZIA<sup>®</sup>. Periodic skin examinations are recommended for all patients, particularly those with risk factors for skin cancer.

### **Heart Failure**

Cases of worsening congestive heart failure (CHF) and new onset CHF have been reported with TNF blockers. CIMZIA<sup>®</sup> has not been formally studied in patients with CHF. Exercise caution when using CIMZIA<sup>®</sup> in patients who have heart failure and monitor them carefully.

### **Hypersensitivity**

Symptoms compatible with hypersensitivity reactions, including angioedema, dyspnea, hypotension, rash, serum sickness, and urticaria, have been reported rarely following CIMZIA<sup>®</sup> administration. Some of these reactions occurred after the first administration of CIMZIA<sup>®</sup>. If such reactions occur, discontinue further administration of CIMZIA<sup>®</sup> and institute appropriate therapy.

### **Hepatitis B Reactivation**

Use of TNF blockers, including CIMZIA<sup>®</sup>, has been associated with reactivation of hepatitis B virus (HBV) in patients who are chronic carriers of this virus. Some cases have been fatal. Test patients for HBV infection before initiating treatment with CIMZIA<sup>®</sup>. Exercise caution in prescribing CIMZIA<sup>®</sup> for patients identified as carriers of HBV, with careful evaluation and monitoring prior to and during treatment. In patients who develop HBV reactivation, discontinue CIMZIA<sup>®</sup> and initiate effective anti-viral therapy with appropriate supportive treatment.

### **Neurologic Reactions**

Use of TNF blockers, including CIMZIA<sup>®</sup>, has been associated with rare cases of new onset or exacerbation of clinical symptoms and/or radiographic evidence of central nervous system demyelinating disease, including multiple sclerosis, and with peripheral demyelinating disease, including Guillain-Barré syndrome. Rare cases of neurological disorders, including seizure disorder, optic neuritis, and peripheral neuropathy have been reported in patients treated with CIMZIA<sup>®</sup>. Exercise caution in considering the use of CIMZIA<sup>®</sup> in patients with these disorders.

### **Hematologic Reactions**

Rare reports of pancytopenia, including aplastic anemia, have been reported with TNF blockers. Medically significant cytopenia (e.g., leukopenia, pancytopenia, thrombocytopenia) has been infrequently reported with CIMZIA<sup>®</sup>. 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<sup>®</sup>. Consider discontinuation of CIMZIA<sup>®</sup> therapy in patients with confirmed significant hematologic abnormalities.

### **Drug Interactions**

An increased risk of serious infections has been seen in clinical trials of other TNF blocking agents used in combination with anakinra or abatacept. Formal drug interaction studies have not been performed with rituximab or natalizumab; however, because of the nature of the adverse events seen with these combinations with TNF blocker therapy, similar toxicities may also result from the use of CIMZIA<sup>®</sup> in these combinations. Therefore, the combination of CIMZIA<sup>®</sup> with anakinra, abatacept, rituximab, or natalizumab is not recommended. Interference with certain coagulation assays has

been detected in patients treated with CIMZIA®. There is no evidence that CIMZIA® therapy has an effect on *in vivo* coagulation. CIMZIA® may cause erroneously elevated aPTT assay results in patients without coagulation abnormalities.

### Autoimmunity

Treatment with CIMZIA® may result in the formation of autoantibodies and, rarely, in the development of a lupus-like syndrome. Discontinue treatment if symptoms of lupus-like syndrome develop.

### Immunizations

Do not administer live vaccines or live-attenuated vaccines concurrently with CIMZIA®.

### Adverse Reactions

In controlled Crohn's clinical trials, the most common adverse events that occurred in ≥5% of CIMZIA® patients (n=620) and more frequently than with placebo (n=614) were upper respiratory infection (20% CIMZIA®, 13% placebo), urinary tract infection (7% CIMZIA®, 6% placebo), and arthralgia (6% CIMZIA®, 4% placebo). The proportion of patients who discontinued treatment due to adverse reactions in the controlled clinical studies was 8% for CIMZIA® and 7% for placebo.

In controlled RA clinical trials, the most common adverse events that occurred in ≥3% of patients taking CIMZIA® 200 mg every other week with concomitant methotrexate (n=640) and more frequently than with placebo with concomitant methotrexate (n=324) were upper respiratory tract infection (6% CIMZIA®, 2% placebo), headache (5% CIMZIA®, 4% placebo), hypertension (5% CIMZIA®, 2% placebo), nasopharyngitis (5% CIMZIA®, 1% placebo), back pain (4% CIMZIA®, 1% placebo), pyrexia (3% CIMZIA®, 2% placebo), pharyngitis (3% CIMZIA®, 1% placebo), rash (3% CIMZIA®, 1% placebo), acute bronchitis (3% CIMZIA®, 1% placebo) and fatigue (3% CIMZIA®, 2% placebo). Hypertensive adverse reactions were observed more frequently in patients receiving CIMZIA® than in controls. These adverse reactions occurred more frequently among patients with a baseline history of hypertension and among patients receiving concomitant corticosteroids and non-steroidal anti-inflammatory drugs. Patients receiving CIMZIA® 400 mg as monotherapy every 4 weeks in RA controlled clinical trials had similar adverse reactions to those patients receiving CIMZIA® 200 mg every other week. The proportion of patients who discontinued treatment due to adverse reactions in the controlled clinical studies was 5% for CIMZIA® and 2.5% for placebo.

The safety profile for patients with psoriatic arthritis (PsA) treated with CIMZIA® was similar to the safety profile seen in patients with RA and previous experience with CIMZIA®.

The safety profile for AS patients treated with CIMZIA® was similar to the safety profile seen in patients with RA.

For full prescribing information, please visit [www.ucb.com](http://www.ucb.com)

### 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.

### **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 $\alpha$  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 $\alpha$ , 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  $\mu\text{g/ml}$  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<sup>®</sup>, minimal transfer of certolizumab pegol from plasma to breast milk was observed. The percentage of the maternal certolizumab pegol dose that was 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<sup>®</sup> in the EU/EEA**

CIMZIA<sup>®</sup> 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<sup>®</sup> and post-marketing were viral infections (includes herpes, 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, 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<sup>®</sup> due to adverse events vs. 2.7% for placebo.

CIMZIA<sup>®</sup> 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<sup>®</sup>. 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<sup>®</sup>. Treatment with CIMZIA<sup>®</sup> must not be initiated in patients with a clinically important active infection. If an infection develops, monitor carefully and stop CIMZIA<sup>®</sup> if infection becomes serious. Before initiation of therapy with CIMZIA<sup>®</sup>, all patients must be evaluated for both active and inactive (latent) tuberculosis infection. If active tuberculosis is diagnosed prior to or during treatment, CIMZIA<sup>®</sup> 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<sup>®</sup>. 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<sup>®</sup>.

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 haematologic 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.

CIMZIA® was studied in 325 patients with active axial spondyloarthritis (axSpA) in a placebo-controlled clinical trial for up to 30 months and in 409 patients with psoriatic arthritis (PsA) in a placebo-controlled clinical trial for up to 30 months. The safety profile for axSpA and PsA patients treated with CIMZIA® was consistent with the safety profile in RA and previous experience with CIMZIA®.

Please consult the full prescribing information in relation to other side effects, full safety and prescribing information. European SmPC date of revision December 2017.

[http://www.ema.europa.eu/docs/en\\_GB/document\\_library/EPAR\\_-\\_Product\\_Information/human/001037/WC500069763.pdf](http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Product_Information/human/001037/WC500069763.pdf)

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

**For further information, UCB:**

**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

**Brand Communications**

Andrea Levin Christopher,  
Immunology Communications, UCB

T +1.404.483.7329  
andrea.levin@ucb.com

**About UCB**

UCB, Brussels, Belgium ([www.ucb.com](http://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 €4.5 billion in 2017. UCB is listed on Euronext Brussels (symbol: UCB). Follow us on Twitter: @UCB\_news.

**Forward looking statements – UCB**

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.

###

## REFERENCES

- <sup>1</sup> Abraham B, Mariette X, Flynn AD, et al. Lack of Placental Transfer of Certolizumab Pegol During Pregnancy: Results from CRIB, a Prospective, Postmarketing, Multicenter, Pharmacokinetic Study. *Gastroenterol.* 2017;S0016-5085(17)34376-7.
- <sup>2</sup> 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.
- <sup>3</sup> Förger F. Treatment with biologics during pregnancy in patients with rheumatic diseases. *Reumatologia.* 2017;55(2):57-58.
- <sup>4</sup> Mahadaven U, Cucchiara S, Hyams J, et al. *Am J Gastroenterol* 2011; 106:214-223; doi: 10.1038/ajg.2010.464; published online 14 December 2010
- <sup>5</sup> Brouwer J, Laven JS, Hazes JM, Dolhain RJ. Miscarriages in Female Rheumatoid Arthritis Patients: Associations With Serologic Findings, Disease Activity, and Antirheumatic Drug Treatment. *Arthritis Rheumatol.* 2015;67(7):1738-43.
- <sup>6</sup> Bharti B, Lee SJ, Lindsay SP, et al. Disease severity and pregnancy outcomes in women with rheumatoid arthritis: results from the Organization of Teratology Information Specialists autoimmune diseases in pregnancy project. *J Rheumatol.* 2015;42:1376-1382.
- <sup>7</sup> Brouwer J, Hazes JMW, Laven JSE, et al. Fertility in Women with Rheumatoid Arthritis: Influence of Disease Activity and Medication. *Annals of the Rheumatic Diseases* 2015;74:1836-1841.
- <sup>8</sup> Jethwa H, Lam S, Giles I. O26. Does Inflammatory Arthritis Really Improve During Pregnancy? A Systematic Review and Meta-Analysis. *Rheumatology.* 2014;53(1):i40-i40.
- <sup>9</sup> Mouyis MA, Thornton CC, Williams D, Giles IP. Pregnancy Outcomes in Patients with Psoriatic Arthritis. *J Rheumatol.* 2017;44:128-129.
- <sup>10</sup> Polachek A, Li S, Polachek IS, et al. Psoriatic arthritis disease activity during pregnancy and the first-year postpartum. *Semin Arthritis Rheum.* 2017;46:740-745.
- <sup>11</sup> de Man YA, Dolhain RJ, van de Geijn FE, Willemsen SP, Hazes JM. Disease activity of rheumatoid arthritis during pregnancy: results from a nationwide prospective study. *Arthritis Rheum.* 2008;59(9):1241-1248.
- <sup>12</sup> Pedersen N, Bortoli A, Duricova D, et al. The course of inflammatory bowel disease during pregnancy and postpartum: a prospective European ECCO-EpiCom Study of 209 pregnant women. *Aliment Pharmacol Ther.* 2013;38:501-512.