Formulary decision guide: Hulio® (adalimumab biosimilar)

**Key points**

- Hulio is citrate free, delivered via a 29-gauge stainless steel needle (with plastic cover), and presentations include a two-step auto-injector and a latex-free, pre-filled syringe with safety device.
- In a 2016 report, the EU Commission said: The availability of biosimilars ... offers potential economic benefit to healthcare systems, while supporting patients' access to new treatment options brought about by advances in medical science.

**Drug name**

Hulio® (adalimumab biosimilar 40 mg)

**Indications**

- Hulio is licensed for all indications associated with the adalimumab reference product
- See the Summary of Product Characteristics for the list of indications: rheumatoid arthritis, juvenile idiopathic arthritis, axial spondyloarthritis, ankylosing spondylitis, psoriatic arthritis, psoriasis, hidradenitis suppurativa, Crohn's disease, ulcerative colitis, and uveitis.

**Dosage in adults**

- Treatment to be initiated by a specialist; adult doses for administration by subcutaneous injection for the three main indications:
  - **rheumatoid arthritis (RA)**—40 mg every 2 weeks, then increased if necessary to 40 mg once weekly, dose to be increased only in patients receiving adalimumab alone, review treatment if no response within 12 weeks.
  - **Crohn's disease**—initially 80 mg, then 40 mg after 2 weeks; maintenance 40 mg every 2 weeks, increased if necessary to 40 mg once weekly, maximum 40 mg administered at a single site, review treatment if no response within 12 weeks of initial dose.
  - **plaque psoriasis**—initially 80 mg, then 40 mg every 2 weeks, to be started 1 week after initial dose, review treatment if no response within 16 weeks.
- See the Summary of Product Characteristics for additional dosage information.

**Delivery**

- Hulio is citrate free, delivered via a 29-gauge stainless steel needle (with plastic cover), and presentations include a two-step auto-injector and a latex-free, pre-filled syringe with safety device.

**Biosimilars**

- The revised position paper on biosimilar medicines from the National Rheumatoid Arthritis Society in 2017 states that:
  - the designation of a biological drug as a ‘biosimilar’ by a regulatory authority demands that extremely rigorous quality controls are met with respect to characterisation of the biosimilar in relation to the originator drug, which can give a great deal of confidence to patients.
  - these quality controls for the biosimilar are much more stringent than those required for originators in the early days of biological disease-modifying anti-rheumatic drugs.
- NICE Key therapeutic topic (KTT15) recommends ensuring that all biological medicines, including biosimilar medicines, are prescribed by brand name so that products cannot be automatically substituted at the point of dispensing.

**Evidence for use—efficacy**

- The ARABESC randomised, double-blind, active-controlled study compared the efficacy and safety of an adalimumab biosimilar (Hulio; FKB327) with the adalimumab reference product (RP; ADL) in patients with RA inadequately controlled on methotrexate:
  - Hulio met the primary study objective establishing equivalence with the RP.
  - ACR20 (American College of Rheumatology definition of 20% improvement in a core set of measures) response rates over time overlapped during weeks 4–24.

**Evidence for use—safety**

- Evidence from the ARABESC study comparing Hulio and the adalimumab RP demonstrated:
  - Hulio; FKB327
  - Adalimumab reference product; ADL
the proportions of patients reporting treatment-emergent adverse events (TEAEs) were similar (55.5% vs 61.6%).

- adverse events were mainly mild or moderate; the most common TEAEs (≥5%) were nasopharyngitis (7.1% vs 8.0%), and upper respiratory tract infection (3.6% vs 5.0%).

- incidences of serious adverse events were similar (4.1% vs 5.2%).

- deaths from treatment-related disseminated tuberculosis (TB) were 1 vs 0, with higher reports of active TB in the RP group (1 vs 3); mean serum trough concentration-time profiles of the two groups were comparable.

- immunogenicity: prevalence and titres of antidrug antibodies were similar, including at final sampling (57.9% vs 55.8%).

### Long-term safety evidence

- The ARABESC study was continued with an open-label extension, called ARABESC-OLE, to compare Hulio with the adalimumab RP for long-term safety, efficacy, and immunogenicity in patients with RA. The study is completed and currently under evaluation, with results scheduled for publication in October 2018.

- at interim analysis, safety profiles were comparable for all treatment sequences, although group sizes were reduced after switching.

- ACR20 response rate at week 30 was comparable after continuous (Hulio–RP, 86.5%; RP–RP, 84.3%) and switched (Hulio–RP, 86.5%; RP–Hulio, 89.1%) treatment.

- no consistent differences in pharmacokinetics and anti-drug antibody profiles were seen between continuous and switched treatments.

### Cost saving

- NHS England’s ambition is to achieve a recurrent annual saving of £200 million to £300 million by 2021, through the increased use of the best value biological medicines in a proactive, systematic, and safe way.

### Side-effects

- The safety profile of Hulio is similar to its RP; the most commonly reported adverse reactions are:
  - infections (such as nasopharyngitis, upper respiratory tract infection, and sinusitis); injection site reactions (erythema, itching, haemorrhage, pain, or swelling); headache; and musculoskeletal pain
  - Serious adverse reactions have been reported for adalimumab:
    - tumour necrosis factor antagonists, such as adalimumab, affect the immune system and their use may affect the body’s defence against infection and cancer.

- See the Summary of Product Characteristics for full details of undesirable effects.

### References


5. NICE. Biosimilar medicines. Key therapeutic topic (KTT15). NICE, 2016 (last updated 2018). Available at: [nice.org.uk/guidance/ktt15](http://nice.org.uk/guidance/ktt15)


7. Genovese M, Glover J, Matsunaga N et al. Efficacy, safety and immunogenicity in randomized, double-blind (DB) and open-label extension (OLE) studies comparing FKB327, an adalimumab biosimilar, with the adalimumab reference product (Humira®; RP) in patients (pts) with active rheumatoid arthritis (RA). *Arthritis Rheumatol* 2017; 69 (suppl 10).

Hulio (adalimumab) 40 mg solution for injection in pre-filled syringe. Hulio (adalimumab) 40 mg vials for paediatric use.

Refer to Summary of Product Characteristics (SmPC) for full information. Presentations and method of administration:
Each 0.8 ml single dose pre-filled syringe, containing 40 mg of adalimumab for subcutaneous injection.

Indications and Dosage:
Paediatric indications:
Hulio treatment should be initiated and supervised by specialist physicians experienced in the diagnosis and treatment of psoriatic arthritis (PsA). Hulio is indicated. Ophthalmologists are advised to consult with an appropriate specialist before initiating treatment with Hulio.

Psoriatic arthritis (PsA): Hulio should be given the patient alert card. After proper training in injection technique, the patient should be instructed on how to administer the drug. The physician determines that it is appropriate and with medical follow-up as necessary. During treatment with conventional therapy (e.g., DMARDs, and with methotrexate or with other non-biologic immunomodulatory agents) should be optimised.

Dosage: 40 mg single dose every other week (EOW). Combination therapy with methotrexate for severe, active RA with inadequate response to or intolerance to conventional therapy, or with other non-biologic immunomodulatory agents.

Dosage: 10 kg to <30 kg: 20 mg single dose EOW; ≥30 kg: 40 mg single dose EOW. Treatment beyond 8 weeks should be reconsidered if no clinical response in that time. In combination with methotrexate for active sJIA with inadequate response to conventional therapy or with other non-biologic immunomodulatory agents.

Dosage: 40 mg single dose EOW. Treatment beyond 8 weeks should be reconsidered if no clinical response in that time.

Psoriatic arthritis (PsA): for active and for children and adolescents from 12 years and above: 40 mg single dose EOW. Treatment beyond 12 weeks should be reconsidered if no clinical response in that time.

Axial spondyloarthritis (AS): for active and for children and adolescents from 12 years and above: 40 mg single dose EOW. Maintenance: 40 mg single dose EOW. For patients with no response by Week 4 may be increased to 80 mg at Week 2; for a more rapid response: 160 mg dose at Week 0, followed by 80 mg at Week 2; for a more rapid induction: 80 mg dose EOW. 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.

Psoriatic arthritis (PsA): for active and for children and adolescents from 12 years and above: 40 mg single dose EOW. Treatment beyond 8 weeks should be reconsidered if no clinical response in that time.

Psoriasis arthropathic (PsA), adults: for active and for children and adolescents from 12 years and above: 40 mg single dose EOW. Treatment beyond 8 weeks should be reconsidered if no clinical response in that time.

Psoriasis arthropathic (PsA), children: for active and for children and adolescents from 12 years and above: 40 mg single dose EOW. Treatment beyond 8 weeks should be reconsidered if no clinical response in that time.

Psoriasis arthropathic (PsA), adults: for active and for children and adolescents from 12 years and above: 40 mg single dose EOW. Treatment beyond 8 weeks should be reconsidered if no clinical response in that time.

Paediatric PsA, 4 years and above: for active and for children and adolescents from 4 years and above: 40 mg single dose EOW. Treatment beyond 8 weeks should be reconsidered if no clinical response in that time.

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Serious infections, including those associated with hospitalisation or death, were reported in patients receiving Hulio. Serious infections were observed in patients receiving Hulio. Other opportunistic infections: Opportunistic infections may occur in patients receiving Hulio for planned surgical procedures. Other opportunistic infections, including tuberculosis (TB), were seen in clinical trials. Other opportunistic infections seen in clinical trials include tuberculosis (TB), histoplasmosis, coccidioidomycosis, histoplasmosis, coccidioidomycosis, hepatitis B reactivation, hepatitis B reactivation, hepatitis C infection, hepatitis C infection, non-infectious intermediate uveitis, non-infectious intermediate uveitis, and developing central demyelinating disorders. Other opportunistic infections seen in clinical trials include tuberculosis (TB), histoplasmosis, coccidioidomycosis, hepatitis B reactivation, hepatitis C infection, non-infectious intermediate uveitis, and developing central demyelinating disorders.

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