BlueCross BlueShield of Arizona
An Independent Licensee of the Blue Cross and Blue Shield Association

MEDICAL COVERAGE GUIDELINES
SECTION: DRUGS

ORIGINAL EFFECTIVE DATE: 09/17/13
LAST REVIEW DATE: 09/16/14
LAST CRITERIA REVISION DATE: 09/16/14
ARCHIVE DATE:

HEREDITARY ANGIOEDEMA MEDICATION THERAPY

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Medical Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.

The section identified as "Description" defines or describes a service, procedure, medical device or drug and is in no way intended as a statement of medical necessity and/or coverage.

The section identified as "Criteria" defines criteria to determine whether a service, procedure, medical device or drug is considered medically necessary or experimental or investigational.

State or federal mandates, e.g., FEP program, may dictate that any drug, device or biological product approved by the U.S. Food and Drug Administration (FDA) may not be considered experimental or investigational and thus the drug, device or biological product may be assessed only on the basis of medical necessity.

Medical Coverage Guidelines are subject to change as new information becomes available.

For purposes of this Medical Coverage Guideline, the terms "experimental" and "investigational" are considered to be interchangeable.

BLUE CROSS®, BLUE SHIELD® and the Cross and Shield Symbols are registered service marks of the Blue Cross and Blue Shield Association, an association of independent Blue Cross and Blue Shield Plans. All other trademarks and service marks contained in this guideline are the property of their respective owners, which are not affiliated with BCBSAZ.

Description:

Injectable medications used for routine prophylaxis against angioedema attacks in individuals with hereditary angioedema (HAE) include:

- Berinert® (C1 esterase inhibitor, human)
- Cinryze™ (C1 esterase inhibitor, human)
- Firazyr® (icatibant)
- Kalbitor® (ecallantide)
- Ruconest® (C1 esterase inhibitor, recombinant)

HEREDITARY ANGIOEDEMA MEDICATION THERAPY (cont.)

Criteria:

See Resources section for FDA-approved dosage.

- Berinert for treatment of acute abdominal, facial or laryngeal angioedema attacks in individuals 13 years of age or older with hereditary angioedema (HAE) is considered ***medically necessary***.

- Berinert for all other indications not previously listed or if above criteria not met is considered ***experimental or investigational*** based upon:

  1. Lack of final approval from the Food and Drug Administration, and
  2. Insufficient scientific evidence to permit conclusions concerning the effect on health outcomes, and
  3. Insufficient evidence to support improvement of the net health outcome, and
  4. Insufficient evidence to support improvement of the net health outcome as much as, or more than, established alternatives, and
  5. Insufficient evidence to support improvement outside the investigational setting.

- Cinryze for routine prophylaxis against angioedema attacks in individuals 13 years of age or older with hereditary angioedema (HAE) is considered ***medically necessary***.

- Cinryze for all other indications not previously listed or if above criteria not met is considered ***experimental or investigational*** based upon:

  1. Lack of final approval from the Food and Drug Administration, and
  2. Insufficient scientific evidence to permit conclusions concerning the effect on health outcomes, and
  3. Insufficient evidence to support improvement of the net health outcome, and
  4. Insufficient evidence to support improvement of the net health outcome as much as, or more than, established alternatives, and
  5. Insufficient evidence to support improvement outside the investigational setting.

- Firazyr for treatment of acute attacks of angioedema in individuals 18 years of age and older with hereditary angioedema (HAE) is considered ***medically necessary***.

- Firazyr for all other indications not previously listed or if above criteria not met is considered ***experimental or investigational*** based upon:

  1. Lack of final approval from the Food and Drug Administration, and
  2. Insufficient scientific evidence to permit conclusions concerning the effect on health outcomes, and
  3. Insufficient evidence to support improvement of the net health outcome, and
  4. Insufficient evidence to support improvement of the net health outcome as much as, or more than, established alternatives, and
  5. Insufficient evidence to support improvement outside the investigational setting.

HEREDITARY ANGIOEDEMA MEDICATION THERAPY (cont.)

Criteria: (cont.)

See Resources section for FDA-approved dosage.

- Kalbitor for treatment of acute attacks of angioedema in individuals 12 years of age and older with hereditary angioedema (HAE) is considered ***medically necessary***.

- Kalbitor for all other indications not previously listed or if above criteria not met is considered ***experimental or investigational*** based upon:

  1. Lack of final approval from the Food and Drug Administration, and
  2. Insufficient scientific evidence to permit conclusions concerning the effect on health outcomes, and
  3. Insufficient evidence to support improvement of the net health outcome, and
  4. Insufficient evidence to support improvement of the net health outcome as much as, or more than, established alternatives, and
  5. Insufficient evidence to support improvement outside the investigational setting.

- Ruconest for treatment of acute attacks in individuals 13 years of age or older with hereditary angioedema (HAE) is considered ***medically necessary***.

- Ruconest for all other indications not previously listed or if above criteria not met is considered ***experimental or investigational*** based upon:

  1. Lack of final approval from the Food and Drug Administration, and
  2. Insufficient scientific evidence to permit conclusions concerning the effect on health outcomes, and
  3. sufficient evidence to support improvement of the net health outcome, and
  4. Insufficient evidence to support improvement of the net health outcome as much as, or more than, established alternatives, and
  5. Insufficient evidence to support improvement outside the investigational setting.

HEREDITARY ANGIOEDEMA MEDICATION THERAPY (cont.)

Resources:

FDA Product Approval Information for Cinryze:

- FDA-approved indication: Routine prophylaxis against angioedema attacks in individuals 13 years of age or older with hereditary angioedema (HAE).

FDA Product Approval Information for Berinert:

- FDA approved indication: Treatment of acute abdominal, facial or laryngeal attacks of hereditary angioedema (HAE) in individuals 13 years of age or older.

FDA Product Approval Information for Kalbitor:

- FDA approved indication: Treatment of acute attacks of hereditary angioedema (HAE) in individuals 12 years of age and older.

FDA Product Approval Information for Firazyr:

- FDA approved indication: Treatment of acute attacks of hereditary angioedema (HAE) in individuals 18 years of age and older.

FDA Product Approval Information for Ruconest:

- FDA-approved indication: Treatment of acute attacks in individuals 13 years of age or older with hereditary angioedema (HAE). Effectiveness has not been established in HAE patients with laryngeal attacks.