

Takhzyro® (lanadelumab-flyo) (Subcutaneous)

Document Number: IC-0392

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I. Length of Authorization

Coverage will be provided for 12 months and may be renewed.

II. Dosing Limits

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

- Takhzyro 150 mg/mL single-dose prefilled syringe: 1 syringe every 14 days
- Takhzyro 300 mg/2 mL single-dose vial and prefilled syringe: 1 vial/syringe 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**
- Will not be used in combination with other prophylactic therapies targeting C1 inhibitor (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 or angiotensin II receptor blockers (ARBs); **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 at least one severe HAE attack 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 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
<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 occur 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); 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**

TAKHZYRO® (lanadelumab-flyo) Prior Auth Criteria

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- 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	<u>Adult and Pediatric Patients ≥12 Years of Age</u>
	<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
	<u>Pediatric Patients 6 to <12 Years of Age</u>
	<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
	<u>Pediatric Patients 2 to <6 Years of Age</u>
	<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, 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 September 2023.
2. Banerji A. Lanadelumab for prevention of attacks in hereditary angioedema: results from the phase 3 HELP study. American College of Allergy, Asthma and Immunology Meeting. 2017, 74: 1-18.
3. Riedl MA, Bernstein JA, Craig T, et al. An open-label study to evaluate the long-term safety and efficacy of lanadelumab for prevention of attacks in hereditary angioedema: design of the HELP study extension. Clin Transl Allergy. 2017 Oct 6;7:36.
4. Bowen T, Cicardi M, Farkas H, et al. Canadian 2003 International Consensus Algorithm For the Diagnosis, Therapy, and Management of Hereditary Angioedema. J Allergy Clin Immunol. 2004 Sep;114(3):629-37.
5. Bygum A, Andersen KE, Mikkelsen CS. Self-administration of intravenous C1-inhibitor therapy for hereditary angioedema and associated quality of life benefits. Eur J Dermatol. Mar-Apr 2009;19(2):147-151.
6. Bowen T, Cicardi M, Farkas H, et al. 2010 International consensus algorithm for the diagnosis, therapy and management of hereditary angioedema. Allergy Asthma Clin Immunol. 2010;6(1):24.
7. Craig T, Aygören-Pürsün E, Bork K, et al. WAO Guideline for the Management of Hereditary Angioedema. World Allergy Organ J. 2012 Dec;5(12):182-99.
8. Gompels MM, Lock RJ, Abinun M, et al. C1 inhibitor deficiency: consensus document. Clin Exp Immunol. 2005;139(3):379.
9. Betschel S, Badiou J, Binkley K, et al. Canadian hereditary angioedema guideline. Asthma Clin Immunol. 2014 Oct 24;10(1):50. doi: 10.1186/1710-1492-10-50.
10. Zuraw BL, Bernstein JA, Lang DM, et al. A focused parameter update: hereditary angioedema, acquired C1 inhibitor deficiency, and angiotensin-converting enzyme inhibitor-associated angioedema. J Allergy Clin Immunol. 2013 Jun;131(6):1491-3. doi: 10.1016/j.jaci.2013.03.034.
11. Zuraw BL, Banerji A, Bernstein JA, et al. US Hereditary Angioedema Association Medical Advisory Board 2013 recommendations for the management of hereditary angioedema due to C1 inhibitor deficiency. J Allergy Clin Immunol Pract. 2013 Sep-Oct;1(5):458-67.
12. Frank MM, Zuraw B, Banerji A, et al. Management of children with Hereditary Angioedema due to C1 Inhibitor deficiency. Pediatrics. 2016 Nov. 135(5)
13. Zuraw BL, Bork K, Binkley KE, et al. Hereditary angioedema with normal C1 inhibitor function: Consensus of an international expert panel. Allergy Asthma Proc. 2012;33 Suppl 1:145-156.
14. Maurer M, Mager M, Ansotegui I, et al. The international WAO/EAACI guideline for the management of hereditary angioedema-The 2017 revision and update. Allergy. 2018 Jan 10. doi: 10.1111/all.13384.
15. Lang DM, Aberer W, Bernstein JA, et al. International consensus on hereditary and acquired angioedema. Ann Allergy Asthma Immunol. 2012;109:395-402.

16. Wintemberger C, Boccon-Gibod I, Launay D, et al. Tranexamic acid as maintenance treatment for non-histaminergic angioedema: analysis of efficacy and safety in 37 patients. Clin Exp Immunol. 2014 Oct; 178(1): 112–117.
17. Saule C, Boccon-Gibod I, Fain O, et al. Benefits of progestin contraception in non-allergic angioedema. Clin Exp Allergy. 2013 Apr;43(4):475-82.
18. Frank MM, Sargent JS, Kane MA, et al. Epsilon aminocaproic acid therapy of hereditary angioneurotic edema; a double-blind study. N Engl J Med. 1972;286:808-812.
19. Betschel S, Badiou J, Binkley K, et al. The International/Canadian Hereditary Angioedema Guideline. Allergy Asthma Clin Immunol. 2019; 15: 72. Published online 2019 Nov 25. doi: 10.1186/s13223-019-0376-8
20. Busse PJ, Christiansen SC, Riedl MA, et al. US HAEA Medical Advisory Board 2020 Guidelines for the Management of Hereditary Angioedema. J Allergy Clin Immunol Pract. 2021 Jan;9(1):132-150.e3. doi: 10.1016/j.jaip.2020.08.046.
21. Maurer M, Magerl M, Betschel S, et al. The international WAO/EAACI guideline for the management of hereditary angioedema – The 2021 revision and update. Allergy. 2021 Nov 22. Doi: 10.1111/all.15214.

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

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Provides free aids and services to people with disabilities to communicate effectively with us, such as:

- Qualified sign language interpreters
- Written information in other formats (large print, audio, accessible electronic formats, other formats)

Provides free language services to people whose primary language is not English, such as:

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Grievance Specialist
PreferredOne Community Health Plan
PO Box 59052
Minneapolis, MN 55459-0052
Phone: 1.800.940.5049 (TTY: 763.847.4013)
Fax: 763.847.4010
customerservice@preferredone.com

You can file a grievance in person or by mail, fax, or email. If you need help filing a grievance, a Grievance Specialist is available to help you.

You can also file a civil rights complaint with the U.S. Department of Health and Human Services, Office for Civil Rights, electronically through the Office for Civil Rights Complaint Portal, available at <https://ocrportal.hhs.gov/ocr/portal/lobby.jsf>, or by mail or phone at:

U.S. Department of Health and Human Services
200 Independence Avenue, SW
Room 509F, HHH Building
Washington, D.C. 20201
1-800-368-1019, 800-537-7697 (TDD)

Complaint forms are available at <http://www.hhs.gov/ocr/office/file/index.html>.

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Minneapolis, MN 55459-0212
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Fax: 763.847.4010
customerservice@preferredone.com

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You can also file a civil rights complaint with the U.S. Department of Health and Human Services, Office for Civil Rights, electronically through the Office for Civil Rights Complaint Portal, available at <https://ocrportal.hhs.gov/ocr/portal/lobby.jsf>, or by mail or phone at:

U.S. Department of Health and Human Services
200 Independence Avenue, SW
Room 509F, HHH Building
Washington, D.C. 20201
1-800-368-1019, 800-537-7697 (TDD)

Complaint forms are available at <http://www.hhs.gov/ocr/office/file/index.html>.

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ATTENTION : Si vous parlez français, des services d'aide linguistique vous sont proposés gratuitement. Appelez le 1.800.940.5049 (TTY: 763.847.4013).

주의: 한국어를 사용하시는 경우, 언어 지원 서비스를 무료로 이용하실 수 있습니다. 1.800.940.5049 (TTY: 763.847.4013). 번으로 전화해 주십시오.

PAUNAWA: Kung nagsasalita ka ng Tagalog, maaari kang gumamit ng mga serbisyo ng tulong sa wika nang walang bayad. Tumawag sa 1.800.940.5049 (TTY: 763.847.4013).