RXADVANCE
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Clinical Policy Title:	lanadelumab-flyo
Policy Number:	RxA.513
Drug(s) Applied:	Takhzyro™
Original Policy Date:	03/06/2020
Last Review Date:	12/07/2020
Line of Business Policy Applies to:	All lines of business

Background

Lanadelumab-flyo (Takhzyro™) is a human monoclonal antibody that inhibits the proteolytic activity of kallikrein to reduce the generation of bradykinin. It is indicated for prophylaxis to prevent attacks of hereditary angioedema (HAE) in patients 12 years and older.

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
lanadelumab-flyo (Takhzyro™)	HAE attack prophylaxis	300 mg SC every 2 weeks	300 mg SC every 2 weeks

Dosage Forms

- Injection: 300 mg/2 mL (150 mg/mL) solution in single dose vial

Clinical Policy

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

I. Initial Approval Criteria

A. Hereditary Angioedema (must meet all)**:**

1. Diagnosis of HAE confirmed by one of the following (a, b or c):
   a. Confirmed monoallelic mutation known to cause HAE in either SERPING1 or F12 gene;
   b. Low C4 level (below the lower limit of normal as defined by the laboratory performing the test) and (i or ii):
      i. Low C1 inhibitor (C1-INH) antigenic level (below the lower limit of normal defined by the laboratory performing the test);
      ii. Low C1-INH functional level (below the lower limit of normal defined by the laboratory performing the test) (see Appendix D);
   c. Normal C4 level and normal C1-INH level, and both of the following (i and ii):
      i. History of recurrent angioedema;
      ii. Family history of angioedema;
2. Prescribed by or in consultation with a/an allergist, hematologist, immunologist or rheumatologist;
3. Age 12 years or older;
4. Member (a, b or c):

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a. experiences more than one (1) moderate to severe attack per month (i.e. airway swelling, debilitating cutaneous or gastrointestinal episodes);
b. is disabled more than five (5) days per month by HAE; or
c. has history of previous airway compromise caused by HAE;

5. Member is not using lanadelumab-flyo in combination with another FDA-approved product for long-term prophylaxis of HAE attacks (e.g., C1 esterase inhibitors);
6. Dose does not exceed 300 mg every 2 weeks.

Approval duration
Commercial: 6 months
Medicaid: 6 months

II. Continued Therapy Approval

A. Hereditary Angioedema (must meet all)**:**

1. Member is currently receiving the medication that has been authorized by RxAdvance or the member has met initial approval criteria listed in this policy;
2. Member is responding positively to therapy as evidenced by reduction in attacks from baseline;
3. Member is not using lanadelumab-flyo in combination with another FDA-approved product for long-term prophylaxis of HAE attacks (e.g., C1 esterase inhibitors);
4. If request is for a dose increase, new dose does not exceed 300 mg every 2 weeks.

Approval duration
Commercial: 12 months
Medicaid: 12 months

III. Appendices

APPENDIX A: Abbreviation/Acronym Key
FDA: Food and Drug Administration
HAE: Hereditary Angioedema
SC: Subcutaneous
C1-INH: C1 Esterase Inhibitor
C4: Complement Component 4

APPENDIX B: Therapeutic Alternatives
Not applicable

APPENDIX C: Contraindications/Boxed Warnings

- Contraindication(s):
  - None.

- Boxed Warning(s):
  - None.

APPENDIX D: General Information

- Diagnosis of HAE:
  - There are two classifications of HAE: HAE with C1-INH deficiency (further broken down into Type I and Type II) and HAE of unknown origin (also known as Type III).
  - In both Type I (approximately 85 percentage of cases) and Type II (approximately 15 percentage of cases), C4 levels are low. C1- INH antigenic levels are low in Type I while C1-INH functional levels

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are low in Type II. Diagnosis of Type I and II can be confirmed with laboratory tests. Reference ranges for C4 and C1-INH levels can vary across laboratories (see below for examples); low values confirming diagnosis are those which are below the lower end of normal.

Laboratory Test & Reference Range	Mayo Clinic	Quest Diagnostics	Lab Corp
C4	14 – 40 mg/dL	16 – 47 mg/dL	13 – 44 mg/dL
C1-INH, antigenic	19 – 37 mg/dL	21 – 39 mg/dL	21 – 39 mg/dL
C1-INH, functional	Normal: more than 67% Equivocal: 41 – 67% Abnormal: less than 41%	Normal: 68% or more Equivocal: 41 – 67% Abnormal: 40% or less	Normal: more than 67% Equivocal: 41 – 67% Abnormal: less than 41%

- Type III, on the other hand, presents with normal C4 and C1-INH levels. Some patients have an associated mutation in the FXII gene, while others have no identified genetic indicators. Type III is very rare (number of cases unknown), and there are no laboratory tests to confirm the diagnosis. Instead the diagnosis is clinical and supported by recurrent episodes of angioedema with a strong family history of angioedema.

References

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3. Cicardi M, Aberer W, Banerji A, et al. Classification, diagnosis, and approach to treatment for angioedema: consensus report from the Hereditary Angioedema International Working Group. Allergy. 2014; 69(5): 602-616. Accessed September 24, 2020.
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5. Lanadelumab, Lexi-Drug. Lexicomp. Wolters Kluwer Health, Inc. Riverwoods, IL. Accessed with subscription at: http://online.lexi.com. Accessed September 24, 2020.

Review/Revision History	Review/Revision Date	P&T Approval Date
Policy established.	01/2020	03/06/2020
Policy was reviewed: 1. Policy title table was updated: Clinical Policy Title was updated to lanadelumab-flyo, Line of business policy applies was updated to All lines of business. 2. Clinical policy criteria were updated. 3. Continued therapy criteria II.A.1 was rephrased to "Currently receiving medication that has been authorized by RxAdvance…".	09/24/2020	12/07/2020

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4. Appendix A was updated: SC, C4 and C1-INH was updated. 5. Appendix D was updated: reference range for Lab Corp C4 has been changed to 13- 44 mg/dL from 9-36 mg/dL. 6. References were reviewed and updated.		

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