

Remicade® 100 mg Powder for Concentrate for Solution for Infusion Infliximab

Prescribing Information

Refer to Summary of Product Characteristics (SmPC) before prescribing.

Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store. Adverse events should also be reported to MSD, UK (Tel: 0208 1548000). By clicking the above link you will leave the MSD website and be taken to the MHRA website.

PRESENTATION

Type I vials, with rubber stoppers and aluminium crimps protected by plastic caps, containing a lyophilised powder (infliximab 100mg). Each vial contains 100mg of infliximab.

USES

Rheumatoid Arthritis (RA): Remicade, in combination with methotrexate (MTX), is indicated for the reduction of signs and symptoms, and the improvement in physical function, in adult patients with active RA when the response to disease-modifying anti-rheumatic drugs (DMARDs), including MTX, has been inadequate; and in adult patients with severe, active and progressive disease not previously treated with MTX or other DMARDs. In these patient populations, a reduction in the rate of the progression of joint damage, as measured by X-ray, has been demonstrated. **Adult Crohn's Disease (CD):** Indicated for treatment of moderately to severely active CD in adult patients who have not responded to, or are intolerant of, a full and adequate course of therapy with a corticosteroid and/or an immunosuppressant; and fistulising active CD in adult patients who have not responded despite a full and adequate course of therapy with conventional treatment (including antibiotics, drainage and immunosuppressive therapy). **Paediatric Crohn's Disease (CD):** Indicated for treatment of severe, active CD in children and adolescents aged 6 to 17 years who have not responded to conventional therapy including a corticosteroid, an immunomodulator and primary nutrition therapy; or who are intolerant to or have contraindications for such therapies. **Ulcerative Colitis (UC):** Indicated for treatment of moderately to severely active UC in adult patients who have had an inadequate response to conventional therapy including corticosteroids and 6-mercaptopurine (6-MP) or azathioprine (AZA), or who are intolerant to or have medical contraindications for such therapies. **Paediatric Ulcerative Colitis (UC):** Indicated for treatment of severely active UC, in

children and adolescents aged 6 to 17 years, who have had an inadequate response to conventional therapy including corticosteroids and 6-MP or AZA, or who are intolerant to or have medical contraindications for such therapies. **Ankylosing Spondylitis (AS):** Indicated for treatment of severe, active AS, in adult patients who have responded inadequately to conventional therapy. **Psoriatic Arthritis (PsA):** Indicated for treatment of active and progressive PsA, in adult patients when the response to previous DMARD drug therapy has been inadequate. Administration should be in combination with MTX or alone in patients who show intolerance to MTX or for whom MTX is contraindicated. A reduction in the rate of progression of peripheral joint damage in patients with polyarticular symmetrical subtypes of PsA has been measured by X-ray. **Psoriasis (PsO):** Indicated for treatment of moderate to severe plaque PsO in adult patients who failed to respond to, or who have a contraindication to, or are intolerant to other systemic therapy including cyclosporine, MTX or PUVA.

DOSAGE AND ADMINISTRATION

To improve traceability the trade name and batch number of the product should be recorded in the patient file. Therapy should be initiated and supervised by physicians experienced in the diagnosis and treatment of RA, CD, UC, AS, PsA and PsO. Administer intravenously over a 2-hour period. Patients should be observed for at least 1 to 2 hours post infusion for acute infusion-related reactions by appropriately trained healthcare professionals. **Shortened infusions across adult indications:** In carefully selected adult patients who have tolerated at least 3 initial 2-hour infusions of Remicade (induction phase) and are receiving maintenance therapy, consideration may be given to administering subsequent infusions over a period of not less than 1 hour. If an infusion reaction occurs in association with a shortened infusion, a slower infusion rate may be considered for future infusions if treatment is to be

continued. Shortened infusions at doses >6 mg/kg have not been studied. RA: 3 mg/kg given as an intravenous infusion followed by additional 3 mg/kg infusion doses at 2 and 6 weeks after the first infusion, then every 8 weeks thereafter. Adult moderately to severely active CD: 5mg/kg given as an intravenous infusion followed by an additional 5mg/kg infusion 2 weeks after the first infusion. If a patient does not respond after 2 doses, no additional treatment should be given. Adult, fistulising, active CD: 5mg/kg intravenous infusion followed by additional 5mg/kg infusions at 2 and 6 weeks after first infusion. If a patient does not respond after 3 doses, no additional treatment should be given. UC: 5mg/kg given as an intravenous infusion followed by additional 5mg/kg infusion doses at 2 and 6 weeks after the first infusion, then every 8 weeks. Clinical response is usually achieved within 14 weeks of treatment (3 doses). AS: 5mg/kg given as an intravenous infusion followed by additional 5mg/kg infusion doses at 2 and 6 weeks after the first infusion, then every 6 to 8 weeks. If a patient does not respond after 2 doses, no additional treatment should be given. PsA: 5mg/kg given as an intravenous infusion followed by additional 5mg/kg infusion doses at 2 and 6 weeks after the first infusion, then every 8 weeks thereafter. PsO: 5mg/kg given as an intravenous infusion followed by additional 5mg/kg infusion doses at 2 and 6 weeks after the first infusion, then every 8 weeks. If a patient shows no response after 4 doses, no additional treatment should be given. Re-administration: in CD or RA Remicade can be re-administered within 16 weeks following the last infusion. Safety and efficacy of re-administration has not been established in: CD or RA after 16 weeks; AS other than every 6 to 8 weeks; PsA and UC other than every 8 weeks. Re-administration with one single Remicade dose in PsO after an interval of 20 weeks suggests reduced efficacy and a higher incidence of mild to moderate infusion reactions when compared to the initial induction regimen. Limited experience from retreatment, using a reinduction regimen suggests a higher incidence of infusion reactions, some serious, when compared to 8 weekly maintenance treatments. If maintenance therapy is interrupted in any indication, and there is a need to restart treatment. Remicade should be reinitiated as a single dose followed by the maintenance dose recommendations. Paediatric population: CD (6 to 17 years): 5 mg/kg given as an intravenous infusion followed by additional 5 mg/kg infusion doses

at 2 and 6 weeks after the first infusion, then every 8 weeks thereafter. If a patient does not respond by 10 weeks, no additional treatment should be given. UC (6 to 17 years): 5 mg/kg given as an intravenous infusion followed by additional 5 mg/kg infusion doses at 2 and 6 weeks after the first infusion, then every 8 weeks thereafter. Available data do not support further infliximab treatment in paediatric patients not responding within the first 8 weeks of treatment.

CONTRAINDICATIONS

Tuberculosis (TB) or other severe infections such as sepsis, abscesses and opportunistic infections; hypersensitivity to infliximab, other murine proteins or any of the excipients; patients with moderate or severe heart failure (NYHA class III/IV).

PRECAUTIONS

Infusion reactions: Acute infusion reactions including anaphylactic reactions may develop during (within seconds) or within a few hours following infusion. If acute infusion reactions occur, the infusion must be interrupted immediately. Emergency equipment, such as adrenaline, antihistamines, corticosteroids and an artificial airway must be available. Antibodies to infliximab may develop and have been associated with increased frequency of infusion reactions. Symptomatic treatment should be given and further Remicade infusions must not be administered.

In clinical studies, delayed hypersensitivity reactions have been reported. Available data suggest an increased risk for delayed hypersensitivity with increasing Remicade-free intervals. Infections: Monitor patients closely for infections, including TB, before, during and up to 6 months after treatment. Exercise caution in patients with chronic infection or a history of recurrent infection. Advise patients of potential risk factors for infections. Suppression of TNF α may mask symptoms of infection such as fever. TB, bacterial infections including sepsis and pneumonia, invasive fungal, viral and other opportunistic infections, have been observed, some of which have been fatal. Infections were reported more frequently in paediatric populations than in adult populations. There have been reports of active TB in patients receiving Remicade. Evaluate patients for active or latent TB before initiating treatment. All tests should be recorded on the Patient Reminder Card provided with the product. If active TB is diagnosed, Remicade therapy must not be initiated. If latent TB is

diagnosed, treatment with anti-TB therapy must be initiated before initiation of Remicade. Advise patients to seek medical advice if symptoms of TB appear. An invasive fungal infection such as aspergillosis, candidiasis, pneumocystosis, histoplasmosis, coccidioidomycosis or blastomycosis should be suspected in patients if a serious systemic illness is developed, a physician with expertise in the diagnosis and treatment of invasive fungal infections should be consulted at an early stage. Patients with fistulising CD and acute suppurative fistulas must not initiate therapy until possible source of infection is excluded.

Hepatitis B (HBV) reactivation: Reactivation of HBV occurred in patients who were chronic carriers. Some cases had a fatal outcome. Patients should be tested for HBV infection before initiating treatment.

Hepatobiliary events: Cases of jaundice and non-infectious hepatitis, some with features of autoimmune hepatitis have been observed. Isolated cases of liver failure resulting in liver transplantation or death have occurred.

Vaccinations/therapeutic infectious agents: Prior to initiation, if possible, it is recommended that vaccinations are brought up to date. Patients may receive concurrent vaccinations, except live vaccines. In infants exposed *in utero* to infliximab, fatal outcome due to disseminated Bacillus Calmette-Guérin (BCG) infection has been reported following administration of BCG vaccine after birth.

Autoimmune processes: Discontinue treatment if a patient develops symptoms suggestive of a lupus-like syndrome and is positive for antibodies against double-stranded DNA.

Neurological events: Anti-TNF α agents have been associated with cases of new onset or exacerbation of clinical symptoms and/or radiographic evidence of peripheral and CNS demyelinating disorders, including Guillain-Barré syndrome and multiple sclerosis. In patients with a history of demyelinating disorders, consider the benefits and risks of anti-TNF treatment before initiation of therapy. Discontinuation of Remicade should be considered if these disorders develop.

Malignancies and lymphoproliferative disorders: A risk of the development of lymphomas and other malignancies in patients (including children and adolescents) cannot be excluded. Use caution in patients with history of malignancy and in patients with increased risk for malignancy due to heavy smoking. Postmarketing cases of hepatosplenic T-cell lymphoma have been reported which were usually fatal. Most

Remicade cases have occurred in patients with CD or UC treated concomitantly with AZA or 6-MP. Exercise caution in patients with PsO and a medical history of extensive immunosuppressant therapy or prolonged PUVA treatment. Patients with UC at increased risk for, or with a prior history of dysplasia or colon carcinoma should be screened for dysplasia before therapy and at regular intervals throughout their disease course. Melanoma and Merkel cell carcinoma have been reported, periodic skin examination is recommended, particularly for patients with risk factors for skin cancer. Increased incidence of cervical cancer in women with RA treated with infliximab including those over 60 years of age has been found, continue periodic screening.

Heart failure: Use caution in patients with mild heart failure (NYHA class I/II) and discontinue in face of new or worsening symptoms of heart failure.

Others: Patients requiring surgery whilst on Remicade therapy should be closely monitored for infections.

Haematologic reactions: Consider discontinuation of therapy in patients with confirmed significant haematologic abnormalities, including pancytopenia, leucopenia, neutropenia and thrombocytopenia.

Special populations: Particular attention should be paid when treating the elderly due to a greater incidence of serious infections seen in Remicade treated patients. Some of these had a fatal outcome.

Drug interactions: No interaction studies have been performed. Combination of Remicade with other biological therapeutics used to treat the same conditions as Remicade, including anakinra and abatacept is not recommended. It is recommended that live vaccines not be given concurrently with Remicade

Fertility, Pregnancy and Lactation

Women of childbearing potential should consider use of adequate contraception and continue use for at least 6 months after the last Remicade treatment. Use during pregnancy only when clearly needed, not recommended when breast-feeding. Administration of live vaccines (e.g. BCG vaccine) to infants exposed to infliximab *in utero* is not recommended for at least 6 months after birth as they may be at risk of infection, including serious disseminated infection. Effects of infliximab on fertility and general reproductive function are unknown.

SIDE-EFFECTS

Refer to Summary of Product Characteristic for complete information on side effects

Very Common $\geq 1/10$: Viral infection, headache, upper respiratory tract infection, sinusitis, abdominal pain, nausea, infusion related reaction, pain.

Common $\geq 1/100$ to $< 1/10$: Bacterial infections, neutropenia, leucopenia, anaemia, lymphadenopathy, allergic respiratory symptom, depression, insomnia, vertigo, dizziness, hypoaesthesia, paraesthesia, conjunctivitis, tachycardia, palpitation, hypotension, hypertension, ecchymosis, hot flush, flushing, lower respiratory tract infection, dyspnoea, epistaxis, gastrointestinal haemorrhage, diarrhoea, dyspepsia, gastroesophageal reflux, constipation, hepatic function abnormal, transaminases increased, new onset or worsening psoriasis including pustular psoriasis (primarily palm & soles), urticaria, rash, pruritus, hyperhidrosis, dry skin, fungal dermatitis, eczema, alopecia, arthralgia, myalgia, back pain, urinary tract infection, chest pain, fatigue, fever, injection site reaction, chills and oedema.

Serious, including fatal adverse reactions have been reported including HBV reactivation, CHF, myocardial ischaemia/infarction, arrhythmia, serious infections (including sepsis, opportunistic infections, TB and Vaccine breakthrough infection (after *in utero* infliximab exposure), serum sickness, haematologic reactions, systemic lupus erythematosus/lupus-like

syndrome, demyelinating disorders, hepatobiliary events, lymphoma, HSTCL, leukaemia, Merkel cell carcinoma, Kaposi's sarcoma, melanoma, cervical cancer, paediatric malignancy, sarcoidosis/sarcoid-like reaction, intestinal or perianal abscess (in CD), toxic epidermal necrolysis, Stevens-Johnson Syndrome, erythema multiforme, linear IgA bullous dermatosis, acute generalised exanthematous pustulosis and serious infusion reactions including cerebrovascular accidents in close temporal association with infusion. The most frequently reported opportunistic infections with a mortality rate of $>5\%$ include pneumocystosis, candidiasis, listeriosis and aspergillosis.

OVERDOSE

No case of overdose has been reported. Single doses up to 20mg/kg have been administered without toxic effects.

PACKAGE QUANTITIES AND BASIC NHS COST

1 vial of 100 mg: £419.62

MARKETING AUTHORISATION NUMBER

Great Britain: PLGB 08563/0012

UK (Northern Ireland): EU/1/99/116/001

MARKETING AUTHORISATION HOLDER

Janssen Biologics B.V.,
Einsteinweg 101, 2333 CB Leiden,
The Netherlands

Legal Category: POM

Date of review of prescribing information: May 2021.

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PI.REM.21.GB-NI.7800.CAP Conversion.No RCN