EDA Assessment Report for Biological Medicinal Product

(Scientific Discussion)

Hulio

Date: November 2024

Unit: Technical Assessment Unit

Assessment report

Hulio

Administrative information:

Trade name of the medicinal product:	Hulio
INN (or common name) of the active substance(s):	Adalimumab 40 mg/0.8 ml
Manufacturer of the finished product	Terumo, Yamaguchi, D and D Corporation 3-22, Azamurayama Sayama, Yamaguchi, JP-754-0894, Japan
Marketing Authorization holder	Viatris Limited, Damastown Industrial Park mulhuddart, Dublin 15-Ireland.
Applied Indication(s):	Hulio is intended for the treatment of the following inflammatory diseases: • Rheumatoid arthritis • Polyarticular juvenile idiopathic arthritis • Enthesitis-related arthritis • Ankylosing spondylitis • Axial spondyloarthritis without Radiographic evidence of ankylosing spondylitis • Psoriatic arthritis • Psoriasis • Hidradenitis suppurativa • Crohn's disease • Ulcerative colitis • Non-infectious uveitis in adults and children
Pharmaceutical form(s) and strength(s):	Solution for injection Prefilled Syringe& Prefilled Pen.

	-40mg/0.8ml
Route of administration	Solution for S.C injection
Approved pack	***For PFS:*** Carton box containing Single-use pre-filled syringe with an automatic needle guard. The syringe is made from colorless & transparent cyclo-olefin polymer plastic with a i-coating™ coated chlorobutyl rubber stopper and a staked stainless needle with a needle cap (butyl /diene blend polymer and polypropylene). Each pack containing PES of 0.8ml with 2 alc. Pads + inner leaflet. ***For PFP*** Carton box containing Single-use pre-filled pen containing syringe with an automatic needle guard. The syringe is made from colorless & transparent cyclo-olefin polymer plastic with a i-coating™ coated chlorobutyl rubber stopper and a staked stainless needle with a needle cap (butyl /diene blend polymer and polypropylene). Each pack containing 2 PEP of 0.8ml with 2 alc. Pads + inner leaflet.

List of abbreviations

CD	Crohn's disease
DP	Drug Product
DS	Drug substance
IBD	Inflammatory bowel disease
GMP	Good manufacturing practice
IgG1	Immunoglobulin gamma 1
mAb	Monoclonal antibody
PFP	Pre-filled Pen
RA	Rheumatoid arthritis
PFS	Pre-filled Syringe
TNF-α	Tumor necrosis factor-alpha

Dossier initial submission and evaluation process:

- The product was submitted for registration via 343/2021 ministerial decree **(Fast Track Pathway)**
- The dossier evaluation by the registration administration units was started on 20.6.2021 after providing all the required documents according to "the Checklist for documents of new biological products registration file".
- Full CTD along with detailed SOPs were provided

1. General introduction about the product including brief description of the AI, its mode of action and indications

- Hulio is a proposed biosimilar to Humira® (adalimumab) which is a recombinant human IgG1 mAb targeting human TNF-α and prevents its interaction with TNF-α receptor.
- Genes coding adalimumab VH and VL were designed according to the available information in the US patent.
- TNF-α has a particularly important role in the regulation of a cascade of pathogenic events in rheumatoid arthritis (RA), Crohn's disease (CD), psoriasis and other inflammatory diseases, suggesting that the inhibition of TNF-α functions is important for treatment of these inflammatory diseases.
- The mechanisms of action of adalimumab, The Fab region of adalimumab has the ability to bind and neutralize sTNF-α to block its binding to TNF-α receptors and following cascade of pathogenic inflammation. Adalimumab also binds to tmTNF-α and is affecting intracellular signaling with the end results such as apoptosis. The direct apoptosis activity induced by Fab region of adalimumab against tmTNF-α expressing cells is believed to be important for inflammatory bowel disease (IBD) treatment.

2. Quality aspects:

- **Manufacturer**
  - **Active substance:**

    Kyowa Kirin Co., Ltd. Takasaki Plant 100-1 Hagiwara-machi, Takasaki, Gunma, 370-0013, Japan.
  - **Finished Product:**

    Terumo, Yamaguchi, D and D Corporation 3-22, Azamurayama Sayama, Yamaguchi, JP-754-0894, Japan

    **Manufacturing of both DS and DP are performed in accordance with cGMP regulations.

- **Stability**

➢ **Drug substance:**

-Store at temperature: (−40 ± 10℃), protect from light.

-Required Shelf Life: 36 months.

➢ **Drug Product:**

-Required Shelf Life: 36 months

-Storage condition:

-Store in a refrigerator (2 - 8℃).

-Don't freeze.

-Keep the PFP& PFS in the outer carton in order to protect from light.

-A single PFP &PFS may be stored at temperatures up to maximum of 25°C for a period up to 14 days.

-The prefilled pen& syringe must be protected from light & discarded if not used within the 14-day period.

3.Non –Clinical aspect & Clinical aspect:

Overall, the nonclinical bio similarity and safety data demonstrate that FKB327 has a similar activity to the reference product Humira

The development program to demonstrate the similarity between Hulio and Humira is in general adequate and was performed according to the guidance on similar biological products and the recommendations given in the CHMP Scientific Advices. The comparability exercise was performed between EU/US sourced reference products and the formulation intended to be marketed in the European Union.

Benefit/ Risk discussion:

In conclusion the overall benefit/risk of Hulio PFP is positive.

4.General Conclusion and Recommendations if any:

Based on the review of CTD modules and other supplementary documents, the product is approved.

For more information, please visit EMA published assessment report link:

https://www.ema.europa.eu/en/documents/assessment-report/hulio-epar-public-assessment-report_en.pdf