EDA Assessment Report for Biological Medicinal Product

(Scientific Discussion)

Abrilada PFP
Abrilada PFS

Date: August 2024

Unit: Technical Assessment Unit

Assessment report

Abrilada

Administrative information:

Trade name of the medicinal product:	Abrilada PFP Abrilada PFS
INN (or common name) of the active substance(s):	Adalimumab 40 mg/0.8ml
Manufacturer of the finished product	Catalent Indiana, LLC 1300 South Patterson Dr. Bloomington, Indiana (IN) 47403 - USA
Marketing Authorization holder	Pfizer Europe MA EEIG, Boulevard de la Plaine 17, 1050 Bruxelles, - BELGIUM
Applied Indication(s):	Rheumatoid arthritis, Juvenile idiopathic arthritis, Enthesitis-related arthritis, Axial spondyloarthritis (Ankylosing spondylitis) , Psoriatic arthritis (PsA) , Psoriasis, Pediatric plaque psoriasis, Hidradenitis suppurativa (HS),Crohn's disease (CD) & Pediatric Crohn's disease, Ulcerative colitis (UC) & Pediatric ulcerative colitis, Uveitis & Pediatric uveitis
Pharmaceutical form(s) and strength(s):	• Solution for subcutaneous injection in pre-filled syringe or prefilled pen. • Strength: 40mg/0.8ml.
Route of administration	Both presentations are intended for S.C injection
Approved pack(s):	PFS: -Carton box containing 2 prefilled syringes with 2 alcohol pads and insert leaflet, each pre-filled syringe is in a blister. -Each pre-filled syringe consists of borosilicate (type I glass) having a (staked) needle, a thermoplastic elastomer needle shield with a polypropylene rigid cover, and a fluoropolymer coated elastomeric chlorobutyl plunger stopper. PFP: -Carton box containing 2 prefilled pens with 2 alcohol pads and insert leaflet.

	- The Prefilled Pen enclosing the syringe is made up of two subassemblies (front subassembly and power pack subassembly), a syringe clip and a label. -Each single-use prefilled pen contains a pre-filled syringe that consists of 1 ml (type I glass) having a (staked) needle, a thermoplastic elastomer needle shield with a polypropylene rigid cover, and a fluoropolymer coated elastomeric chlorobutyl plunger stopper.

List of abbreviations

CD	Crohn's disease
CHO	Chinese hamster ovary
CTD	Common technical document
DS	Drug substance
EMA	European Medicines Agency
GMP	Good manufacturing practice
mAb	Monoclonal antibody
PFP	Pre-filled pen
PFS	Pre-filled syringe
S.C	subcutaneous
TNF	Tumor necrosis factor
UC	Ulcerative colitis

Dossier initial submission and evaluation process.

- The product was submitted for registration via reliance model level 1
- The applicant applied for scientific advice unit on 21.7.2022.
- The dossier was initially received by the registration administration units on 6.12.2023 after providing EMA detailed assessment report along with Full CTD for the product.

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

- The finished product is presented as a single-use, sterile, preservative-free solution for administration via SC injection containing 40 mg of adalimumab as active substance in 0.8 mL.
- Abrilada is developed as a biosimilar product to Humira (adalimumab, AbbVie Deutschland GmbH & Co. KG).

- Adalimumab (active substance) is an IgG1 kappa monoclonal antibody (mAb) expressed in Chinese Hamster Ovary (CHO) cells with two identical heavy(H) chains and two identical light (L) chains, covalently linked with four inter-chain disulfide bonds.
  The active substance is capable of binding to human TNF in a dose dependent manner and neutralizing its effects. TNF is a naturally occurring cytokine that promotes normal inflammatory and immune responses when bound to its receptor. However, overexpressed TNF-α has been implicated in numerous autoimmune diseases. Blocking the TNF receptors results in the inhibition of pro-inflammatory pathways leading to decreased cytokine release and reduced inflammatory cell infiltration.

2. Quality aspects:

- **Manufacturer(s)**

  -Adalimumab drug substance (DS) is manufactured, tested and released at Wyeth BioPharma, Andover, MA, USA.

  -The finished product is manufactured at: Catalent Indiana, LLC, 1300 South Patterson Dr. Bloomington, Indiana (IN) 47403 - USA

  -All manufacturers are authorized according to current GMP regulations.

- **Stability**

  Drug Substance:
  -Suggested Storage Conditions of the active substance: -20 ± 5°C
  -required shelf life for the active substance 60 months.

  Drug product (PFP and PFS):
  -required shelf life for the drug product is 36 months
  - The finished product is Stored in a refrigerator (2°C–8°C). Do not freeze. Keep the pre-filled syringe/pen in its outer carton in order to protect from light.

- **Biosimilarity assessment:**

  - Abrilada has been developed as a biosimilar to the reference medicinal product Humira (adalimumab). For the biosimilarity analysis, the company performed comparability exercise including Abrilada versus Humira (EU) and Humira (US). The comparability exercise is mostly based on comparison of analytical characterization data collected during the years of pharmaceutical development. For most quality attributes, a high degree of similarity has been demonstrated.
  - the data indicate that the nonclinical biological activity appears similar between Abrilada, Humira-US, and Humira-EU, and further, the systemic exposure, ADA formation, and in vivo biological effects in cynomolgus monkeys appear similar between Abrilada and

Humira-EU. Thus, the nonclinical data, when combined with other analytical/quality and clinical data, supports the totality of the evidence that demonstrates the similarity of Abrilada and Humira.

3. Non-clinical and clinical aspects

-In conclusion the overall benefit/risk of Abrilada is favorable in the treatment of Rheumatoid arthritis (RA), polyarticular juvenile idiopathic arthritis (PJIA), psoriatic arthritis, ankylosing spondylitis (AS), adult and paediatric Crohn's disease (CD), ulcerative colitis (UC) , adult and adolescent hidradenitis suppurativa, adult and paediatric plaque psoriasis, adult and paediatric uveitis, juvenile enthesitis-related arthritis, and axial spondyloarthritis (radiographic-negative).

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/amsparity-epar-public-assessment-report_en.pdf

****knowing that Abrilada was approved by EMA under the name "Amsparity"**