

### **Prescribing Information**

**Humira (adalimumab) 20mg and 40mg solution for injection in pre-filled syringe,**

**Humira 40mg and 80mg solution for injection in pre-filled pen.**

**Refer to Summary of Product Characteristics (SmPC) for full information.**

**Presentation and method of administration:** Each single dose 0.2 ml pre-filled syringe contains 20 mg of adalimumab for subcutaneous injection. Each single dose 0.4 ml pre-filled pen or 0.4 ml pre-filled syringe contains 40mg of adalimumab for subcutaneous injection. Each single dose 0.8 ml pre-filled pen contains 80 mg of adalimumab for subcutaneous injection.

**Indications and Dosage:** Humira 20mg pre-filled syringe and Humira 80 mg pen are only approved for use in specific indications with a therapeutic requirement, **please refer to SmPCs for full information.** Humira treatment should be initiated and supervised by specialist physicians experienced in the diagnosis and treatment of conditions for which Humira is indicated. Ophthalmologists are advised to consult with an appropriate specialist before initiation of treatment with Humira. Patients treated with Humira should be given the Patient Reminder Card. After proper training in injection technique, patients may self-inject with Humira if their physician determines that it is appropriate and with medical follow-up as necessary. During treatment with Humira, other concomitant therapies (e.g., corticosteroids and/or immunomodulatory agents) should be optimised.

**Rheumatoid arthritis (RA), adults:** In combination with methotrexate (MTX) for moderate to severe, active RA with inadequate response to disease-modifying anti-rheumatic drugs (DMARDs) including MTX. In combination with MTX for severe, active and progressive RA when not previously treated with MTX. Can be given as monotherapy if intolerance to or when continued treatment with MTX is inappropriate. Reduces rate of progression of joint damage on X-ray and improves physical function, in combination with MTX. Dosage: 40 mg single dose every other week (EOW). Concomitant MTX should be continued. In monotherapy, patients may require 40 mg every week or 80mg EOW if they experience a decrease in clinical response. Treatment beyond 12 weeks should be reconsidered if no clinical response in that time. Consider need for dose interruption, e.g. before surgery or if serious infection occurs. Reintroduction of Humira after discontinuation for 70 days or longer gave same magnitudes of clinical response and similar safety profile as before dose interruption.

**Polyarticular juvenile idiopathic arthritis (pJIA), paediatrics 2 years and above:** In combination with MTX, for active pJIA, with inadequate response to one or more DMARDs. Can be given as monotherapy if intolerance to or when continued treatment with MTX is inappropriate. Dosage: 10 kg to <30 kg: 20 mg EOW. If ≥ 30 kg: 40 mg EOW. Treatment beyond 12 weeks should be reconsidered if no clinical response in that time.

**Enthesitis-related arthritis (ERA), paediatrics 6 years and above:** For active ERA with inadequate response or intolerance to conventional therapy. Dosage: 15 kg to < 30 kg: 20 mg EOW. If ≥ 30 kg: 40 mg EOW.

**Ankylosing spondylitis (AS), adults:** For severe active AS with inadequate response to conventional therapy. Dosage: adults: 40 mg single dose EOW. Treatment beyond 12 weeks should be reconsidered if no clinical response in that time.

**Axial spondyloarthritis without radiographic evidence of AS (nr-axSpA), adults:** For severe nr-axSpA with objective signs of inflammation (elevated CRP and / or MRI), and an inadequate response to, or intolerance to nonsteroidal anti-inflammatory drugs. Dosage: 40 mg single dose EOW. Treatment beyond 12 weeks should be reconsidered if no clinical response in that time.

**Psoriatic arthritis (PsA), adults:** For active and progressive PsA with inadequate response to DMARDs. Reduces rate of progression of peripheral joint damage on X-ray in polyarticular symmetrical subtypes of the disease and improves physical function. Dosage: 40 mg single dose EOW. Treatment beyond 12 weeks should be reconsidered if no clinical response in that time.

**Psoriasis (Ps), adults:** For moderate to severe chronic plaque psoriasis in candidates for systemic therapy. Dosage: 80 mg initial dose at Week 0, followed by 40 mg EOW from Week

1. Treatment beyond 16 weeks should be reconsidered if no clinical response in that time. Beyond 16 weeks, patients with inadequate response can increase dosage to 40 mg every week or 80mg EOW (refer to SmPC). If adequate response is achieved with 40mg every week or 80mg EOW, dosage may subsequently be reduced to 40 mg every other week.

**Psoriasis, paediatrics 4 years and above:** For severe chronic plaque psoriasis with inadequate response to or if topical therapy and phototherapies are inappropriate. Dosage: 15 kg to < 30 kg: 20 mg dose initially followed by 20 mg EOW starting one week after initial dose. If ≥ 30 kg: 40 mg dose initially followed by 40 mg EOW starting one week after initial dose. Treatment beyond 16 weeks should be reconsidered if no clinical response in that time.

**Hidradenitis suppurativa (HS), adults and adolescents from 12 years of age:** For active moderate to severe HS (acne inversa) in patients with an inadequate response to conventional systemic HS therapy. Dosage: HS, adults: 160 mg dose initially at Day 1, followed by 80 mg two weeks later at Day 15. Two weeks later (Day 29) continue with a dose of 40 mg every week or 80mg EOW. Reintroduction after treatment interruption: 40 mg every week or 80 mg EOW.

Dosage: HS, adolescents from 12 years and ≥30 kg: 80 mg initial dose at Week 0, followed by 40 mg EOW from Week 1. If there is inadequate response to 40 mg EOW, an increase in dosage to 40 mg every week or 80mg EOW may be considered. Treatment interruption: Humira may be re-introduced as appropriate.

Adults and adolescents from 12 years of age: Antibiotics may be continued if necessary. Concomitant topical antiseptic wash on HS lesions is recommended to be used on a daily basis. Treatment beyond 12 weeks should be reconsidered if no improvement in that time. Evaluate periodically the benefit and risk of continued long-term treatment.

**Crohn's disease (CD), adults:** For moderately to severely active CD in patients who have not responded despite a full and adequate course of therapy with a corticosteroid and/or an immunosuppressant, or are intolerant to or have medical contraindications for such therapies. Dosage: Induction: 80 mg dose at Week 0, followed by 40 mg at Week 2. For a more rapid response: 160 mg at Week 0, followed by 80 mg at Week 2; risk of adverse events higher during rapid induction. Maintenance: 40 mg dose EOW. During maintenance, corticosteroids may be tapered in accordance with clinical guidelines. If decrease in clinical response, can increase dosage to 40 mg every week or 80mg EOW. Patients with no response by Week 4 may benefit from continued maintenance therapy to Week 12. Treatment beyond 12 weeks should be reconsidered if no clinical response in that time.

**Paediatric Crohn's disease (CD), 6 years and above:** For moderately to severely active CD with inadequate response to, intolerance to or contraindication for conventional therapy including primary nutrition therapy and a corticosteroid, and/or an immunomodulator.

Dosage: < 40 kg: Induction: 40 mg dose at Week 0, followed by 20 mg at Week 2. For a more rapid response: 80 mg at Week 0, followed by 40 mg at Week 2; risk of adverse events higher during rapid induction. Maintenance: 20 mg dose EOW. If insufficient response, consider an increase in dosage to 20 mg every week. If ≥ 40 kg: Induction: 80 mg dose at Week 0, followed by 40 mg at Week 2. For a more rapid response: 160 mg dose at Week 0, followed by 80 mg at Week 2; risk of adverse events higher during rapid induction. Maintenance: 40 mg dose EOW. If insufficient response, consider an increase in dosage to 40 mg every week or 80 mg EOW. Treatment beyond 12 weeks should be reconsidered if no clinical response in that time.

**Ulcerative colitis (UC), adults:** For moderately to severely active UC with inadequate response to, intolerance to or contraindication for conventional therapy including corticosteroids and 6-mercaptopurine (6-MP) or azathioprine (AZA). Dosage: Induction: 160 mg dose at Week 0, followed by 80 mg at Week 2. Maintenance: 40 mg dose EOW. During maintenance, corticosteroids may be tapered in accordance with clinical guidelines. If insufficient response, consider an increase in dosage to 40 mg every week or 80mg EOW. Treatment beyond 8 weeks should be reconsidered if no clinical response in that time.

**Paediatric ulcerative colitis (UC), 6 years and above:** For moderately to severely active ulcerative colitis in paediatric patients who have had an inadequate response to conventional

therapy including corticosteroids and/or 6-mercaptopurine (6-MP) or azathioprine (AZA), or who are intolerant to or have medical contraindications for such therapies.

**Dosage:** < 40 kg: **Induction:** 80 mg dose at Week 0, followed by 40 mg at Week 2.

**Maintenance:** 40 mg dose EOW. **If ≥ 40 kg:** **Induction:** 160 mg dose at Week 0, followed by 80 mg at Week 2. **Maintenance:** 80 mg dose EOW. Paediatric patients who turn 18 years of age while on Humira should continue their prescribed maintenance dose. Treatment beyond 8 weeks should be reconsidered if no clinical response in that time.

**Uveitis, adults:** For non-infectious intermediate, posterior and panuveitis with inadequate response to corticosteroids, in patients in need of corticosteroid-sparing, or in whom corticosteroid treatment is inappropriate. **Dosage:** 80 mg initial dose at Week 0, followed by 40 mg EOW from Week 1. Treatment can be initiated in combination with corticosteroids and/or with other non-biologic immunomodulatory agents. Concomitant corticosteroids may be tapered in accordance with clinical practice starting two weeks after initiating treatment with Humira. Evaluate on a yearly basis the benefit and risk of continued long-term treatment.

**Paediatric Uveitis, 2 years and above:** For chronic non-infectious anterior uveitis with inadequate response or intolerance to conventional therapy, or in whom conventional therapy is inappropriate. **Dosage:** < 30 kg: 20 mg dose EOW in combination with MTX. Optional 40 mg loading dose one week prior to start of maintenance therapy. No clinical data in use of loading dose < 6 years of age (see SmPC). **If ≥ 30 kg:** 40 mg dose EOW in combination with MTX. Optional 80 mg loading dose one week prior to start of maintenance therapy. Evaluate on a yearly basis the benefit and risk of continued long-term treatment.

**Contraindications:** Hypersensitivity to the active substance or any of the excipients (see SmPC). Active tuberculosis (TB) or other severe infections such as sepsis and opportunistic infections; Moderate to severe heart failure (NYHA class III/IV).

**Warnings and precautions:** Clearly record trade name and batch number of administered product to improve traceability of biological medicinal products. **Infections:** Patients taking Tumour Necrosis Factor (TNF)-antagonists are more susceptible to serious infections especially if impaired lung function. Monitor for infections, including TB, before, during and for 4 months after treatment. Do not initiate treatment with an active infection, until it is controlled. Consider risk/benefit prior to treatment in patients exposed to high risk of TB or who have travelled in areas of high risk of TB or endemic mycoses. Evaluate new infections during treatment and monitor closely. Stop treatment if new serious infection or sepsis, and treat appropriately. Exercise caution in patients with a history of recurring infections or who are predisposed to infections, including the use of concomitant immunosuppressive medications. **Serious infections:** Serious infections, including those with hospitalisation or death reported in patients receiving treatment. **TB:** Consult SmPC for details. Reactivation and new onset TB, both pulmonary and extra-pulmonary (disseminated) reported. Screen all patients before therapy initiation for active or latent TB. Appropriate screening tests (i.e. tuberculin skin test and chest X-ray) should be performed in all patients. If active TB is diagnosed Humira therapy must not be initiated. If latent TB is suspected, consult a physician with appropriate expertise and follow local treatment recommendations for prophylaxis prior to initiation of Humira. Despite prophylaxis, TB reactivation has occurred on Humira. **Other opportunistic infections:** Opportunistic infections have been observed in patients receiving Humira. Stop treatment in patients with signs and symptoms of such infections. Consult with physician with appropriate expertise for diagnosis and administration of empiric antifungal therapy in these patients. **Hepatitis B Reactivation:** Reactivation of HBV has occurred in chronic carriers (surface antigen positive). Patients should be tested for HBV infection before initiating treatment. HBV carriers should consult with a specialist physician and be closely monitored for reactivation of HBV infection throughout therapy and for several months following termination of Humira. If reactivation occurs stop treatment and initiate appropriate anti-viral and supportive treatment. **Neurological events:** Caution in patients with pre-existing or recent-onset central or peripheral nervous system demyelinating disorders. Discontinuation of treatment should be considered if any of these disorders develop. Neurological evaluation should be performed in patients with non-infectious intermediate uveitis before therapy initiation and regularly during treatment, to assess for pre-existing or

developing central demyelinating disorders. **Allergic reactions:** Reports of serious allergic reactions including anaphylaxis received. For serious allergic or anaphylactic reaction, stop Humira immediately and initiate appropriate therapy. **Malignancies and lymphoproliferative disorders:** A possible risk of malignancy, including lymphoma and leukaemia, in all patients including paediatric patients, treated with TNF antagonists. Examine all patients, especially those with a medical history of extensive immunosuppressant or PUVA treatment for non-melanoma skin cancer prior to and during treatment, caution in COPD patients, and in patients with increased risk of malignancy due to heavy smoking. Consider the potential risk with the combination of AZA or 6-MP and Humira (hepatosplenic T-cell lymphoma has occurred). Risk of hepatosplenic T-cell lymphoma cannot be excluded. Caution in patients with a history of malignancy. Risk of developing dysplasia or colon cancer is unknown. Patients with UC, history of dysplasia or colon carcinoma to be screened for dysplasia before and during treatment. **Haematologic reactions:** Adverse events of the haematologic system reported with Humira. Patients should seek immediate medical attention if signs and symptoms of blood dyscrasias develop while on treatment. **Vaccinations:** Patients may receive concurrent vaccinations, except for live vaccines. Bring paediatric patients up to date with all immunisations prior to Humira treatment. **Congestive heart failure:** See contraindications. Caution is advised in mild heart failure (NYHA class I/II). Discontinue treatment for new or worsening symptoms of congestive heart failure. **Autoimmune processes:** Autoimmune antibodies may form with Humira. Stop treatment if development of a lupus-like syndrome with positive antibodies against double-stranded DNA. **Surgery:** Consider the long half-life of Humira for planned surgical procedures. Closely monitor for infections. **Small bowel obstruction:** Failure to respond to treatment for CD may indicate the presence of fixed fibrotic stricture requiring surgical treatment. **Elderly:** Serious infections were higher in patients over 65 years of age, some of which had a fatal outcome. Consider risk of infections in these patients.

**Interactions:** Antibody formation was lower when Humira was given together with MTX in comparison with use as monotherapy. Combination of Humira with other biologic DMARDs (e.g. anakinra and abatacept) or other TNF-antagonists is not recommended.

**Fertility, pregnancy and lactation:** Humira should only be used during pregnancy if needed. Women of childbearing potential should consider the use of adequate contraception and continue its use for at least five months after the last Humira treatment. No administration of live vaccines (e.g. BCG) to infants exposed to Humira in utero for 5 months following mother's last Humira treatment during pregnancy. Humira can be used during breast-feeding.

**Adverse Reactions:** *Very common*  $\geq 1/10$ : Respiratory tract Infections (including lower and upper respiratory tract infection, pneumonia, sinusitis, pharyngitis, nasopharyngitis and pneumonia herpes viral), leukopenia (including neutropenia and agranulocytosis), anaemia, lipids increased, headache, abdominal pain, nausea and vomiting, elevated liver enzymes, rash (including exfoliative rash), musculoskeletal pain, injection site reaction (including injection site erythema).

**Serious, including fatal, adverse reactions have been reported.** including infections/sepsis, TB, opportunistic infections, allergic reactions (including anaphylaxis), HBV reactivation and malignancies (including leukaemia, lymphoma and hepatosplenic T-cell lymphoma). Serious haematological, neurological and autoimmune reactions have also been reported. These include rare reports of pancytopenia, aplastic anaemia, central and peripheral demyelinating events and reports of lupus, lupus-related conditions and Stevens-Johnson syndrome.

**Prescribers should consult the SmPC for the complete list of reported side effects.**

**Legal Category:** POM (S1A).

**Marketing Authorisation Numbers:** EU/1/03/256/022, EU/1/03/256/013, EU/1/03/256/017, EU/1/03/256/021.

**Further information:** available from AbbVie Limited, 14 Riverwalk, Citywest Business Campus, Dublin 24.

**HCPs are asked to report any suspected adverse reactions via HPRA**

**Pharmacovigilance; website: [www.hpria.ie](http://www.hpria.ie).**

**Date of revision of PI:** November 2020, PI/256/025