Takhzyro® (lanadelumab-flyo)
(Subcutaneous)

Document Number: IC-0392

Last Review Date: 03/02/2023
Date of Origin: 09/05/2018
Dates Reviewed: 10/2018, 10/2019, 03/2020, 10/2020, 10/2021, 10/2022, 03/2023

I. Length of Authorization

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

II. Dosing Limits

A. Quantity Limit (max daily dose) [NDC Unit]:

- Takhzyro 150 mg/mL single-dose prefilled syringe: 1 unit every 14 days
- Takhzyro 300 mg/2 mL single-dose vial and prefilled syringe: 1 unit every 14 days

B. Max Units (per dose and over time) [HCPCS Unit]:

- 300 billable units per 14 days

III. Initial Approval Criteria [1]

Coverage is provided in the following conditions:

- Patient is at least 2 years of age; **AND**

Universal Criteria [1,14,19]

- Must be prescribed by, or in consultation with, a specialist in: allergy, immunology, hematology, pulmonology, or medical genetics; **AND**
- Must not be used in combination with C1 inhibitor prophylaxis (e.g., Cinryze or Haegarda) or berotralstat (Orladeyo); **AND**
- Confirmation the patient is avoiding the following possible triggers for HAE attacks:
  - Estrogen-containing oral contraceptive agents AND hormone replacement therapy; **AND**
  - Antihypertensive agents containing ACE inhibitors; **AND**
  - Dipeptidyl peptidase IV (DPP-IV) inhibitors (e.g., sitagliptin); **AND**
  - Neprilysin inhibitors (e.g., sacubitril); **AND**

Prophylaxis to prevent Hereditary Angioedema (HAE) attacks † Φ [1,14,19,20,21]

- Patient has a history of one of the following criteria for long-term HAE prophylaxis:

- History of two (2) or more severe HAE attacks per month (i.e., airway swelling, debilitating cutaneous or gastrointestinal episodes)
- Patient is disabled more than 5 days per month by HAE
- History of at least one laryngeal attack caused by HAE; **AND**

- Treatment of patient with "on-demand" therapy (i.e., Kalbitor, Firazyr, Ruconest, or Berinert) did not provide satisfactory control or access to "on-demand therapy" is limited; **AND**
- Patient has one of the following clinical presentations consistent with a 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) § [14,19,20,21]

• 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); **AND**
• Low C4 level (C4 below the lower limit of normal as defined by the laboratory performing the test); **AND**
• Low C1-INH functional level (C1-INH functional level below the lower limit of normal as defined by the laboratory performing the test); **AND**
  ○ Patient has a family history of HAE; **OR**
  ○ Acquired angioedema has been ruled out (i.e., patient onset of symptoms occur prior to 30 years old, normal C1q levels, patient does not have underlying disease such as lymphoma or benign monoclonal gammopathy [MGUS], etc.)

HAE II (C1-Inhibitor dysfunction) § [19,21]
• Normal to elevated C1-INH antigenic level; **AND** • Low C4 level (C4 below the lower limit of normal as defined by the laboratory performing the test); **AND** • Low C1-INH functional level (C1-INH functional level below the lower limit of normal as defined by the laboratory performing the test)
HAE with normal C1INH (formerly known as HAE III) § [19,20,21]

• Prophylaxis for HAE with normal C1-INH is not routinely recommended and will be evaluated on a case by case basis
  ○ Prior to consideration of long-term prophylaxis, the patient must have demonstrated:
  ▪ An inadequate response or intolerance to an adequate trial of prophylactic therapy with an antifibrinolytic agent (e.g., tranexamic acid (TXA) or aminocaproic acid) and/or a 17α-alkylated androgen (e.g., danazol) unless contraindicated. Female patients may derive additional benefit from progestins[16,17,18]; **AND**
  ▪ Response to therapy from an agent indicated for the treatment of acute attacks (i.e., C1 esterase inhibitor, icatibant, ecallantide, etc.)

† FDA Approved Indication(s); ‡ Compendia Recommended Indication(s); Φ Orphan Drug

IV. Renewal Criteria [1,14,19,20,21]

Coverage may be renewed based upon the following criteria:

- Patient continues to meet the universal and other indication-specific relevant criteria identified in section III; **AND**

- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include: severe hypersensitivity reactions, etc.; **AND**
- Significant improvement in severity, frequency, and/or duration of attacks have been achieved and sustained; **AND**
- Patients 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.

V. Dosage/Administration [1]

Indication	Dose
Prophylaxis of Hereditary Angioedema (HAE) attacks	Adult and Pediatric Patients ≥12 Years of Age • 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 Pediatric Patients 6 to <12 Years of Age • Administer 150 mg subcutaneously every 2 weeks. • A dosing interval of 150 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 Pediatric Patients 2 to <6 Years of Age • Administer 150 mg subcutaneously every 4 weeks. ***NOTE:*** • *Adult and pediatric patients ≥12 years of age: Takhzyro may be administered by the patient or caregiver after being trained by a healthcare professional.* • *Pediatric patients 2 to <12 years of age: Takhzyro should be administered by a healthcare provider or caregiver.*

VI. Billing Code/Availability Information

HCPCS Code:

- J0593 – Injection, lanadelumab-flyo, Takhzyro, 1 mg; 1 billable unit = 1 mg (*code may be used for Medicare when drug administered under direct supervision of a physician, not for use when drug is self-administered)*

NDC:

- Takhzyro 150 mg/mL single-dose prefilled syringe: 47783-0645-xx
- Takhzyro 300 mg/2 mL single-dose prefilled syringe: 47783-0646-xx
- Takhzyro 300 mg/2 mL single-dose vial: 47783-0644-xx

VII. References

1. Takhzyro [package insert]. Lexington, MA; Dyax Corp.; February 2023. Accessed February 2023.
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Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
D84.1	Defects in the complement system

Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determination (NCD), Local Coverage Determinations (LCDs), and Local Coverage Articles (LCAs) may exist and compliance with these policies is required where applicable. They can be found at: https://www.cms.gov/medicare-coverage-database/search.aspx. Additional indications may be covered at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCD/LCA): N/A

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
E (1)	CA, HI, NV, AS, GU, CNMI	Noridian Healthcare Solutions, LLC
F (2 & 3)	AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ	Noridian Healthcare Solutions, LLC
5	KS, NE, IA, MO	Wisconsin Physicians Service Insurance Corp
6	MN, WI, IL	National Government Services, Inc. (NGS)
H (4 & 7)	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions, Inc.
8	MI, IN	Wisconsin Physicians Service Insurance Corp

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
N (9)	FL, PR, VI	First Coast Service Options, Inc.
J (10)	TN, GA, AL	Palmetto Government Benefit Administrators, LLC
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA, LLC
L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA)	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC