Takhzyro (lanadelumab)
Policy Number: C15446-A

CRITERIA EFFECTIVE DATES:

ORIGINAL EFFECTIVE DATE	LAST REVIEWED DATE	NEXT REVIEW DATE
1/2019	07/17/2019	07/17/2020
J CODE	**TYPE OF CRITERIA**	**LAST P&T APPROVAL**
J3590 (NOC) C9399 (NOC)	RxPA	Q3 2019 20190828C15446-A

PRODUCTS AFFECTED: Takhzyro (lanadelumab-flyo)

DRUG CLASS: Plasma Kallikrein Inhibitors- monoclonal antibodies

ROUTE OF ADMINISTRATION: Subcutaneous, self-administered

PLACE OF SERVICE: Specialty Pharmacy
The recommendation is that medications in this policy will be for pharmacy benefit coverage and will be self-administered

AVAILABLE DOSAGE FORMS: NDC: 47783-0644-01, 300 mg/2 ml vial

FDA-APPROVED USES: Prophylaxis to prevent attacks of hereditary angioedema (HAE) in patients 12 years and older

COMPENDIAL APPROVED OFF-LABELED USES: None

COVERAGE CRITERIA: INITIAL AUTHORIZATION

DIAGNOSIS: ICD-10 Diagnosis: D84.1 Defects in the complement system

REQUIRED MEDICAL INFORMATION:
A. PREVENTION OF HAE ATTACKS:

1. Documentation of confirmed diagnosis of hereditary angioedema type I or II, via blood tests for C1 INH and C4 levels
AND
2. Documentation that patient experiences at least 2 HAE attacks per month
AND
3. Documentation that medication will be used for prophylaxis- not for acute treatment
AND
4. Patient has a documented trial/failure or contraindication or unable to receive treatment with danazol
AND
5. Takhzyro will not be used in combination with other approved treatments to PREVENT HAE attacks

DURATION OF APPROVAL: Initial authorization: 9 months, continuing authorization: 6 months

QUANTITY: 2 VIALS (4ml) per 28 day supply- If attack free for 6 months- 1 vial (2ml) per 28 days

PRESCRIBER REQUIREMENTS: Prescribed by or in consultation with a board certified allergist, immunologist, hematologist or dermatologist.

AGE RESTRICTIONS: 12 years of age and older

GENDER: Male and Female

CONTINUATION OF THERAPY:
A. PREVENTION OF HAE ATTACKS:
1. Documentation of frequency and severity of attacks since starting Takhzyro therapy
AND
2. (a) If ZERO attacks have occurred within 6 months since starting Takhzyro therapy, documentation of patient evaluation for extended dosing interval of 300mg every 4 weeks
OR
(b) If documentation provided show patient is not attack free- must demonstrate improvement from baseline in severity, duration or frequency of attacks
AND
3. Documentation of confirmed diagnosis of hereditary angioedema type I or II, via blood tests for C1 INH and C4 levels
AND
4. Documentation that medication will be used for prophylaxis- not for acute treatment
AND
5. Takhzyro will not be used in combination with other approved treatments to PREVENT HAE attacks

CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION: All other uses of Takhzyro (lanadelumab-flyo) are considered experimental/investigational and therefore, will follow Molina's Off-Label policy.

OTHER SPECIAL CONSIDERATIONS: Takhzyro is distributed by a limited network of 5 specialty pharmacies: Accredo, Briova, CVS Caremark, Option Care, Orsini.

BACKGROUND:
Hereditary angioedema (HAE) is a chronic autosomal dominant genetic disorder characterized by recurrent episodes of tissue swelling in various parts of the body, including the face, hands, feet, airways, and intestinal tract. Attacks can happen at any age after birth. Most cases of HAE are caused by mutations in the gene that codes for C1 esterase inhibitor (C1-INH). The mutations lead to either deficient C1-INH levels (HAE Type I, 85%) or dysfunctional C1-INH (HAE Type II, 15%). Type III HAE, also known as HAE with normal C1-INH, is extremely rare and occurs primarily in women. Type III HAE may be estrogen dependent and although some patients will demonstrate activating mutations in the coagulation factor XII. Bradykinin is a key mediator of HAE symptoms for all three types of HAE due to absent or abnormal components in bradykinin metabolizing pathways. C1-INH plays an important role in the regulation of the kallikrein-kinin system, preventing the accumulation of bradykinin, which is a potent vasodilator. It is the dysfunction of the kallikrein-kinin pathway that leads to the development of HAE symptoms. It is the uncontrolled levels of bradykinin that can lead to episodes of extreme dilation of blood vessels, resulting in leakage of plasma and tissue swelling. C1-INH titers less than 30% of normal with profoundly depressed C4 levels confirm the diagnosis of HAE. The signs and symptoms associated with acute HAE attacks include intense and painful swelling of the face, larynx, gastrointestinal (GI) tract, limbs, or genitalia. Approximately

50% of individuals with untreated HAE have monthly exacerbations and another 40% have 6 to 11 attacks annually. Episodic attacks of HAE produce edema in three primary areas: periphery, abdomen, and larynx. Peripheral attacks are associated with painful disfigurement and physical disability. Abdominal attacks result in severe abdominal pain, nausea, and vomiting, while laryngeal attacks may result in death by asphyxiation. Medications for HAE can be categorized into on-demand therapies taken during an acute attack and therapies for prophylaxis of attacks. International guidelines and consensus documents recommend that all attacks be considered for treatment and that long- term prophylaxis be considered in all patients for whom on-demand therapy is insufficient to minimize effects of the disease.
The efficacy of Takhzyro for the prevention of angioedema attacks in patients 12 years of age and older with Type I or II HAE was demonstrated in a multicenter, randomized, double-blind, placebo-controlled parallel- group study. The study included 125 adult and adolescent patients with HAE who experienced at least one investigator-confirmed attack per 4 weeks during the run-in period. Patients were randomized into 1 of 4 parallel treatment arms for the 26-week treatment period. All Takhzyro treatment arms produced clinically meaningful and statistically significant reductions in the mean HAE attack rate compared to placebo across all primary and secondary endpoints in the intent-to-treat (ITT) population. An open-label, long-term safety and efficacy study is ongoing and expected to complete in November 2019. The HELP study also collected exploratory endpoints that included the percentage of patients who were attack free for the entire 26-week treatment period. The percentage of attack-free patients for the entire 26-week treatment period is listed in the chart above. The attack-free rate was used to determine whether and how patients could step down in dosing frequency. For patients on the 300 mg every 2 weeks, the attack-free rate increased to 77% when measured from days 70-182 on treatment. The lower attack-free rate seen in the first 6 months was likely due to the long half-life of Takhzyro and that patients did not reach steady state until around 70 days. There have been no head-to-head comparisons among any of the products for HAE. According to the individual product prescribing information, the reduction in monthly attack rate versus placebo of all three products remain comparable.

APPENDIX:

REFERENCES:

1. Takhzyro ® [prescribing information]. Lexington, MA:Dyax Corp (Shire). September 2018.
2. Craig T, Pursun EA, Bork K, et al. WAO guideline for the management of hereditary angioedema. WAO Journal. 2012;5:182-199.
3. Craig TJ, Schneider LC, MacGinnitie AJ.Plasma-derived C1-INH for managing hereditary angioedema in pediatricpatients: A systematic review. Pediatr Allergy Immunol. 2015 Sep;26(6):537-44.
4. Agostoni, Angelo, et al.“"Hereditary and acquired angioedema: problems and progress: proceedings of the third C1 esterase inhibitor deficiency workshop and beyond”" Journal of Allergy and Clinical Immunology 114.3 (2004): S51-S131.
5. Weiler CR, van Dellen RG. Genetic test indications and interpretations in patients with hereditary angioedema. Mayo Clin Proc. 2006 Jul;81(7):958-72
6. Maurer M, Magerl M, Ansotegui I, et al. The International WAO/EAACI guideline for the management of hereditary angioedema – the 2017 revision and update. World Allergy Organization Journal. 2018;11(5).