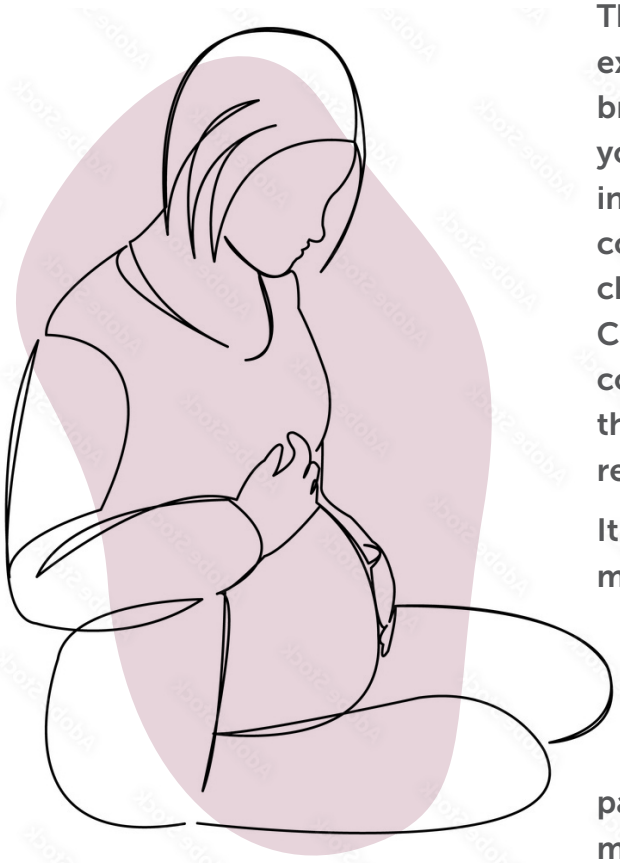
CIMZIA® (certolizumab pegol) in Pregnancy and Breastfeeding

Cimzia For Her



This factsheet aims to provide information about exposure to CIMZIA during pregnancy and breastfeeding, to aid your clinical practice and help you advise your patients. CIMZIA should only be used in pregnancy if clinically needed. The use of adequate contraception should be considered for women of childbearing potential who have been prescribed CIMZIA. For women planning pregnancy, continued contraception may be considered for 5 months after the last CIMZIA dose due to its elimination rate. Please refer to the SmPC for further information.[1]

It is understandable for women to want to review any medications they are on when they find out they are pregnant. However, it is important that they do not stop or make any changes to how they take their medication before talking to their healthcare professional. Healthcare professionals should advise patients of the benefits and/or risks of taking any medication whilst pregnant or breastfeeding.

What is CIMZIA?

CIMZIA® (certolizumab pegol) is indicated for the treatment of moderate to severe plaque psoriasis in adults who are candidates for systemic therapy.[1] Full indications can be found at the end of this document.

CIMZIA is a recombinant, humanised antibody Fab' fragment against tumour necrosis factor alpha (TNFα) expressed in Escherichia coli and conjugated to polyethylene glycol (PEG).[1] CIMZIA has a unique molecular structure and is the only Fc-free biologic in moderate to severe chronic plaque psoriasis.[2-4]

This document is for UK and ROI healthcare professionals only and has been initiated and funded by UCB Pharma Ltd.
Prescribing information and adverse event reporting can be found at the end of this document.

CIMZIA® (certolizumab pegol) in Pregnancy and Breastfeeding

Cimzia For Her

Can CIMZIA affect fertility?

Effects on sperm motility measures and a trend of reduced sperm count in male rodents have been observed with no apparent effect on fertility.[1]

Does taking CIMZIA increase the chance of miscarriage?

Miscarriage can occur in any pregnancy. However, prospective and retrospective studies reporting on pregnancy outcomes following maternal CIMZIA exposure have not indicated an increased risk of foetal death.[5-7]

Does taking CIMZIA increase the chance of birth defects?

Every infant carries at least 3-5% risk of being born with a malformation or deformation and approximately 10% risk of being born with internal abnormalities or functional deficits.[8] Data from 1,392 prospectively collected pregnancies exposed to CIMZIA with known pregnancy outcomes, including 1,021 who had at least first-trimester CIMZIA exposure, does not indicate a malformative effect of CIMZIA.[6,a] Further data are being collected as the available clinical experience is still limited to conclude that there is no increased risk associated with CIMZIA administration during pregnancy.[1]

Can taking CIMZIA during pregnancy increase the chance of any other pregnancy related problems?

Disease flares during pregnancy are associated with an increased risk of miscarriage, preterm delivery and low birth weight and may be more detrimental to neonatal outcomes than potential risks associated with anti-TNF therapy.[9] Therefore it is important that their conditions remain controlled during pregnancy and women should continue to take their medication if necessary.

In the CRIB[b] study, 16 women were treated with CIMZIA during pregnancy.[9] Only 1 infant was born preterm, only 1 infant had low birth weight, and infection was reported in 1 infant.[9]

This study measured drug levels in both pregnant women as well as in the umbilical cord blood and infant blood.[9] Due to its Fc-free structure, CIMZIA is not expected to undergo active placental transfer.[9] The results of the CRIB study suggest no to minimal placental transfer of CIMZIA during the third trimester, and the minimal level detected in one infant at birth (<0.1% of the adult therapeutic level) can be assumed to have no effect on immune system development.[9] Of the 14 infants in the per-protocol set, 13 had no quantifiable CIMZIA plasma levels at birth (<0.032 µg/mL).[9] Of 15 available umbilical cord samples, 14 had no quantifiable glycol (PEG) levels; the remaining cord had 9.8 µg/mL PEG (corresponding CIMZIA level was below lower limit of quantification (LLOQ)).[9] It was only found in very small amounts in the cord blood of 1 baby.[9] The results of this study support the continuation of treatment with CIMZIA when necessary to maintain disease control.[9]

CIMZIA® (certolizumab pegol) in Pregnancy and Breastfeeding

Cimzia For Her

Does taking CIMZIA in pregnancy increase the chance of the child having any behaviour or learning issues?

A prospective, observational, multicentre study of 869 pregnant women exposed to a number of biologic medications including CIMZIA found no differences in infant achievement of developmental milestones up to one year.[10]

Can women breastfeed after taking CIMZIA?

CIMZIA is a large protein and only minimal amounts of medication is expected to pass into breastmilk and be absorbed by the baby.[11] The CRADLE[c] study was specifically designed to measure CIMZIA levels in the breastmilk of mothers. It found very low or undetectable levels in mothers' breastmilk.[11] In addition, since CIMZIA 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.[1]

Can a baby receive live vaccines before one year of age if the mother takes CIMZIA later in pregnancy?

It is important that babies receive the recommended vaccination schedule on time for the best protection.[12] Due to its inhibition of TNFα, CIMZIA administered during pregnancy could affect the normal immune response in the newborn.[1] It is advised that if this drug is taken during pregnancy, the baby should not be given any live or live-attenuated vaccines until at least five months after the last dose was received during pregnancy unless the benefit of the vaccination clearly outweighs the theoretical risk of administration of the vaccines to the infants.[1]

The risks and benefits of live vaccines should be discussed with a healthcare provider.

References. **1**. CIMZIA. Summary of Product Characteristics. Available from: https://www.medicines.org.uk/emc/product/4450/smpc#gref (accessed February 2025). **2**. Nesbitt A, et al. Inflamm Bowel Dis 2007;1 3(11): 1323–1332. **3**. Pasut G. BioDrugs 2014; 28(suppl 1): S15–S23. **4**. Porter C, et al. J Reprod Immunol 2016; 116: 7–12. **5**. Clowse MEB, et al., Arthritis Rheumatol. 2018;70(9):1399-1407. **6**. Clowse MEB, et al. Ther Adv Musculoskelet Dis. 2022;14. **7**. Strain J, et al. Skin Therapy. 2021;26(2):1-5. **8**. Graham JM. Society for Birth Defects Research and Prevention. Teratology Primer, 3rd edition. Available at: https://www.birthdefectsresearch.org/primer/Gene-Risk-Birth-Defect.asp. (accessed February 2025). **9**. Mariette X, et al. Ann Rheum Dis 2018; 77(2):228-233. **10**. Mahadevan U, et al. Gastroenterology 2021;160(4):1131-1139. **11**. Clowse MEB, et al. Ann Rheum Dis. 2017;76(11):1890-1896. **12**. NHS vaccinations and when to have them. Available at: https://www.nhs.uk/vaccinations/nhs-vaccinations-and-when-to-have-them/ (accessed February 2025).

CIMZIA is indicated for the treatment of[1]:

Moderate to severe, active rheumatoid arthritis (RA) in adult patients when the response to disease-modifying antirheumatic drugs (DMARDs) including methotrexate (MTX), has been inadequate. CIMZIA can be given as monotherapy in case of intolerance to MTX or when continued treatment with MTX is inappropriate.

Severe, active and progressive RA in adults not previously treated with MTX or other DMARDs.

Severe active ankylosing spondylitis (AS) in adults who have had an inadequate response to, or are intolerant to nonsteroidal anti-inflammatory drugs (NSAIDs).

Severe active axial spondyloarthritis in adults 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.

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 methotrexate or when continued treatment with methotrexate is inappropriate.

Moderate to severe plaque psoriasis in adults who are candidates for systemic therapy.

Special warnings and precautions for use

Fertility, pregnancy and lactation in women of childbearing potential: The use of adequate contraception should be considered for women of childbearing potential who have been prescribed CIMZIA. For women planning pregnancy, continued contraception may be considered for 5 months after the last CIMZIA dose due to its elimination rate.[1]

Pregnancy: CIMZIA should only be used during pregnancy if clinically needed.[1]

CIMZIA® (certolizumab pegol) in Pregnancy and Breastfeeding

Cimzia For Her

Footnotes:

[a]Data from 1392 prospective pregnancies with maternal CIMZIA exposure and known pregnancy outcomes (n = 1425) were reported; 1021 had at least first-trimester CIMZIA exposure.[6] Live birth was reported in 1259/1425 (88.4%) of all prospective outcomes.[6] There were 150/1425 (10.5%).[6]

[b]**CRIB**: Based on a pharmacokinetic study of women ≥30 weeks pregnant (n=16), all 16 mothers who entered the sampling period completed the study (no missed visits) and received commercial CIMZIA for a locally approved indication (RA, axSpA/AS, PsA, and CD*; last dose ≤35 days prior to delivery), 15 mothers received CIMZIA 200 mg Q2W, and 1 received CIMZIA 400 mg Q4W.[9]

[c]**CRADLE**: Based on a pharmacokinetic study of lactating mothers (n=17), at least 6 weeks post-partum with no upper age limit for infants, receiving commercial CIMZIA for a locally approved indication (RA, axSpA/AS, PsA, and CD*), from whom 137 samples were collected, and at an approved dose at the time the study was conducted (n=16 received CIMZIA 200 mg Q2W, n=1 received CIMZIA 400 mg Q4W).[11]

*CIMZIA is not approved for use in Crohn's disease in the European Union.

Abbreviations:

AS, ankylosing spondylitis; axSpA, axial spondyloarthritis; CD, Crohn's disease; CRP, C-reactive protein; DMARD, disease-modifying antirheumatic drug; Fc, fragment-crystallisable; MRI, magnetic resonance imaging; MTX, methotrexate; NSAID, nonsteroidal anti-inflammatory drug; PEG, polyethylene glycol; PsA, psoriatic arthritis; RA, rheumatoid arthritis; SmPC, summary of product characteristics; TNFα, tumour necrosis factor alpha; Q2W, every 2 weeks; Q4W, every 4 weeks.

PRESCRIBING INFORMATION FOR HCP'S IN REPUBLIC OF IRELAND (Please consult the Summary of Product Characteristics (SPC) before prescribing)

Cimzia® (Certolizumab Pegol) Active Ingredient: Certolizumab pegol 200 mg in one ml in a pre-filled syringe, pre-filled pen or dose dispenser cartridge **Indication(s):** *Rheumatoid arthritis (RA):* Cimzia, in combination with methotrexate (MTX), is indicated for moderate to severe, active RA in adult patients with inadequate response 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. Cimzia in combination with methotrexate (MTX), is also indicated in 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. *Axial spondyloarthritis:* Cimzia is indicated in adult patients with severe active axial spondyloarthritis, comprising: *Ankylosing spondylitis (AS):* Adults with severe active ankylosing spondylitis who have had an inadequate response to, or are intolerant to nonsteroidal anti-inflammatory drugs (NSAIDs). *Axial spondyloarthritis without radiographic evidence of AS:* Adults with severe active axial spondyloarthritis without radiographic evidence of AS but with objective signs of inflammation by elevated CRP and/or MRI, who have had an inadequate response to, or are intolerant to NSAIDs. *Psoriatic arthritis:* Cimzia in combination with MTX, is indicated for active psoriatic arthritis in adults with inadequate response to previous DMARD therapy. Cimzia can be given as monotherapy in case of intolerance to MTX or when continued treatment with MTX is inappropriate. *Plaque psoriasis:* Cimzia is indicated in moderate to severe plaque psoriasis in adults who are candidates for systemic therapy. **Dosage and Administration:** Should be initiated and supervised by specialist experienced physicians. Provide patients with the reminder alert card. For RA and psoriatic arthritis, continue MTX during treatment with Cimzia where appropriate. *Loading dose:* Recommended starting dose is 400 mg (2 subcutaneous injections of 200 mg each) at weeks 0, 2 and 4. *Maintenance dose: RA and Psoriatic Arthritis:* Recommended maintenance dose is 200 mg every 2 weeks. Once clinical response confirmed, can consider an alternative maintenance dose of 400 mg every 4 weeks. *Axial spondyloarthritis:* Recommended maintenance dose is 200 mg every 2 weeks or 400 mg every 4 weeks. After at least 1 year of treatment, in axSpA patients with sustained remission, can consider a reduced maintenance dose of 200 mg every 4 weeks. (see SPC). For indications above, carefully reconsider continued therapy in patients with no evidence of therapeutic benefit in the first 12 weeks of treatment. *Plaque psoriasis:* Recommended maintenance dose is 200 mg every 2 weeks. Can consider 400 mg every 2 weeks if insufficient response. Carefully reconsider continued therapy in patients with no evidence of therapeutic benefit in first 16 weeks of treatment. *Missed dose:* Advise patients to inject the next dose as soon as they remember and inject subsequent doses as originally instructed. **Contraindications:** Hypersensitivity to active substance or any excipients; active tuberculosis or other severe infections such as sepsis or opportunistic infections; moderate to severe heart failure (NYHA classes III/IV). **Warnings & Precautions:** Before starting Cimzia, screen for active and inactive tuberculosis and record results on the patient reminder alert card. If a past history of latent tuberculosis, use of anti-tuberculosis therapy must be started before initiation of Cimzia. If active tuberculosis diagnosed before or during treatment, Cimzia must not be initiated and must be discontinued. Some patients who have been successfully treated for active tuberculosis have redeveloped tuberculosis while being treated with Cimzia. Advise patients to seek advice if sign/symptoms of tuberculosis occur during/after therapy. Consult SPC for details. Monitor patients closely for signs of infection before, during and up to 5 months after treatment. Must not initiate if clinically important active infection until infection controlled. Monitor if develops new infection during treatment and discontinue if develops serious new infection until infection controlled. Serious infections and opportunistic infections have been reported with some fatal outcomes. Caution in patients with a history of recurring or opportunistic infections including those on concomitant corticosteroid or immunosuppressive medications or elderly. Test for HBV infection before starting Cimzia. If HBV carriers are treated with Cimzia, monitor throughout and after treatment. HBV reactivation has occurred in chronic carriers with some fatal outcomes. If develop HBV reactivation, discontinue Cimzia and initiate antiviral therapy and supportive treatments. Possible risk for lymphomas, leukaemia or other malignancies with TNF-antagonist treatment cannot be excluded. Caution if history of malignancy and when considering continuing therapy in patients who develop malignancy. Melanoma and Merkel cell carcinoma have been reported. Periodic skin exam recommended, especially if risk factors for skin cancer. Advise patients to seek immediate medical attention if they develop signs and symptoms suggestive of tuberculosis, blood dyscrasias or infection. Medical significant cytopaenia has been reported with Cimzia. Advise patients to seek immediate medical advice if signs/symptoms suggestive of blood dyscrasias or infection. Consider discontinuation if confirmed significant haematological abnormalities. Rare cases reported of demyelinating disease including multiple sclerosis. Consider benefit-risk if pre-existing or recent onset demyelinating disorder. Rare cases of neurological disorders reported with Cimzia. Rare reports of severe hypersensitivity reactions, some after first Cimzia administration – discontinue Cimzia immediately and treat appropriately. Use with caution if history of severe hypersensitivity to another TNF-antagonist. Cimzia has been associated with formation of antinuclear antibodies (ANA) and development of a lupus-like syndrome. If patient develops lupus-like syndrome, discontinue treatment. Use with caution in mild heart failure; discontinue if new or worsening symptoms of congestive heart failure. Use with caution in COPD patients and those with history of heavy smoking due to increased risk for malignancy. Patients receiving Cimzia may receive vaccination except live vaccines. Cimzia may cause erroneously elevated aPTT assay results in patients without coagulation abnormalities. The needle shield contains a natural rubber latex derivative which may cause allergic reactions. Record name and batch number of administered product to improve traceability of biological products. **Interactions:** The combination of Cimzia and anakinra or abatacept is not recommended. **Fertility, pregnancy and lactation:** The use of adequate contraception to prevent pregnancy 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. Data from more than 1300 prospectively collected pregnancies exposed to Cimzia with known pregnancy outcomes, including more than 1000 pregnancies exposed during the first trimester, does not indicate a malformative effect of Cimzia. Further data are being collected as the available clinical experience is still limited to conclude that there is no increased risk associated with Cimzia administration during pregnancy. 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. In a clinical study, 16 women were treated with certolizumab pegol 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 µg/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. In a clinical study in 17 lactating women treated with Cimzia, minimal transfer of certolizumab pegol from the plasma to breast milk was observed. The percentage of the maternal Cimzia dose that reaches an infant during a 24-hour period was estimated to 0.04% to 0.3%. 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. **Effects on ability to drive:** Dizziness (including vertigo, vision disorder, fatigue) may occur after Cimzia administration. **Side Effects:** Common adverse-effects (≥ 1/100 to <1/10): bacterial and viral infections, eosinophilic disorders, leukopenia, headaches, sensory abnormalities, hypertension, nausea, hepatitis (including hepatic enzyme increased), rash, pyrexia, pain, asthenia, pruritus (any site), injection site reactions. **Serious Side effects**: Infections including sepsis, tuberculosis, fungal infections, blood and lymphatic system malignancies, solid organ tumours, non-melanoma skin cancers, pre-cancerous lesions, benign tumours and cysts, gastrointestinal tumours, melanoma, Merkel cell carcinoma, Kaposi's sarcoma, eosinophilic disorders, leukopaenia (including neutropaenia, lymphopaenia), anaemia, lymphadenopathy, thrombocytopaenia, thrombocytosis, pancytopaenia, splenomegaly, erythrocytosis, vasculitides, lupus erythematosus, drug hypersensitivity (including anaphylactic shock), angioneurotic oedema, sarcoidosis, thyroid disorders, haemosiderosis, suicide attempt, delirium, mental impairment, anxiety disorders, sensory abnormalities, peripheral neuropathies, seizure, cranial nerve inflammation, multiple sclerosis, Guillain-Barré syndrome, visual disorder, tinnitus, vertigo, cardiomyopathies, ischaemic coronary artery disorders, arrhythmias, palpitations, pericarditis, atrioventricular block, hypertension, haemorrhage or bleeding (any site), hypercoagulation, syncope, cerebrovascular accident, arteriosclerosis, Raynaud's phenomenon, asthma, pleural effusion, interstitial lung disease, pneumonitis, ascites, gastrointestinal ulceration and perforation, gastrointestinal tract inflammation, odynophagia, hepatitis (including hepatic enzyme increased), hepatopathy, cholelithiasis, new onset or worsening of psoriasis, bullous conditions, Stevens-Johnson syndrome, erythema multiforme, lichenoid reactions, renal impairment, nephropathy, fistula, coagulation time prolonged. **Consult SPC in relation to other side effects. Pharmaceutical Precautions**: Store in refrigerator (2°-8°C). Do not freeze. Keep the pre-filled syringe and pre-filled pen in the outer carton to protect from light. **Legal Category**: POM. **Marketing Authorisation Number(s):** EU/1/09/544/001, EU/1/09/544/005 and EU/1/09/544/008. **Marketing Authorisation Holder**: UCB Pharma S.A., Allée de la Recherche 60, 1070 Brussels, Belgium. **Further information is available from**: *Republic of Ireland:* UCB (Pharma) Ireland Ltd, United Drug House, Magna Drive, Magna Business Park, City West Road, Dublin 24, Ireland Tel: +353 1 4632371 Fax: +353 14637396. Email: UCBCares.IE@ucb.com

Date of Revision: Jan 2025 (IE-CZ-2500004). Cimzia is a registered trademark

Click here or Scan QR Code to access the United Kingdom Prescribing Information for **CIMZIA®** (certolizumab pegol)

Adverse events should be reported. Reporting forms and information can be found at **www.mhra.gov.uk/yellowcard** for the UK and **www.hpra.ie/homepage/about-us/report-an-issue** for Republic of Ireland. Adverse events should also be reported to UCB Pharma Ltd at **ucbcares.uk@ucb.com** or **0800 2793177** for the UK and UCB (Pharma) Ireland Ltd at **ucbcares.ie@ucb.com** or **1800 930075** for Republic of Ireland.

IE-CZ-2400118 Date of preparation: February 2025

208 Bath Road, Slough, Berkshire, SL1 3WE

BECAUSE YOU KNOW CIMZIA® (certolizumab pegol)

Inspired by patients. Driven by science.