

Takhzyro® (lanadelumab-flyo) (Subcutaneous)

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I. Length of Authorization

- Initial: Prior authorization validity will be provided initially for 12 months.
- Renewal: Prior authorization validity may be renewed every 12 months thereafter.

II. Dosing Limits

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**
- Will not be used in combination with other prophylactic therapies targeting C1 inhibitor (e.g., Cinryze or Haegarda), activated Factor XII (e.g., Andembry), or kallikrein (e.g., 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 or angiotensin II receptor blockers (ARBs); **AND**
 - Dipeptidyl peptidase IV (DPP-IV) inhibitors (e.g., sitagliptin, etc.); **AND**
 - Neprilysin inhibitors (e.g., sacubitril); **AND**

Prophylaxis to Prevent Hereditary Angioedema (HAE) Attacks † Φ ^{1,4,14,19,20,21}

- Patient requires long-term prophylactic treatment based on the provider's assessment of the patient's disease activity, quality of life, availability of health care resources, and/or failure to achieve adequate control by appropriate on-demand therapy (i.e., Kalbitor, Firazyr, Ruconest, or Berinert); **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}
<ul style="list-style-type: none"> • 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 <ul style="list-style-type: none"> ○ Patient has a family history of HAE; OR ○ Acquired angioedema has been ruled out (i.e., patient onset of symptoms occurs prior to 30 years of age, 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}
<ul style="list-style-type: none"> • 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}
<ul style="list-style-type: none"> • Prophylaxis for HAE with normal C1-INH is not routinely recommended and will be evaluated on a case by case basis <ul style="list-style-type: none"> ○ Prior to consideration of long-term prophylaxis, the patient must have demonstrated: <ul style="list-style-type: none"> ▪ 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); Ⓢ 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 to Prevent Hereditary Angioedema (HAE) attacks	<p><u>Adult and Pediatric Patients ≥12 Years of Age</u></p> <ul style="list-style-type: none"> 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 <p><u>Pediatric Patients 6 to <12 Years of Age</u></p> <ul style="list-style-type: none"> 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 <p><u>Pediatric Patients 2 to <6 Years of Age</u></p> <ul style="list-style-type: none"> Administer 150 mg subcutaneously every 4 weeks. <p><u>NOTE:</u></p> <ul style="list-style-type: none"> <u>Adult and pediatric patients ≥12 years of age:</u> Takhzyro may be administered by the patient or caregiver after being trained by a healthcare professional. <u>Pediatric patients 2 to <12 years of age:</u> Takhzyro should be administered by a healthcare provider or caregiver.

VI. Billing Code/Availability Information

HCPCS Code:

- J0593 – Injection, lanadelumab-flyo, 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(s):

- 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

- Takhzyro [package insert]. Cambridge, MA; Takeda Pharmaceuticals U.S.A., Inc.; January 2025. Accessed June 2025.
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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)

The preceding information is intended for non-Medicare coverage determinations. 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 Determinations (NCDs) and/or Local Coverage Determinations (LCDs) may exist and compliance with these policies is required where applicable. Local Coverage Articles (LCAs) may also exist for claims payment purposes or to clarify benefit eligibility under Part B for drugs which may be self-administered. The following link may be used to search for NCD, LCD, or LCA documents:

<https://www.cms.gov/medicare-coverage-database/search.aspx>. Additional indications, including any preceding information, may be applied 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 (WPS)
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 (WPS)
N (9)	FL, PR, VI	First Coast Service Options, Inc.
J (10)	TN, GA, AL	Palmetto GBA
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA

Medicare Part B Administrative Contractor (MAC) Jurisdictions

Jurisdiction	Applicable State/US Territory	Contractor
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