Lanadelumab-flyo

NDC CODE(S) 47783-0644-XX TAKHZYRO 300MG/2ML Solution (SHIRE US INC)

DESCRIPTION

Lanadelumab-flyo is a non-plasma derived, recombinant, fully human monoclonal antibody (IgG1/κ-light chain) that binds plasma kallikrein and inhibits its proteolytic activity. Plasma kallikrein is a protease that cleaves high-molecular-weight-kininogen (HMWK) to generate cleaved HMWK (cHMWK) and bradykinin, a potent vasodilator that increases vascular permeability resulting in swelling and pain associated with HAE. In patients with HAE due to C1-inhibitor (C1-INH) deficiency or dysfunction, normal regulation of plasma kallikrein activity is not present, which leads to uncontrolled increases in plasma kallikrein activity and results in angioedema attacks. Lanadelumab-flyo decreases plasma kallikrein activity to control excess bradykinin generation in patients with HAE.

Individuals with an inherited deficiency or dysfunction of C1-INH suffer from sudden, recurrent edematous swellings of the subcutaneous or submucosal tissues. This condition is known as hereditary angioedema (HAE).

POLICY

- Lanadelumab-flyo for the prevention of angioedema attacks of Hereditary Angioedema (HAE) is considered ***medically necessary*** if the medical appropriateness criteria are met. **(See Medical Appropriateness below.)**
- Lanadelumab-flyo for the treatment or prevention of other conditions/diseases is considered investigational.

MEDICAL APPROPRIATENESS

INITIAL APPROVAL

- Lanadelumab-flyo is considered **medically appropriate** for the prevention of angioedema attacks of Hereditary Angioedema (HAE) if **ALL** of the following criteria are met:
  - Individual is 12 years of age or older
  - Not used in combination with C1 inhibitor prophylaxis (e.g., Cinryze® or Haegarda®)
  - Confirmation of avoidance of the following possible triggers of HAE attacks:
    - Estrogen-containing oral contraceptive agents AND hormone replacement therapy
    - Antihypertensive agents containing ACE inhibitors
    - Dipeptidyl peptidase IV (DPP-IV) inhibitors (e.g., sitagliptin)
    - Neprilysin inhibitors (e.g., sacubitril)
  - Individual has history of **ANY ONE** of the following criteria for long-term HAE prophylaxis:
    - History of two (2) or more severe HAE attacks per month (e.g., airway swelling, debilitating cutaneous or gastrointestinal episodes
    - Individual disabled more than five days per month by HAE
    - History of at least one laryngeal attack caused by HAE
  - "On demand" HAE therapy (e.g., Kalbitor®, Firazyr®, Berinert®, Ruconest®) does not offer satisfactory control or access to "on-demand therapy" is limited
  - Individual has **ANY ONE** of the following clinical presentations consistent with HAE subtype, which must be confirmed by repeat blood testing (treatment for acute attack should not be delayed for confirmatory testing):
    - **HAE I (C1-Inhibitor deficiency**) if **ALL** of the following:
      - Low C1 inhibitor (C1-INH) antigenic level (C1-INH antigenic level below the lower limit of normal as defined by the laboratory performing the test)
      - Low C4 level (C4 below the lower limit of normal as defined by the performing lab)

- Low C1-INH functional level (C1-INH functional level below the lower limit of normal as defined by the performing lab) and **ANY ONE** of the following:
  - Individual has positive family history of HAE
  - Acquired angioedema has been ruled out (i.e., individual onset of symptoms occurred prior to 30 years old normal C1q levels, individual does not have underlying disease such as lymphoma or benign monoclonal gammopathy [MGUS], etc.)

- **HAE II (C1-Inhibitor dysfunction)** if **ALL** of the following:
  - Normal to elevated C1-INH antigenic level
  - Low C4 level (C4 below the lower limit of normal as defined by the performing lab)
  - Low C1-INH functional level (C1-INH functional level below the lower limit of normal as defined by the performing lab)
- **HAE with normal C1-INH (formerly known as HAE III)** prophylaxis for HAE with normal C1-INH is not routinely recommended and will be evaluated on a case by case basis.

RENEWAL CRITERIA

- Lanadelumab-flyo is considered **medically appropriate** for renewal if **ALL** of the following criteria are met:
  - Individual continues to meet initial approval criteria
  - Significant improvement in severity and duration of attacks have been achieved and sustained
  - Absence of unacceptable toxicity from the drug, Examples of unacceptable toxicity include the following: severe hypersensitivity reactions, etc.
  - Individuals who have demonstrated improvement/stabilization of disease and are well-controlled (e.g., attack free) for at least 6 months should attempt a trial of every 4 week dosing

INDICATION(S)	DOSAGE & ADMINISTRATION
Prophylaxis of Hereditary Angioedema (HAE) attacks	Administer 300 mg subcutaneously every 2 weeks *-A dosing interval of 300 mg every 4 weeks is also effective and may be considered if the patient is well-controlled (e.g., attack free) for more than 6 months.*

LENGTH OF AUTHORIZATION

Coverage will be provided 6 months and may be renewed annually thereafter.

Refer to **DOSAGE LIMITS** below

APPLICABLE TENNESSEE STATE MANDATE REQUIREMENTS

BlueCross BlueShield of Tennessee's Medical Policy complies with Tennessee Code Annotated Section 56-7-2352 regarding coverage of off-label indications of Food and Drug Administration (FDA) approved drugs when the off-label use is recognized in one of the statutorily recognized standard reference compendia or in the published peer-reviewed medical literature.

IMPORTANT REMINDER

We develop Medical Policies to provide guidance to Members and Providers. This Medical Policy relates only to the services or supplies described in it. The existence of a Medical Policy is not an authorization, certification, explanation of benefits or a contract for the service (or supply) that is referenced in the Medical Policy. For a determination of the benefits that a Member is entitled to receive under his or her health plan, the Member's health

plan must be reviewed. If there is a conflict between the Medical Policy and a health plan, the express terms of the health plan will govern.

ADDITIONAL INFORMATION

For appropriate chemotherapy regimens, dosage information, contraindications, precautions, warnings, and monitoring information, please refer to one of the standard reference compendia (e.g., the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) published by the National Comprehensive Cancer Network®, Drugdex Evaluations of Micromedex Solutions at Truven Health, or The American Hospital Formulary Service Drug Information).

SOURCES

Betschel, S., Badiou, J., Binkley, K., Borici-Mazi, R., Hébert, J., Kanani, A., et al. (2019). The International/Canadian Hereditary Angioedema Guideline. *Allergy, Asthma & Clinical Immunology.* 2019. 15:72. Published online 2019 Nov 25. doi: 10.1186/s13223-019-0376-8.

Lexi-Comp Online. (2020, March). AHFS DI. *Lanadelumab-flyo*. Retrieved November 25, 2020 from Lexi-Comp Online with AHFS.

Mauer M, Magerl M, Ansotegui I, et al. The international WAO/EAACI guideline for the management of hereditary angioedema—The 2017 revision and update. Allergy. 2018 73(8):1575-1596.

MICROMEDEX Healthcare Series. Drugdex Evaluations. (2020, September). *Lanadelumab-flyo.* Retrieved November 25, 2020 from MICROMEDEX Healthcare Series.

U.S. Food and Drug Administration. (2018, November). Center for Drug Evaluation and Research.*Takhzyro® (lanadelumab-flyo) injection for subcutaneous use.* Retrieved November 25,, 2020 from https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/761090s001lbl.pdf

EFFECTIVE DATE 4/2/21

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