CIMZIA ABBREVIATED PRODUCT INFORMATION

Name of the medicinal product:
Cimzia® (Certolizumab pegol) Pharmaceutical form: Solution for injection. Each pre-filled syringe contains 200 mg certolizumab pegol in one ml.

Therapeutic indications:

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

Axial spondyloarthritis
Adult patients with severe active axial spondyloarthritis,comprising: 1) *Ankylosing spondylitis (AS):*Adults with severe active ankylosing spondylitis who have had an inadequate response to, or are intolerant to NSAIDs. 2) *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 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 methotrexate or when continued treatment with methotrexate is inappropriate.

Posology and Method of administration:

Loading dose
The recommended starting dose of Cimzia for adult patients is 400 mg (given as 2 subcutaneous injections of 200 mg each) at weeks 0, 2 and 4. For rheumatoid arthritis and psoriatic arthritis, MTX should be continued during treatment with Cimzia where appropriate.

Maintenance dose
Rheumatoid arthritis:
After the starting dose, the recommended maintenance dose of Cimzia for adult patients with rheumatoid arthritis is 200 mg every 2 weeks. Once clinical response is confirmed, an alternative maintenance dosing of 400 mg every 4 weeks can be considered. MTX should be continued during treatment with Cimzia where appropriate.
Axial spondyloarthritis:
After the starting dose, the recommended maintenance dose of Cimzia for adults patients with axial spondyloarthritis is 200 mg every 2 weeks or 400 mg every 4 weeks.
Psoriatic arthritis:
After the starting dose, the recommended maintenance dose of Cimzia for adult patients with psoriatic arthritis is 200 mg every 2 weeks. Once clinical response is confirmed, an alternative maintenance dosing of 400 mg every 4 weeks can be considered. MTX should be continued during treatment with Cimzia where appropriate.

Contraindications:
Hypersensitivity to the active substance or any of the excipients, active tuberculosis or other severe infections such as sepsis or opportunistic infections, moderate to severe heart failure (NYHA classes III/IV).

Special warnings and precautions for use:
Serious infections, sepsis, tuberculosis (including miliary, disseminated and extrapulmonary disease) and opportunistic infections have been reported in patients receiving Cimzia®. Some of these events have been fatal. Patients must be monitored closely for signs and symptoms of infections inclusing tuberculosis before, during and up to 5 months after treatment with Cimzia®. Patients who develop a new infection should be monitored closely. Administration of Cimzia® should be discontinued if a patient develops a new serious infection until the infection is controlled. Physicians should exercise caution when considering the use of Cimzia® in patients with a history of recurring infection, or with underlying conditions which may predispose patients to infections including the use of concomitant immunosuppressive medications. Before initiation of therapy with Cimzia®, all patients must be evaluated for both active and inactive (latent) tuberculosis infection including a detailed medical history for patients with a personal history of tuberculosis, with possible previous exposure to others with active tuberculosis, and with previous and/or current use of immunosuppressive therapy. If latent tuberculosis is diagnosed, appropriate anti-tuberculosis therapy must be started before initiating treatment with Cimzia® and the benefit/risk balance of therapy with Cimzia® should be very carefully considered. 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®. TNF blockers including Cimzia® may increase the risk of reactivation of Hepatitis B Virus (HBV) in patients who are chronic carriers of the virus. Patients at risk for HBV infection should be evaluated for prior evidence of HBV infection before initiating Cimzia® therapy. Carriers of HBV who require treatment with TNF antagonists should be closely monitored for clinical and laboratory signs of active HBV infection throughout therapy and for up to 5 months after therapy, especially if the patient is on concomitant corticosteroid therapy. In patients who develop HBV reactivation, Cimzia® should be discontinued and effective antiviral therapy with appropriate supportive treatment should be initiated. As the potential role of TNF antagonist therapy in the development of malignancies is not known, caution should be exercised when considering TNF antagonist therapy for patients with a history of malignancy or when considering continuing treatment in patients who develop malignancy. With the current knowledge, a possible risk for the development of lymphomas or other malignancies in patients treated with a TNF antagonist cannot be excluded.Caution should be exercised when using any TNF antagonist in chronic obstructive pulmonary disease patients, as well as in patients with increased risk for malignancy due to heavy smoking. Cases of congestive heart failure have been reported in RA patients receiving Cimzia® and it hence should be used with caution in patients with mild heart failure (NYHA class I/II). Treatment with Cimzia® must be discontinued in patients who develop new or worsening symptoms of congestive heart failure. Adverse reactions of the hematologic system, including medically significant cytopenia (e.g. leukopaenia, pancytopaenia, thrombocytopaenia) have been reported with Cimzia®. All patients should be advised 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®. Discontinuation of Cimzia® therapy should be considered in patients with confirmed significant hematological abnormalities. Use of TNF antagonists has been associated with rare cases of new onset or exacerbation of clinical symptoms and/or radiographic evidence of demyelinating disease, including multiple sclerosis. In patients with preexisting or recent onset of demyelinating disorders, the benefits and risks of TNF antagonist treatment should be carefully considered before initiation of Cimzia® therapy. Rare cases of neurological disorders, including seizure disorder, neuritis and peripheral neuropathy, have been reported in patients treated with Cimzia®. Severe hypersensitivity reactions have been reported rarely following Cimzia® administration in trials. If severe reactions occur, administration of Cimzia® should be discontinued immediately and appropriate therapy instituted. Since TNF mediates inflammation and modulates cellular immune responses, the possibility exists for TNF antagonists, including Cimzia®, to cause immunosuppression, affecting host
defences against infections and malignancies. Treatment with Cimzia® may result in the formation of antinuclear antibodies (ANA) and, uncommonly, in the development of a lupus like syndrome. If a patient develops symptoms suggestive of a lupus-like syndrome following treatment with Cimzia®, treatment must be discontinued. As no data are available, live vaccines or attenuated vaccines should not be administered concurrently with Cimzia

Undesirable effects: Cimzia® was studied in 2367 patients with RA in controlled and open label trials for up to 57 months. The commonly reported adverse reactions (1-10%) in clinical trials with Cimzia® were viral infections (includes herpes, papillomavirus, influenza), bacterial infections (including abscess), rash, headache (including migraine), asthenia, leukopaenia (including lymphopaenia, neutropaenia), eosinophilic disorder, pain (any sites), pyrexia, sensory abnormalities, hypertension, pruritis (any sites), hepatitis (including hepatic enzyme increase), injection site reactions. Serious adverse reactions include sepsis, opportunistic infections, tuberculosis, herpes zoster, lymphoma, solid organ tumors, angioneurotic edema, cardiomyopathies (includes heart failure), ischemic coronary artery disorders, pancytopaenia, peripheral embolism and thrombosis, cerebrovascular accident, vasculitis, hepatitis/hepatopathy (includes cirrhosis), and renal impairment/nephropathy (includes nephritis). In RA controlled clinical trials, 5% of patients discontinued taking Cimzia® due to adverse events vs 2.5% for placebo.

Please refer to Summary of Product Characteristics before prescribing Cimzia®.

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