Prescribing Information (PI)

Hulio ▼ (adalimumab) 40 mg solution for injection in pre-filled syringe, Hulio (adalimumab) 40 mg solution for injection in pre-filled pen and Hulio (adalimumab) 40 mg vial for paediatric use.

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

Presentation and method of administration: Each 0.8 ml single dose pre-filled syringe, pre-filled pen or vial contains 40 mg of adalimumab for subcutaneous injection.

Indications and Dosage: **please refer to SmPC for full information.**

Hulio treatment should be initiated and supervised by specialist physicians experienced in the diagnosis and treatment of conditions for which Hulio is indicated. Ophthalmologists are advised to consult with an appropriate specialist before initiation of treatment with Hulio. Patients treated with Hulio should be given the patient alert card.

After proper training in injection technique, patients may self-inject with Hulio if their physician determines that it is appropriate and with medical follow-up as necessary.

During treatment with Hulio, other concomitant therapies (e.g., corticosteroids and/or immunomodulatory agents) should be optimised.

Rheumatoid arthritis (RA), adults: In combination with methotrexate for moderate to severe, active RA with inadequate response to disease-modifying anti-rheumatic drugs (DMARDs) including methotrexate. In combination with methotrexate for severe, active and progressive RA when not previously treated with methotrexate. Can be given as monotherapy if intolerance to or when continued treatment with methotrexate is inappropriate. Reduces rate of progression of joint damage on X-ray and improves physical function, in combination with methotrexate.

Dosage: 40 mg single dose every other week (EOW). Concomitant methotrexate should be continued. Glucocorticoids, salicylates, nonsteroidal anti-inflammatory drugs, or analgesics can be continued. In monotherapy, patients may require 40 mg every week or 80 mg 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 after 70 days or longer of discontinuation 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 methotrexate for active pJIA with inadequate response to one or more DMARDs. Can be given as monotherapy if intolerance to or when continued treatment with methotrexate is inappropriate.

Dosage: 10 kg to <30 kg 20 mg single dose EOW. If ≥30 kg: 40 mg single dose 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 to or intolerance to conventional therapy.

Dosage: 15 kg to <30 kg: 20 mg single dose EOW. If ≥30 kg: 40 mg single dose EOW.

Ankylosing spondylitis (AS), adults: For severe active AS with inadequate response to conventional therapy.

Dosage: 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, 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 (refer to SmPC).

Paediatric Plaque Psoriasis, 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 and above: For active moderate to severe HS (acne inversa) with 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 80 mg every other week. 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. Reintroduction of after treatment interruption: 40 mg every week or 80 mg EOW. Evaluate periodically the benefit and risk of continued long-term treatment.

Crohn's disease (CD), adults: For moderately to severely active CD with no response despite a full and adequate course of, intolerance to or contraindication for a corticosteroid and/or an immunosuppressant therapy.

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 dosing frequency to 40 mg every week or 80 mg 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 dosing frequency 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 dosing frequency 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 dosing frequency to 40 mg every week or 80 mg EOW. 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 Hulio. 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 to 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. Hulio may be available in other strengths and/or presentations depending on the individual treatment needs.

Contraindications: Hypersensitivity to the active substance or to any 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 the name and batch number of administered product to improve traceability of biological products.

Infections: Patients taking 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 during an active infection, until infection is controlled. Consider risk/benefit prior to treatment in patients exposed to 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 sepsis, due to bacterial, mycobacterial, invasive fungal, parasitic, viral, or other opportunistic infections such as listeriosis, legionellosis and pneumocystis have been reported.

Other serious infections seen in clinical trials include pneumonia, pyelonephritis, septic arthritis and septicaemia.

Serious infections, including those associated with hospitalisation or death, were reported in patients receiving treatment.

Tuberculosis (TB): Consult SmPC for details. Reactivation and new onset TB, both pulmonary and extra-pulmonary (i.e. disseminated), were reported. Screen all patients before therapy initiation for active or inactive (latent) TB. Appropriate screening tests (i.e. tuberculin skin test and chest X-ray) should be performed in all patients. If latent TB is suspected, consult physician with appropriate expertise and follow local treatment recommendations for prophylaxis prior to initiation of Hulio. Despite prophylaxis, TB reactivation has occurred on Hulio. If active TB is diagnosed, do not initiate Hulio treatment.

Other opportunistic infections: Opportunistic infections were observed in patients receiving Hulio. Stop treatment in patients with signs and symptoms (i.e. fever, malaise, weight loss, sweats, cough, dyspnoea, and/or pulmonary infiltrates) 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 a specialist physician and be closely monitored for reactivation of HBV infection throughout therapy and for several months following termination of treatment. If reactivation occurs, stop treatment and initiate appropriate antiviral 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. Neurologic evaluation should be performed in patients with non-infectious intermediate uveitis prior to initiation of treatment 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 Hulio immediately and initiate appropriate therapy.

Malignancies and lymphoproliferative disorders: A possible risk has been reported of malignancy, including lymphomas and leukaemia, in all patients, including paediatric patients, treated with Tumour Necrosis Factor (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 for malignancy due to heavy smoking. Consider the potential risk with the combination of AZA or 6-MP and Hulio (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 Hulio. 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 initiating Hulio treatment.

Congestive heart failure: See contraindications. Caution is advised with mild heart failure (NYHA class I/II). Discontinue treatment if new or worsening symptoms of congestive heart failure.

Autoimmune processes: Autoimmune antibodies may form with Hulio. Stop treatment if development of a lupus-like syndrome with positive antibodies against double-stranded DNA.

Surgery: Consider the long half-life of Hulio for planned surgical procedures. Monitor closely for infections.

Elderly patients: 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 Hulio was given together with MTX in comparison with use as monotherapy. Combination of Hulio with other biologic DMARDs (e.g. anakinra and abatacept) or other TNF-antagonists is not recommended.

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

Adverse Reactions: *Very common ≥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).

Common ≥1/100 to <1/10: Systemic infections (including sepsis, candidiasis and influenza), intestinal infections (including gastroenteritis viral), skin and soft tissue infections (including paronychia, cellulitis, impetigo, necrotising fasciitis and herpes zoster), ear infections, oral infections (including herpes simplex, oral herpes and tooth infections), reproductive tract infections (including vulvovaginal mycotic infection), urinary tract infections (including pyelonephritis), fungal infections, joint infections, skin cancer excluding melanoma (including basal cell carcinoma and squamous cell carcinoma), benign neoplasm, leucocytosis, thrombocytopenia, hypersensitivity, allergies (including seasonal allergy), hypokalaemia, uric acid increased, blood sodium abnormal, hypocalcaemia, hyperglycaemia, hypophosphatemia, dehydration, mood alterations (including depression), anxiety, insomnia, paraesthesias (including hypoesthesia), migraine, nerve root compression, visual impairment, conjunctivitis, blepharitis, eye swelling, vertigo, tachycardia, hypertension, flushing, haematoma, asthma, dyspnoea, cough, GI haemorrhage, dyspepsia, gastroesophageal reflux disease, sicca syndrome, worsening or new onset of psoriasis (including palmoplantar pustular psoriasis), urticaria, bruising (including purpura), dermatitis (including eczema), onychoclasis, hyperhidrosis, alopecia, pruritus, muscle spasms (including blood creatine phosphokinase increased), renal impairment, haematuria, chest pain, oedema, pyrexia, coagulation and bleeding disorders (including activated partial thromboplastin time prolonged), autoantibody test positive (including double stranded DNA antibody), blood lactate dehydrogenase increased, impaired healing.

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.

For other rare and very rare adverse reactions, please refer to SmPC.

Name and Address of Marketing Authorisation Holder: Mylan S.A.S. 117 allée des Parcs 69800 Saint Priest France. **Marketing Authorisation Number**: EU/1/18/1319/002 (pre-filled syringe), EU/1/18/1319/005 (pre-filled pen) and EU/1/18/1319/007 (vials). **Basic NHS price**: Hulio 40 mg £616.25 (for 2 syringes or 2 pens or 2 vials).

Legal Category: POM. **Date of Revision**: September 2018; Ref No: ADA-2018-0008

Detailed information on this medicinal product is available on the website of the European Medicines Agency http://www.ema.europa.eu. and from Mylan Medical Information, Building 4, Trident Place, Hatfield Business Park, Mosquito Way, Hatfield, Hertfordshire, AL10 9BW, phone no. 01707 853000, Email: info@mylan.co.uk

Adverse events should be reported. Reporting forms and information can be found at www.yellowcard.gov.uk or search for MHRA Yellow Card in the Google Play or Apple App Store. Adverse events should be reported to Medical Information, Mylan, Building 4, Trident Place, Hatfield Business Park, Mosquito Way, Hatfield, Hertfordshire, AL10 9BW, on phone no. 01707 853000, Email: info@mylan.co.uk