EDA Assessment Report for Biological Medicinal Product

(Scientific Discussion)

Takhzyro 300mg/2ml

Takhzyro 150 mg/1ml

Date: November 2024

Unit: Technical Assessment Unit

Assessment report

Takhzyro

Administrative information:

Trade name of the medicinal product:	Takhzyro 300mg/2ml Takhzyro 150 mg/1ml
INN (or common name) of the active substance(s):	Lanadelumab
Manufacturer of the finished product	Vetter Pharma-Fertigung GmbH and Co. KG, Schuetzenstrasse 87 and 99-101 88212 Ravensburg – Germany.
Marketing Authorization holder	Takeda Pharmaceuticals International AG Ireland Branch, Block 2 Miesian Plaza, 50-58 Baggot Street Lower, Dublin 2, D02 HW68 – Ireland.
Applied Indication(s):	Takhzyro is indicated for routine prevention of recurrent attacks of hereditary angioedema (HAE) in patients aged 2 years and older.
Pharmaceutical form(s) and strength(s):	Solution for injection, the solution is colorless to slightly yellow, appearing either clear or slightly opalescent. -150 mg /ml
Route of administration	Subcutaneous injection.

Approved pack	Carton box containing as unit packs of one prefilled syringe of borosilicate Type I clear glass syringe barrel with staked 27 G ½ inch special thin–wall needle with rigid needle shield and Bromo butyl rubber formulation with Fluro Tec and B2–40 coating -Plunger rod Polystyrene L with large Flange with inner leaflet.

List of abbreviations

EDA	Egyptian Drug Authority
CTD	Common Technical Document
EMA	European medicines Agency
B2-Receptors	Bradykinin receptors
DP	Drug Product
DS	Drug Substance
HAE	Hereditary Angioedema
HMWK	high-molecular-weight-kininogen
IgG	Immunoglobulin G
pKal	plasma kallikrein
SC	Subcutaneous

Dossier initial submission and evaluation process:

The file evaluated according to EDA Reliance level I & the company submitted data which are the followings:

1. Full CTD for the product.
2. EMA full Assessment report.

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

-Lanadelumab is a recombinant fully human IgG1 monoclonal antibody inhibitor of active pKal that binds both soluble and membrane-bound forms of the enzyme. It is hypothesized that by specifically inhibiting pKal,

-Lanadelumab will prevent the release of bradykinin from HMWK, thereby preventing the vascular leak and swelling that is initiated when bradykinin binds to the B2 receptor.

- Takhzyro is indicated for routine prevention of recurrent attacks of hereditary angioedema (HAE) in patients aged 2 years and older

2. **Quality aspects:**

- **Manufacturer(s)**

➢ **Drug substance:**

1. Rentschler Biopharma SE, Erwin-Rentschler-Str. 21, 88471 Laupheim - Germany.
2. Shire Human Genetic Therapies Inc., 400 Shire Way, Lexington, MA 02421, United States of America.

➢ **finished product:**

-Vetter Pharma-Fertigung GmbH and Co. KG, Schuetzenstrasse 87 and 99-101 88212 Ravensburg – Germany.
- Manufacturing of both DS and DP are performed in accordance with cGMP regulations.

- **Stability**

➢ **Drug substance:**

-Approved Shelf Life: 60 months
-Approved Storage Conditions: Store at (-60 -90°C)

➢ **Drug Product:**

-Approved Shelf Life: 24 months
-Store in a refrigerator: (2-8° C)

3. Non –Clinical aspect & Clinical aspect:

-Overall, the nonclinical studies demonstrate that lanadelumab did not demostrate adverse effects on vital functions or produce adverse target organ pathologies in rats or cynomolgus monkeys. Taken together, the highly specific and potent lanadelumab has the potential to offer significant benefits to patients with angioedema as a prophylactic treatment with infrequent SC dosing.

Clinical Efficacy conclusion
The administration via subcutaneous route and frequency of lanadelumab offers an improvement for patient status.

Benefit/ Risk discussion:
Benefit The benefit of landamub has been adequately shown for prevention of HAE attacks that occurred as significant attacks rate reduction and achievement of attack-free status, also improve the quality of life for each efficacy evaluation period. Risk There were some adverse events occurred during the studies period e.g. infections and infestations, general disorders administration site

conditions, musculoskeletal and connective tissue disorders and elevation in liver enzyme and creatine phosphokinase should be monitoring and inform PV department.
In conclusion the overall benefit/risk of landamub is favourable in the Routine prevention of recurrent attacks of hereditary angioedema (HAE) in patients aged 2 years & older.

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