Pharmacy Management Drug Policy

SUBJECT: Hereditary Angioedema (HAE) For Andembry, Berinert, Cinryze, Dawnzera, Ekterly, Firazyr, Icatibant, Haegarda, Kalbitor, Orladeyo, Ruconest, Sajazir, and Takhzyro
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If the member's subscriber contract excludes coverage for a specific service or prescription drug, it is not covered under that contract. In such cases, medical or drug policy criteria are not applied. This drug policy applies to the following line/s of business:

Policy Application

Category:	☒ Commercial Group (e.g., EPO, HMO, POS, PPO)	☒ Medicare Advantage
	☒ On Exchange Qualified Health Plans (QHP)	☐ Medicare Part D
	☒ Off Exchange Direct Pay	☒ Essential Plan (EP)
	☒ Medicaid & Health and Recovery Plans (MMC/HARP)	☒ Child Health Plus (CHP)
	☐ Federal Employee Program (FEP)	☐ Ancillary Services
	☒ Dual Eligible Special Needs Plan (D-SNP)	

DESCRIPTION:

Hereditary angioedema (HAE) is an autosomal dominant disease caused by a deficiency in functional C1 esterase inhibitor, which leads to increases in bradykinin levels. The increase in bradykinin produces an increase in vascular permeability which leads to episodes of nonpruritic, nonpitting, subcutaneous or submucosal edema. Symptoms involve the arms, legs, hands, feet, bowels, genitalia, trunk, face, tongue, or larynx and typically begin in early childhood (2-3 years of age). Attacks can be precipitated by minor trauma and stress but may occur without an apparent trigger.

The following are measured to help confirm a diagnosis of HAE.

- Serum complement factor 4 (C4)
- C1 inhibitor (C1-INH) antigenic protein
- C1 inhibitor (C1-INH) functional level

HAE can be broadly divided into 2 fundamental types: HAE-C1INH (HAE due to a deficiency of C1-INH) or HAE-nl-C1INH (HAE with normal C1-INH). HAE-C1INH is further divided into 2 subtypes: type I HAE, characterized by deficient levels of C1INH protein and function; and type II HAE, characterized by the normal level of C1INH protein that is dysfunctional, resulting in diminished C1INH functional activity. HAE-nl-C1INH (previously referred to as type III HAE), in which the C4, C1-INH protein and C1-INH functional activity are all normal or near normal, is not as well understood as HAE-C1INH.

HAE can be treated by Andembry (garadacimab), Berinert (Human C1 Esterase Inhibitor), Cinryze (Human C1 Esterase Inhibitor), Dawnzera (donidalorsen), Ekterly (sebetralstat), Haegarda (Human C1 Esterase Inhibitor), Kalbitor (Ecallantide), Firazyr (Icatibant), Sajazir (Icatibant), Ruconest (Recombinant C1 Esterase Inhibitor), Takhzyro (Lanadelumab-flyo) or Orladeyo (Berotralstat) each of which is FDA approved to reduce edema symptoms. Berinert, Cinryze, Haegarda, and Ruconest treat HAE by replacing Human C1 Esterase Inhibitor deficiencies. Kalbitor treats HAE attacks by inhibiting plasma kallkrein which cleaves high molecular weight kininogen and results in bradykinin release. Firazyr, Sajazir and generic Icatibant inhibits bradykinin from binding the B2 receptor. Takhzyro is a plasma kallikrein inhibitor (monoclonal antibody). Orladeyo and Ekterly are oral kallikrein inhibitors. Andembry is a Factor XIIa inhibitor (monoclonal antibody), which decreases the activation of prekallikrein to kallikrein and the generation of bradykinin. Dawnzera is an antisense oligonucleotide that targets prekallikrein messenger RNA, reducing prekallikrein production and disrupting the pathways that lead to bradykinin production.

POLICY:

Based upon our assessment and review of the peer-reviewed literature Andembry, Berinert, Cinryze, Dawnzera, Ekterly, Firazyr, Haegarda, Icatibant, Kalbitor, Orladeyo, Ruconest, Sajazir, and Takhzyro have been medically proven to be effective and therefore, **medically necessary** for the prophylactic and acute attack treatment of Hereditary Angioedema (HAE) following diagnoses if specific criteria are met:

A. **To be considered for drug treatment, individuals must meet the following criteria in addition to drug specific criteria listed below**:
   1. Medication must be prescribed by an allergist, immunologist, hematologist, or dermatologist **AND**
   2. Must have a confirmed diagnosis of HAE based on the following:
      a. HAE-C1INH (HAE due to a deficiency of C1-INH: Type I or II HAE)
         i. A history of recurrent angioedema in the absence of concomitant urticaria and no concomitant use of medication known to cause angioedema (i.e., ACE-Inhibitors, estrogens, angiotensin II receptor blockers, DPP-IV inhibitors, and neprilysin inhibitors) **AND**
         ii. Low C1INH antigenic or functional level **AND**
         iii. Low C4 level (either at baseline or during an attack) **OR**
      b. HAE-nl-C1INH (HAE with normal C1-INH)
         i. A history of recurrent angioedema in the absence of concomitant urticaria and no concomitant use of medication known to cause angioedema (i.e., ACE-Inhibitors, estrogens, angiotensin II receptor blockers, DPP-IV inhibitors, and neprilysin inhibitors) **AND**
         ii. Documented normal or near normal C4, C1-INH antigen, and C1-INH function **AND**
         iii. Demonstration of EITHER:
            A. A mutation associated with the disease (i.e., mutations of the F12 gene, ANGPT1 gene, PLG gene, or KNG1 gene) **OR**
            B. A positive family history of recurrent angioedema and documented lack of efficacy of high-dose antihistamine therapy (i.e., cetirizine at 40 mg/d or the equivalent) for at least 1 month.

B. **Drug specific criteria**

Acute Treatments
Berinert (C1 esterase inhibitor [Human]) – Medical or Rx
1. Must have a diagnosis of **acute** attacks associated with hereditary angioedema (progress notes required) 2. Must be used for acute attacks--Safety and efficacy as prophylactic therapy has not been established and therefore will not be covered 3. Berinert has been proven to be both safe and effective in adult and pediatric patients 4. **For New starts only**: For patients 18 years of age and older, requests for Berinert will require documentation of therapeutic failure, severe intolerance, **OR** a contraindication to generic icatibant. a. Applies to Commercial, Essential Plan, Exchange, Child Health Plus, Medicare Advantage, Medicaid and HARP members when requested under the **medical benefit** b. Applies to Commercial, Essential Plan, Exchange, and Child Health Plus members when request under the **pharmacy benefit** 5. Berinert will be reviewed under the **medical benefit** when administered by a health care professional. If the member transitions to self-administration, then Berinert can be authorized under the **pharmacy benefit**. 6. Dose is 20 units per kg by IV infusion. 7. Maximum quantity limit of 10 vials per 30 days on Rx benefit 8. Authorization on the medical benefit will be for 1 month initially then every 6 months

9. Authorization on the pharmacy benefit will be for 6 months at a time
10. Recertification will require documentation of decrease in severity or duration of attacks. Documentation including frequency of administration will also be required at time of recertification to monitor for appropriate use.

Ekterly (sebetralstat) - Rx

1. Must have a diagnosis of **acute** attacks associated with hereditary angioedema (progress notes required)
2. Must be used for acute attacks- Safety and efficacy as prophylactic therapy has not been established and therefore will not be covered
3. Safety and efficacy in children under the age of 12 has not been established and therefore will not be covered.
4. Ekterly is an oral medication and will therefore be covered under the **pharmacy benefit**
5. Requests for Ekterly will require documentation of therapeutic failure, severe intolerance, **OR** a contraindication to generic icatibant.
    a. This does not apply to members under the age of 18.
6. The recommended dose is 600 mg (2 x 300mg tablets) orally at the earliest recognition of an acute HAE attack. A second 600 mg dose may be taken 3 hours after the first dose if response is inadequate, or if symptoms worsen or recur. Maximum of 4 tablets (1,200 mg) in a 24-hour period.
7. Quantity limit of 4 tablets per 30-days.
8. Authorization will be for 6 months at a time.
    a. Recertification will require documentation of a decrease in severity or duration of attacks. Documentation including frequency of administration will also be required at the time of administration to monitor for appropriate use.

Firazyr, icatibant and Sajazir - Rx

1. Must have a diagnosis of **acute** attacks associated with hereditary angioedema (progress notes required)
2. Must be used for acute episodic attacks--Safety and efficacy as prophylactic therapy has not been established and therefore will not be covered
3. Firazyr, Sajazir, and icatibant have potential to attenuate antihypertensive effects of ACE inhibitors and should not be administered to patients taking ACE inhibitors since there are no clinical trials in this population
4. Safety and Efficacy in anyone under 18 years old is not established and therefore will not be covered.
5. Firazyr, Sajazir, and icatibant can be self-administered upon recognition of an HAE attack after training under the guidance of a healthcare professional and therefore will be covered under the **pharmacy benefit.**
6. Step therapy applies: Both initial and recertification/continuation of therapy requests for brand Firazyr will require documentation of therapeutic failure, severe intolerance, or a contraindication to a trial with generic Icatibant.
7. Standard dosing is 30mg subcutaneously injected into abdominal area; if response is inadequate or symptoms recur additional injections of 30mg may be administered at intervals of at least 6 hours with no more than 3 doses per 24-hour period.
8. Quantity limit of #3 (3ml each) pre-filled syringes – 9ml/30 days.
9. Authorization will be for 6 months at a time.
    a. Recertification will require documentation of decrease in severity or duration of attacks. Documentation including frequency of administration will also be required at time of recertification to monitor for appropriate use.

Kalbitor (ecallantide) - Medical

1. Must have a diagnosis of **acute** attacks associated with hereditary angioedema (progress notes required)

2. Must be used for acute attacks--Safety and efficacy as prophylactic therapy has not been established and therefore will not be covered
3. Safety and efficacy have not been established in children under the age of 12 and therefore will not be covered
4. Anaphylaxis has been reported after administration of Kalbitor. Because of the risk of anaphylaxis, it should only be administered by a healthcare professional with appropriate medical support to manage anaphylaxis and HAE and is therefore covered under the **medical benefit**.
5. **For New starts only:** For patients 18 years of age and older, requests for Kalbitor will require documentation of therapeutic failure, severe intolerance, **OR** a contraindication to generic icatibant.
6. The recommended dose of Kalbitor is 30 mg (3 mL), administered subcutaneously in three 10 mg (1mL) injections. If the attack persists, an additional dose of 30 mg may be administered within a 24-hour period.
7. Authorization will be for 1 month initially then every 6 months
    a. Recertification will require documentation of decrease in severity or duration of attacks. Documentation including frequency of administration will also be required at time of recertification to monitor for appropriate use

Ruconest (C1 esterase inhibitor [Recombinant]) – Medical or Rx

1. Must have a diagnosis of **acute** attacks associated with hereditary angioedema (progress notes required)
2. Ruconest will not be covered for laryngeal attacks as efficacy has not been established in patients with laryngeal HAE attacks
3. Safety and efficacy in children under the age of 13 has not been established and therefore will not be covered
4. Ruconest will be reviewed under the **medical benefit** when administered by a health care professional. If the member transitions to self-administration, then Ruconest can be authorized under the **pharmacy benefit**.
5. **For New starts only**: For patients 18 years of age and older, request for Ruconest will require documentation of therapeutic failure, severe intolerance, OR a contraindication to generic Icatibant
    a. Applies to Commercial, Essential Plan, Exchange, Child Health Plus, Medicare Advantage, Medicaid and HARP members when requested under the **medical benefit**
    b. Applies to Commercial, Essential Plan, Exchange, and Child Health Plus members when request under the **pharmacy benefit**
6. Dose is 50 IU per kg by IV injection.
    a. Maximum dose is 4200 IU with no more than 2 doses within a 24-hour time-period
7. Quantity limit of 100 ml per 30 days.
8. Authorization on the medical benefit will be for 1 month initially then every 6 months
9. Authorization on the pharmacy benefit will be for 6 months at a time
10. Recertification will require documentation of decrease in severity or duration of attacks. Documentation including frequency of administration will also be required at time of recertification to monitor for appropriate use.

Prophylactic Treatments

Andembry (garadacimab) - Rx

1. Must have a diagnosis of hereditary angioedema (progress notes required)
2. Must be used as prophylaxis – not for acute treatment
3. For long term prophylaxis, the patient must meet the following:
    a. History of at least one laryngeal attack or at least two severe HAE attacks (i.e., debilitating cutaneious or gastrointestinal episodes) per month that resulted in loss of work/school

productivity or ER/unscheduled doctor visits **OR** disability for > 5 days per month due to HAE
4. Safety and efficacy in children under the age of 12 has not been established and therefore will not be covered.
5. Andembry is intended for self-administered or administration by a caregiver and therefore will be covered under the **pharmacy benefit.**
6. Requests for Andembry will require documentation of therapeutic failure, severe intolerance, **OR** a contraindication to Haegarda **AND** Takhzyro
7. Standard dosage is an initial loading dose of 400 mg (two 200 mg injections) administered subcutaneously on the first day of treatment, followed by a maintenance dosage of 200 mg administered subcutaneously every month.
8. Quantity limit of 1.2 mL (1 injection) per 28 days.
    a. A quantity limit of 2.4 mL (2 injections) will be allowed for the initial month of therapy in order to obtain the proper loading dose.
9. Authorization will be provided for 6 months at a time
    a. Recertification will require documentation of decrease in the severity, duration, and/or frequency of attacks.

Cinryze (C1 esterase inhibitor [Human]) – Medical or Rx

1. Must have a diagnosis of hereditary angioedema (progress notes required)
2. Must be used as a prophylaxis – not for acute treatment
3. Cinryze will be allowed for short-term prophylaxis if being requested prior to medical, surgical, or dental procedure. Approval will be for one month only.
4. For long term prophylaxis, the patient must meet the following:
    a. History of at least one laryngeal attack or at least two severe HAE attacks (i.e., debilitating cutaneous or gastrointestinal episodes) per month that resulted in loss of work/school productivity or ER/unscheduled doctor visits **OR** disability for > 5 days per month due to HAE
5. Safety and efficacy in children under the age of 6 has not been established and therefore will not be covered
6. Cinryze will be reviewed under the **medical benefit** when administered by a health care professional. If the member transitions to self-administration, then Cinryze can be authorized under the **pharmacy benefit.**
7. Step therapy applies for New Starts as follows:
    a. For all lines of business: Requests for Cinryze for long term prophylaxis will require documentation of therapeutic failure, severe intolerance, OR a contraindication to Haegarda **AND** Takhzyro.
    b. This step does not apply to:
        i. Requests for short-term prophylaxis prior to medical, surgical, or dental procedure.
8. Standard dosage for pediatric patient's ages 6-11 years old is 500-unit IV infusion over 5 minutes every 3-4 days. This dose may be adjusted according to individual response, up to 1000 unit every 3-4 days.
9. Standard dosage for adolescent and adult patients (12 years old and above) is 1000-unit IV infusion over 10 minutes every 3-4 days.
10. Quantity limit of 20 vials per 30 days.
    a. Requests for quantities in excess of the establish quantity limit for adolescent and adult patients (12 years old and above), will be considered based on Cinryze package labeling:
        i. For patients who have not responded adequately to 1000 unit every 3 or 4 days, doses up to 2000 units (not exceeding 80 U/kg) every 3 or 4 days may be considered based on individual patient response.
    b. Requests will require documentation of a previous trial with the standard dosage (1000 unit) and outcome of the trial, to document the need for the increased dose.
    c. No more than 50 vials per 30 days will be authorized.

11. Authorization on either the medical benefit or the pharmacy benefit will be for 6 months.
    a. Recertification will require documentation of decrease in the severity, duration, and/or frequency of attacks. Documentation including frequency of administration will also be required at time of recertification to monitor for appropriate use

Dawnzera (donidalorsen) - Rx

1. Must have a diagnosis of hereditary angioedema (progress notes required)
2. Must be used as a prophylaxis – not for acute treatment
3. For long term prophylaxis, the patient must meet the following:
    a. History of at least one laryngeal attack or at least two severe HAE attacks (i.e., debilitating cutaneous or gastrointestinal episodes) per month that resulted in loss of work/school productivity or ER/unscheduled doctor visits **OR** disability for > 5 days per month due to HAE
4. Safety and efficacy in children under the age of 12 has not been established and therefore will not be covered
5. Dawnzera is intended for self-administration or administration by a caregiver and therefore will be covered under the **pharmacy benefit.**
6. Requests for Dawnzera will require documentation of therapeutic failure, severe intolerance, **OR** a contraindication to Haegarda **AND** Takhzyro.
7. Recommended dosage is 80mg administered subcutaneously every 4 weeks. A dosage of 80mg subcutaneously every 8 weeks may be considered.
8. Quantity limit of 0.8 mL (1 injection) per 28 days.
9. All recertification requests (initial and subsequent) will require documentation of the frequency and severity of attacks experienced and the frequency of administration of Dawnzera to monitor for appropriate use.
10. Initial authorization will be provided for 9 months.
    a. If 0 attacks have occurred during the prior 6 months while on the medication, a trial with an extended dosing interval of 80mg every 8 weeks will be required.
    b. If documentation is provided that the patient is not attack free (has experienced at least 1 attack), but has had a decrease in severity, duration and/or frequency of attacks while on the medication compared to baseline, a dosing frequency of 80mg every 4 weeks can be continued.
    c. If documentation is provided that the patient has not experienced a decrease in severity, duration and/or frequency of attacks while on the medication compared to baseline (no benefit from the medication), further treatment will not be authorized.
11. Subsequent recertification requests will be for 6 months at a time and will be reviewed using the same criteria as above:
    a. If 0 attacks have occurred during the prior 6 months while on the medication, a trial with an extended dosing interval of 80mg every 8 weeks will be required.
    b. If documentation is provided that the patient is not attack free (has experienced at least 1 attack), but has had a decrease in severity, duration and/or frequency of attacks while on the medication compared to baseline, a dosing frequency of 80mg every 4 weeks can be continued.
    c. If documentation is provided that the patient has not experienced a decrease in severity, duration and/or frequency of attacks while on the medication compared to baseline (no benefit from the medication), further treatment will not be authorized.

Haegarda (C1 esterase inhibitor [Human]) - Rx

1. Must have a diagnosis of hereditary angioedema (progress notes required)
2. Must be used as a prophylaxis – not for acute treatment
3. Haegarda will be allowed for short-term prophylaxis if requested prior to medical, surgical, or dental procedure. Approval will be for one month only.
4. For long term prophylaxis, the patient must meet the following:
    a. History of at least one laryngeal attack or at least two severe HAE attacks (i.e., debilitating

cutaneous or gastrointestinal episodes) per month that resulted in loss of work/school productivity or ER/unscheduled doctor visits **OR** disability for > 5 days per month due to HAE
5. Safety and efficacy in children under the age of 6 has not been established and therefore will not be covered
6. Haegarda can be self-administered after training under the guidance of a healthcare professional and therefore will be covered under the **pharmacy benefit.**
7. Standard dosage is 60 International Units (IU) per kg body weight by subcutaneous injection twice weekly.
   a. Quantity limit of 16 vials per 28 days (defined as the combined total amount of 2000 unit vials **AND** 3000-unit vials)
   b. Requests will require documentation of patient's weight to verify requested dosing is in accordance with the FDA approved dosing.
   c. Requests for dosing every three days will require documentation of a previous trial of twice weekly dosing that did not lead to a decrease in the severity, duration and/or frequency of attacks.
8. Authorization will be for 6 months at a time.
   a. Recertification will require documentation of decrease in the severity, duration, and/or frequency of attacks. Documentation including frequency of administration will also be required at time of recertification to monitor for appropriate use

Orladeyo (berotralstat) - Rx

1. Must have a diagnosis of hereditary angioedema (progress notes required)
2. Must be used as a prophylaxis – not for acute treatment
3. For long term prophylaxis, the patient must meet the following:
   a. History of at least one laryngeal attack or at least two severe HAE attacks (i.e., debilitating cutaneous or gastrointestinal episodes) per month that resulted in loss of work/school productivity or ER/unscheduled doctor visits **OR** disability for > 5 days per month due to HAE
4. Safety and efficacy in children under the age of 2 has not been established and therefore will not be covered
5. Orladeyo is an oral medication and will therefore be covered under the **pharmacy benefit**.
6. Standard dosage for ages 12 and older is 150 mg orally once daily. Dose reductions to 110 mg orally once daily are recommended for moderate-severe hepatic impairment and can be considered in patients with persistent GI reactions.
7. Oral pellets are indicated for pediatric patients age 2 to less than 12 years of age. Dosage is weight based and administered once daily.
8. Quantity limit of 28 capsules or 28 pellet packets per 28 days.
9. Authorization will be for 6 months at a time.
   a. Recertification will require documentation of decrease in the severity, duration, and/or frequency of attacks.

Takhzyro (lanadelumab) – Medical or Rx

1. Must have a diagnosis of hereditary angioedema (progress notes required)
2. Must be used as a prophylaxis – not for acute treatment
3. For long term prophylaxis, the patient must meet the following:
   a. History of at least one laryngeal attack or at least two severe HAE attacks (i.e., debilitating cutaneous or gastrointestinal episodes) per month that resulted in loss of work/school productivity or ER/unscheduled doctor visits **OR** disability for > 5 days per month due to HAE
4. The prescribing information has the following recommended dosages based on age:
   a. The recommended starting dosage in adult and pediatric patients 12 years of age and older is 300mg subcutaneously every two weeks.
   b. The recommended starting dosage in pediatric patients 6 to less than 12 years of age is 150

mg administered subcutaneously every two weeks.
   c. The recommended dosage in pediatric patients 2 to less than 6 years of age is 150 mg administered subcutaneously every four weeks.
5. The product is commercially available in the following dosage forms and has the following quantity limits:
   a. 150mg/mL pre-filled syringe, quantity limit of 1mL per 28 days
   b. 300mg/2mL pre-filled syringe, quantity limit of 2mL per 28 days
   c. 300mg/2mL single-dose vial, quantity limit of 2mL per 28 days
6. Takhzyro 150mg/mL syringe can be considered for coverage under the **pharmacy benefit** (caregiver administered) or **medical benefit** (healthcare provider administer).
   a. Requests for Takhzyro 150mg/mL syringe under the **medical benefit** (healthcare provider administered) for patients < 12 years of age will require documentation of an inability to self-inject or documentation of an inability of a caregiver to administer the medication.
   b. Coverage under the medical benefit for patients 12 years of age and older will be excluded
   c. Once a patient turns 12 years old, they will be required to obtain treatment under the pharmacy benefit, as the 300mg/2mL syringe/vial is not covered under the medical benefit (see below).
7. Takhzyro 300mg/2mL pre-filled syringe and single-dose vial can be self-administered after training under the guidance of a healthcare professional and therefore will be covered under the **pharmacy benefit only** for all lines of business.
8. All recertification requests (initial and subsequent) will require documentation of the frequency and severity of attacks experienced and the frequency of administration of Takhzyro to monitor for appropriate use.
9. Requests for Adult and Pediatric Patients 12 years of Age and Older:
   a. Initial approval will be for 9 months.
      i. If 0 attacks have occurred during the prior 6 months while on the medication, a trial with an extended dosing interval of 300mg every four weeks will be required based on package labeling which states that a dose of 300 mg every four weeks is also effective.
      ii. If documentation is provided that the patient is not attack free (has experienced at least 1 attack), but has had a decrease in severity, duration, and/or frequency of attacks while on the medication compared to baseline, a dosing frequency of 300mg every 2 weeks can be continued.
      iii. If documentation is provided that the patient has not experienced a decrease in severity, duration, and/or frequency of attacks while on the medication compared to baseline (no benefit from the medication), further treatment will not be authorized.
   b. Subsequent recertification requests will be for 6 months at a time and will be reviewed utilizing the same criteria above:
      i. If documentation has been submitted that 0 attacks have occurred during the 6 months prior, a trial with 300mg every four weeks will be required.
      ii. If documentation is provided that the patient is not attack free (has experienced at least 1 attack), but has had a decrease in severity, duration, and/or frequency of attacks while on the medication compared to baseline, a dosing frequency of 300mg every 2 weeks can be continued.
      iii. If documentation is provided that the patient has not experienced a decrease in severity, duration, and/or frequency of attacks while on the medication compared to baseline (no benefit from the medication), further treatment will not be authorized.
10. Requests for Pediatric Patients 6 to less than 12 years of age:
   a. Initial approval will be for 9 months.
      i. If 0 attacks have occurred during the prior 6 months while on the medication, a trial with an extended dosing interval of 150mg every four weeks will be required based on package labeling which states that a dose of 150 mg every four weeks may be considered if the

patient is well-controlled (e.g., attack free) for more than 6 months
   ii. If documentation is provided that the patient is not attack free (has experienced at least 1 attack), but has had a decrease in severity, duration, and/or frequency of attacks while on the medication compared to baseline, a dosing frequency of 150mg every 2 weeks can be continued.
   iii. If documentation is provided that the patient has not experienced a decrease in severity, duration, and/or frequency of attacks while on the medication compared to baseline (no benefit from the medication), further treatment will not be authorized.
b. Subsequent recertification requests will be for 6 months at a time and will be reviewed utilizing the same criteria above:
   i. If documentation has been submitted that 0 attacks have occurred during the 6 months prior, a trial with 150mg every four weeks will be required.
   ii. If documentation is provided that the patient is not attack free (has experienced at least 1 attack), but has had a decrease in severity, duration, and/or frequency of attacks while on the medication compared to baseline, a dosing frequency of 150mg every 2 weeks can be continued.
   iii. If documentation is provided that the patient has not experienced a decrease in severity, duration, and/or frequency of attacks while on the medication compared to baseline (no benefit from the medication), further treatment will not be authorized.

11. Requests for Pediatric Patients 2 to less than 6 years of age:
   a. Initial approval and subsequent recertification requests will be approved for 6 months at a time.
      i. Recertification requests will require documentation that the patient has had a decrease in severity, duration, and/or frequency of attacks while on the medication compared to baseline.
      ii. If documentation is provided that the patient has not experienced a decrease in severity, duration, and/or frequency of attacks while on the medication compared to baseline (no benefit from the medication), further treatment will not be authorized.

POLICY GUIDELINES:

1. Utilization Management are contract dependent and coverage criteria may be dependent on the contract renewal date. Additionally, coverage of drugs listed in this policy are contract dependent. Refer to specific contract/benefit language for exclusions.
2. Clinical documentation must be submitted for each request (initial and recertification) unless otherwise specified (e.g., provider attestation required). Supporting documentation includes, but is not limited to, progress notes documenting previous treatments/treatment history, diagnostic testing, laboratory test results, genetic testing/biomarker results, and imaging.
   - Continued approval at time of recertification will require documentation that the drug is providing ongoing benefit to the patient in terms of improvement or stability in disease state or condition.
3. This policy does not apply to Medicare Part D and D-SNP pharmacy benefits. The drugs in this policy may apply to all other lines of business including Medicare Advantage.
4. For members with Medicare Advantage, medications with a National Coverage Determination (NCD) and/or Local Coverage Determination (LCD) will be covered pursuant to the criteria outlined by the NCD and/or LCD. NCDs/LCDs for applicable medications can be found on the CMS website at https://www.cms.gov/medicare-coverage-database/search.aspx. Indications that have not been addressed by the applicable medication's LCD/NCD will be covered in accordance with criteria determined by the Health Plan (which may include review per the Health Plan's Off-Label Use of FDA Approved Drugs policy). Step therapy requirements may be imposed in addition to LCD/NCD requirements.

5. Not all contracts cover all Medical Infusible drugs. Refer to specific contract/benefit plan language for exclusions of Injectable Medications.
6. For contracts where Insurance Law § 4903(c-1), and Public Health Law § 4903(3-a) are applicable, if trial of preferred drug(s) is the only criterion that is not met for a given condition, and one of the following circumstances can be substantiated by the requesting provider, then trial of the preferred drug(s) will not be required.
   - The required prescription drug(s) is (are) contraindicated or will likely cause an adverse reaction or physical or mental harm to the member;
   - The required prescription drug is expected to be ineffective based on the known clinical history and conditions and concurrent drug regimen;
   - The required prescription drug(s) was (were) previously tried while under the current or a previous health plan, or another prescription drug or drugs in the same pharmacologic class or with the same mechanism of action was (were) previously tried and such prescription drug(s) was (were) discontinued due to lack of efficacy or effectiveness, diminished effect, or an adverse event;
   - The required prescription drug(s) is (are) not in the patient's best interest because it will likely cause a significant barrier to adherence to or compliance with the plan of care, will likely worsen a comorbid condition, or will likely decrease the ability to achieve or maintain reasonable functional ability in performing daily activities;
   - The individual is stable on the requested prescription drug. The medical profile of the individual (age, disease state, comorbidities), along with the rational for deeming stability as it relates to standard medical practice and evidence-based practice protocols for the disease state will be taken into consideration.
   - The above criteria are not applicable to requests for brand name medications that have an AB rated generic. We can require a trial of an AB-rated generic equivalent prior to providing coverage for the equivalent brand name prescription drug.
7. This policy is applicable to drugs that are included on a specific drug formulary. If a drug referenced in this policy is non-formulary, please reference the Coverage Exception Evaluation Policy for All Lines of Business Formularies policy for review guidelines.
8. A normal C4 particularly during an edema attack should make one question the diagnosis of HAE
9. Some medications may trigger or worsen angioedema events in patients with HAE and should be avoided including estrogen contraceptives, hormone replacement therapy, and ACE-Inhibitors.
10. Individuals' who are authorized for prophylactic Andembry, Cinryze, Dawnzera, Haegarda, Takhzyro or Orladeyo and have an acute attack while on therapy, should be re-evaluated to determine if there is an identifiable cause (adherence, misdiagnosis, etc.) for the breakthrough.
11. Individuals will only be authorized for **one acute** HAE medication at one time.
12. Individuals will only be authorized for **one prophylactic** HAE medication at one time.
13. The above quantity limits have been established in order to be sufficient to cover a patient in the event of an attack. Due to lack of evidence for more frequent administration, requests for quantities in excess of the established limits will not be approved. In the event, a patient is completely out of medication, a one-time override for early refill may be considered. One-time overrides will be approved after the submission of documentation (via provider progress notes, hospital progress notes, etc.) clarifying the patient's exacerbation details including date of exacerbation, date of medication administration, dose administered, as well as response.
14. All requests will be reviewed to ensure they are being used for an appropriate indication and may be subject to an off-label review in accordance with our Off-Label Use of FDA Approved Drugs Policy (Pharmacy-32).
15. All utilization management requirements outlined in this policy are compliant with applicable New York State insurance laws and regulations. Policies will be reviewed and updated as necessary to ensure ongoing compliance with all state and federally mandated coverage requirements.

UPDATES:

Date:	Revision:
03/05/2026	Revised
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03/19	Revision
10/18	Revision
09/18	Revision
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08/18	Revision
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08/16	Revision
03/16	Revision

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12/14	Revision
05/14	Revision
05/13	Revision
02/13	Revision
02/12	Created

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