Medical and Behavioral Health Policy Activity

Policies Effective: October 5, 2020 Notification Posted: August 3, 2020

Policies Developed

- **Expanded Gastrointestinal Biomarker Panels, VI-59**
  Expanded gastrointestinal biomarker panels are considered **EXPERIMENTAL/INVESTIGATIVE** for all indications, including but not limited to evaluation of intestinal dysbiosis, irritable bowel syndrome, malabsorption, or small intestinal overgrowth of bacteria, and nutrition status due to the lack of clinical evidence demonstrating an impact on improved health outcomes.

- **Intravenous Iron Replacement Therapy, II-243**
  Note:
  - **This policy addresses only ferumoxytol (Feraheme®), ferric carboxymaltose (Injectafer®), and ferric derisomaltose (Monoferric®) intravenous iron therapies.**
  - **This policy does NOT address iron replacement therapy for use in patients with chronic kidney disease (CKD) on dialysis.**

  I. Initial Review for ferumoxytol (Feraheme®), ferric carboxymaltose (Injectafer®), ferric derisomaltose (Monoferric®)

  Use of ferumoxytol, ferric carboxymaltose, or ferric derisomaltose may be considered **MEDICALLY NECESSARY AND APPROPRIATE** when **ALL** of the following criteria are met:
  - Age 18 years or older; **AND**
  - Diagnosis of ONE of the following:
    - Iron deficiency anemia (IDA) without chronic kidney disease (CKD), as indicated by ONE of the following:
      - Serum ferritin < 30 ng/mL; or
      - Transferrin saturation (TSAT) < 20%; or
      - Absence of stainable iron in bone marrow;

      OR
    - Iron deficiency anemia (IDA) with chronic kidney disease (CKD) in patients not requiring dialysis, as indicated by ONE of the following:
      - Serum ferritin < 100 ng/mL; or
      - Transferrin saturation (TSAT) < 30%;

    AND
  - ONE of the following:
    - Inadequate response to full course of treatment (at least 3 to 6 months) of oral iron; or
    - Anatomic or physiologic condition that interferes with oral iron absorption; or
    - Documented intolerance, FDA labeled contraindication, or hypersensitivity to oral iron;

    AND
  - ONE of the following:
    - Inadequate response to BOTH iron dextran (Infed®) and iron sucrose (Venofer®); or
    - Documented intolerance, FDA labeled contraindication, or hypersensitivity to BOTH iron dextran (Infed®) and iron sucrose (Venofer®);

    AND
  - No FDA labeled contraindications to the requested agent (see table 1 below); **AND**
  - Requested dose is within the FDA labeled dose for the indication (see table 2 below); **AND**
  - For commercial health plan members only, step therapy supplement criteria may apply for select conditions (see policy II-242: Step Therapy Supplement).

II. Renewal Review for ferumoxytol (Feraheme®), ferric carboxymaltose (Injectafer®), ferric derisomaltose (Monoferric®)

Use of ferumoxytol, ferric carboxymaltose, or ferric derisomaltose may be considered **MEDICALLY NECESSARY AND APPROPRIATE** for retreatment in adult patients when **ALL** of the following criteria are met:

- Previously approved for the requested agent through the initial review process; **AND**
- Demonstrated positive clinical response to the requested agent (e.g., increased hemoglobin level); **AND**
- Recent laboratory results (within the past 4 weeks) since last administration of the requested agent demonstrating a need for additional therapy; **AND**
- No FDA labeled contraindications to the requested agent (see table 1 below); **AND**
- Requested dose is within the FDA labeled dose for the indication (see table 2 below).

III. Experimental/Investigative Uses

All other uses of ferumoxytol (Feraheme®) for iron deficiency anemia in patients not requiring dialysis are considered **EXPERIMENTAL/INVESTIGATIVE** due to the lack of evidence demonstrating an impact on improved health outcomes.

All other uses of ferric carboxymaltose (Injectafer®) or ferric derisomaltose (Monoferric®) are considered **EXPERIMENTAL/INVESTIGATIVE** due to the lack of evidence demonstrating an impact on improved health outcomes.

Table 1. FDA Labeled Contraindications

Agent	FDA Labeled Contraindications
Ferumoxytol (Feraheme®)	• Known hypersensitivity to Feraheme® or any of its components. • History of allergic reaction to any intravenous iron product.
Ferric carboxymaltose (Injectafer®)	• Hypersensitivity to Injectafer® or any of its inactive components.
Ferric derisomaltose (Monoferric®)	• Serious hypersensitivity to Monoferric® or any of its components

Table 2. Dosing

NOTE: See documentation submission requirements below if the requested dose is higher or more frequent than the dosing criteria provided in this table.

Agent	Dosing
Ferumoxytol (Feraheme®)	Initial 510 mg dose in intravenous infusion followed by a second 510 mg dose 3 to 8 days later.
Ferric carboxymaltose (Injectafer®)	For patients weighing 50 kg (110 lb) or more: • Two doses separated by at least 7 days. • Each dose of 750 mg for a total cumulative dose of 1500 mg of iron per course. For patients weighing less than 50 kg (110 lb): • Two doses separated by at least 7 days • Each dose as 15 mg/kg body weight.

	Treatment may be repeated if iron deficiency anemia reoccurs
Ferric derisomaltose (Monoferric®)	For patients weighing 50 kg or more: • Administer 1,000 mg of drug as an intravenous infusion. For patients weighing less than 50 kg: • Administer drug as 20 mg/kg actual body weight as an intravenous infusion. Repeat treatment if iron deficiency anemia reoccurs

Documentation Submission:
Documentation supporting the medical necessity criteria described in the policy must be included in the prior authorization, when prior authorization is required. In addition, the following documentation must also be submitted:

Initial Review
1. Clinical notes describing the diagnosis and clinical features of the diagnosis.
2. Laboratory values demonstrating treatment failure of oral or intravenous therapy after at least 3 weeks of therapy.
3. Laboratory values should be obtained within 1 to 3 weeks following the last dose of intravenous iron in a treatment course.
4. The dose being requested and patient's weight if requested agent includes weight-based dosing. If the requested dose is higher or more frequent than the dosing guidelines provided in the table above, a clear explanation for the medical necessity of the requested dose MUST be submitted, including prior dosing (strength and frequency) associated with inadequate response.
5. For commercial health plan members only, when step therapy requirements apply for the requested indication, documentation for one or more of the step therapy supplement criteria MUST be provided (see policy II-242).

Renewal Review
1. Documentation of prior approval for the requested agent through the initial review process.
2. Documentation supporting the positive clinical response (e.g., increased hemoglobin level).
3. Laboratory results indicating need for further intravenous iron therapy.
4. The dose being requested, including the patient's weight. If the requested dose is higher or more frequent than the dosing guidelines provided in the table above, a clear explanation for the medical necessity of the requested dose MUST be submitted, including prior dosing (strength and frequency) associated with inadequate response.
5. For commercial health plan members only, when step therapy requirements apply for the requested indication, documentation for one or more of the step therapy supplement criteria MUST be provided (see policy II-242).

- **Implantable Hypoglossal Nerve Stimulation for the Treatment of Obstructive Sleep Apnea, IV-80**
NOTE: For other treatments of obstructive sleep apnea, please see medical policy IV-07, *Treatment of Obstructive Sleep Apnea and Snoring in Adults*.

I. Hypoglossal nerve stimulation may be considered **MEDICALLY NECESSARY AND APPROPRIATE** in adults with obstructive sleep apnea when **ALL** of the following criteria are met:
- Age ≥ 22 years; **AND**
- Body mass index (BMI) ≤ 32 kg/m^2; **AND**
- Apnea/hypopnea index (AHI), respiratory disturbance index (RDI), or respiratory event index (REI) ≥ 15 with less than 25% central apneas; **AND**
- Inability to use PAP (greater than 5 nights per week of usage; usage defined as greater than 4 hours of use

per night), including documentation that the patient was intolerant of PAP for a minimum of 12 weeks, despite multiple models of facial masks and nasal pillows, and consultation with a sleep specialist; **AND**

- Absence of the following:
  - Complete concentric collapse at the soft palate level;
  - Severe or restricted obstructive pulmonary disease;
  - Neuromuscular disease affecting the respiratory tract;
  - Severe valvular heart disease;
  - Pregnancy or planned pregnancy;
  - Any other anatomical findings that would compromise performance of the device (e.g., tonsil size 3 or 4 per tonsillar hypertrophy grading scale).

II. Hypoglossal nerve stimulation may be considered **MEDICALLY NECESSARY AND APPROPRIATE** in adolescents or young adults with Down syndrome and obstructive sleep apnea syndrome (OSA) when **ALL** of the following criteria are met:

- Age 10 to 21 years; **AND**
- Body mass index ≤ 95th percentile for age; **AND**
- AHI >10 and <50 with less than 25% central apneas after prior adenotonsillectomy; **AND**
- Have either tracheotomy or ineffectively treated with CPAP due to noncompliance, discomfort, undesirable side effects, persistent symptoms despite compliance use, or refusal to use the device; **AND**
- Non-concentric retropalatal obstruction on drug-induced sleep endoscopy.

III. All other uses of hypoglossal nerve stimulation are considered **EXPERIMENTAL/INVESTIGATIVE** due to the lack of clinical evidence demonstrating an impact on improved health outcomes.

Documentation Submission:

Documentation supporting the medical necessity criteria described in the policy must be included in the prior authorization, when prior authorization is required. In addition, the following documentation must also be submitted:

1. Sleep study confirming diagnosis of sleep apnea must show moderate to severe OSA, performed within the previous year;
2. A summary of all conservative OSA treatments attempted, including length of trial and results;
3. Results of drug-induced sleep endoscopy procedure.

- **Site of Service for Selected Specialty Medical Drugs, XI-06**

NOTE:

- **This policy applies to commercial health plan members only.**
- **See table below for medical drugs included in the site of service program.**
- **Medical necessity of the drug may be separately reviewed against the appropriate criteria.**
- **When policy criteria for use of a hospital outpatient facility are not met, a non-hospital outpatient setting (e.g., freestanding infusion center or home infusion) should be used.**

I. Use of a hospital outpatient facility for infusion or injection of a medical drug may be considered **MEDICALLY NECESSARY AND APPROPRIATE** when **ANY** of the following criteria are met:

- Age <18 years; OR
- Nearest in-network non-hospital outpatient facility with supervised infusion or injection capabilities is >25 miles from patient's home AND patient is not eligible for home infusion; OR
- First dose or <60 days from the first dose; OR
- Reinitiating therapy after not being on therapy for ≥6 months (Note: this does not include maintenance therapy); OR
- History of a severe adverse event with prior infusion or injection therapy (e.g. anaphylaxis, seizure, thromboembolism, myocardial infarction, renal failure); OR

- History of adverse events with prior infusion or injection therapy (e.g. hypersensitivity or allergic reactions), which have not been successfully managed through standard premedications or infusion rate adjustments; OR
- Comorbidity or medical condition that increases the risk of an adverse event, including but not limited to the following:
  - o Cardiopulmonary conditions; or
  - o Inability to safely tolerate intravenous volume loads, including unstable renal function; or
  - o Difficult or unstable vascular access;

  OR
- Physical or cognitive impairment such that infusion or injection in a non-hospital outpatient setting would present an unnecessary health risk; OR
- Concurrent treatment with medications that require a higher level of monitoring (e.g. intravenous cytotoxic chemotherapy, blood products).

II. Use of a hospital outpatient facility for infusion or injection of a medical drug when the criteria in section I are not met is considered **NOT MEDICALLY NECESSARY**.

Table 1. Specialty Medical Drugs Included in the Site of Service Program

Drug(s)	Policy #
Abatacept (Orencia®)	II-161
Agalsidase Beta (Fabrazyme®)	II-26
Alglucosidase Alfa (Lumizyme®)	II-186
Alpha-1 Proteinase Inhibitors • Alpha-1 Antitrypsin (Aralast NP™) • Alpha-1 Antitrypsin (Glassia®) • Alpha-1 Antitrypsin (Prolastin-C®) • Alpha-1 Antitrypsin (Zemaira®)	II-206
Belimumab (Benlysta®)	II-152
Benralizumab (Fasenra®)	II-203
Burosumab (Crysvita®)	II-212
Certolizumab Pegol (Cimzia®)	II-179
Eculizumab (Soliris®)	II-196
Edaravone (Radicava®)	II-178
Elosulfase alfa (Vimizim®)	II-218
Galsufase (Naglazyme®)	II-217
Golimumab (Simponi Aria®)	II-180
Idursulfase (Elaprase®)	II-215
Immunoglobulin Therapy (e.g., Hizentra®, Gamunex®-C, Gammaked™, Gammagard Liquid®, Cuvitru™, HyQvia)	II-51
Infliximab (Remicade®, Inflectra®, Renflexis®, Ixifi®)	II-97
Intravenous Enzyme Replacement Therapy for Gaucher Disease • Imiglucerase (Cerezyme®) • Taliglucerase Alfa (Elelvso®) • Velaglucerase Alfa (Vpriv®)	II-214
Laronidase (Aldurazyme®)	II-216
Mepolizumab (Nucala®)	II-201
Natalizumab (Tysabri®)	II-49
Ocrelizumab (Ocrevus®)	II-185
Omalizumab (Xolair®)	II-34
Patisiran (Onpattro™)	II-220

Pegloticase (Krystexxa®)	II-147
Pharmacologic Therapies for Hereditary Angioedema • C1 Esterase Inhibitor (Berinert®) • C1 Esterase Inhibitor (Cinryze®) • Ecallantide (Kalbitor®) • C1 Esterase Inhibitor (Ruconest®)	II-102
Reslizumab (Cinqair®)	II-202
Rituximab (Rituxan®)	II-47
Romiplostim (Nplate®)	II-211
Sebelipase Alfa (Kanuma®)	II-200
Tildrakizumab (Ilumya™)	II-222
Tocilizumab (Actemra™)	II-181
Ustekinumab (Stelara®)	II-168
Vedolizumab (Entyvio®)	II-182
Vestronidase Alfa (Mepsevii™)	II-219

Policies Revised

- **Site of Service for Selected Outpatient Procedures: Outpatient Hospital and Ambulatory Surgery Center, XI-03**

NOTE:

- **This policy applies to commercial health plan members and Minnesota Health Care Program subscribers to Families and Children and MinnesotaCare.**
- **See table below for outpatient procedures included in the ambulatory surgery center (ASC) site of service program.**

Outpatient Hospital Site of Service

I. When the criteria in Section II are not met, use of a hospital outpatient facility for an outpatient procedure is considered **NOT MEDICALLY NECESSARY** and a non-hospital outpatient setting (e.g., ambulatory surgery center, office-based surgical suite) should be used.

II. Use of a hospital outpatient facility for an outpatient procedure may be considered **MEDICALLY NECESSARY AND APPROPRIATE** when any of the following criteria are met:

- Age <18 years;
- Nearest in-network, non-hospital outpatient facility with procedural capabilities is >25 miles from patient's home;
- Planned length of stay >24 hours;
- Anesthesia risk
  - American Society of Anesthesiologists (ASA) Physical Status (PS) Classification IV or higher (see definition);
  - History of complications from anesthesia (e.g., malignant hyperthermia);
  - Alcohol dependence at risk for withdrawal syndrome;
  - Recent history of drug abuse (e.g., cocaine) (<3 months);
  - Prolonged surgery (>3 hours);
  - Known or suspected difficult airway;
- Increased cardiovascular risk, including but not limited to:
  - Uncompensated chronic heart failure (NYHA class III or IV) (see definition);
  - Recent history of myocardial infarction (MI) (<6 months);
  - Poorly controlled, resistant hypertension;
  - Recent history of cerebrovascular accident or transient ischemic attack (<3 months);
  - Increased risk for cardiac ischemia (cardiac or vascular stent placed <1 year or angioplasty <90 days);

- Cardiac arrhythmia that increases periprocedural or anesthesia risk;
- Moderate or severe valvular heart disease;
- Implantable cardioverter-defibrillator (ICD);
- Mechanical cardiovascular support (e.g., left ventricular assist device [LVAD] or total artificial heart);

- Increased pulmonary risk, including but not limited to:
  - Moderate to severe chronic obstructive pulmonary disease (COPD) (FEV1 <50% or 2 or more exacerbations in the past year);
  - Moderate or severe persistent asthms (FEV1 <80% despite treatment);
  - Moderate to severe obstructive sleep apnea (OSA) (AHI or RDI ≥15);
  - Dependent on a ventilator;
  - Dependent on continuous supplemental oxygen;
- Increased liver risk, including but not limited to:
  - Advanced liver disease (MELD Score >8);
- Increased renal risk, including but not limited to:
  - End stage renal disease on dialysis;
- Increased bleeding risk, including but not limited to:
  - Bleeding disorder requiring replacement factor, blood products, DDAVP/desmopressin, or special infusion product;
  - Anticipated need for transfusion(s);
- Other
  - Morbid obesity (BMI ≥40);
  - Brittle diabetes or HbA1C ≥ 8.5%;
  - Pregnancy;
  - Cannot transfer independently;
  - Known or suspected foreign body in the target organ or tissue;
  - Significant cognitive impairment (e.g., unable to participate in pre-procedure planning and/or understand discharge instructions).

Inpatient Hospital Site of Service

III. Use of an inpatient hospital facility solely for a procedure noted in the table below is considered **NOT MEDICALLY NECESSARY**.

Procedure Codes
See table below.

Table. Outpatient Procedures Included in the Site of Service Program

CPT Codes
Ear, Nose, Throat (ENT) Procedures
21320, 30140, 30520, 69436, 69631
Gynecologic Procedures
57522, 58353, 58558, 58563, 58565
Hernia Procedures
49505, 49585, 49650, 49651, 49652, 49654

Orthopedic Arthroscopy & Foot Procedures
28285, 28289, 28291, 28292, 28296, 28297, 28298, 28299, 29805, 29806, 29807, 29819, 29820, 29821, 29822, 29823, 29824, 29825, 29826, 29827, 29828, 29830, 29834, 29835, 29836, 29837, 29838, 29840, 29844, 29845, 29846, 29847, 29848, 29860, 29861, 29862, 29863, 29870, 29873, 29874, 29875, 29876, 29877, 29879, 29880, 29881, 29882, 29883, 29884, 29885, 29886, 29887, 29888, 29889, 29891, 29892, 29893, 29894, 29895, 29897, 29898, 29899, 29914, 29915, 29916
Upper & Lower Gastrointestinal Endoscopy
43235, 43239, 43249, 45378, 45380, 45384, 45385

- **Treatment of Obstructive Sleep Apnea and Snoring in Adults, IV-07**
  Note: For hypoglossal nerve stimulation to treat obstructive sleep apnea, please see medical policy IV-80, Hypoglossal Nerve Stimulation for the Treatment of Obstructive Sleep Apnea.

I. Medical Management

- **Intraoral Appliances**
  - Intraoral appliances (e.g., mandibular advancing/positioning devices or tongue-retaining devices) may be considered **MEDICALLY NECESSARY AND APPROPRIATE** when ALL of the following criteria are met:
    1. Patient has been diagnosed with OSA defined by:
       - An AHI or RDI of 15 or greater events per hors; **OR**
       - An AHI or RDI between 5 and 14 events per hour with any of the following associated symptoms:
         1. Excessive daytime sleepiness
         2. Documented hypertension
         3. Ischemic heart disease
         4. History of stroke; **AND**
    2. Central sleep apnea has been ruled out, as documented by a sleep study; **AND**
    3. There is absence of temporomandibular dysfunction, periodontal disease, or gross dental decay; **AND**
    4. PAP therapy has not been effective despite a documented trial of at least one month; **AND**
    5. The device is prescribed after a face-to-face clinical evaluation, and diagnosis of OSA has been established by a physician (MD or DO) who is either a diplomate of the American Board of Medical Specialties; **AND**
    6. The device is custom made by a qualified dentist, referred by one of the above specialties.
  - Prefabricated oral devices are considered **NOT MEDICALLY NECESSARY.**
- **Continuous Positive Airway Pressure (CPAP)**
  - Continuous positive airway pressure (CPAP) may be considered **MEDICALLY NECESSARY AND APPROPRIATE** in patients with confirmed OSA with:
    1. An AHI or RDI of 15 events per hour or greater; **OR**
    2. An AHI or RDI between 5 and 14 events per hour with any of the following associated symptoms:
       - Excessive daytime sleepiness
       - Documented hypertension
       - Ischemic heart disease
       - History of stroke
- **Bi-level Positive Airway Pressure (BiPAP)**
  - BiPAP may be considered **MEDICALLY NECESSARY AND APPROPRIATE** in patients who:
    1. Meet the criteria for CPAP; **AND**

2. Have failed a prior trial of CPAP; **OR**
3. For whom BiPAP is found to be more effective than CPAP in the sleep laboratory.

- **Auto-Adjusting PAP (APAP)**
  - APAP may be considered **MEDICALLY NECESSARY AND APPROPRIATE** in patients who:
    1. Meet the criteria for CPAP above; **AND**
    2. Have no evidence by history or physical examination of the following conditions:
       - Central sleep apnea
       - Congestive heart failure
       - Chronic pulmonary disease such as chronic obstructive pulmonary disease
       - Pulmonary hypertension
       - Obesity hypoventilation syndrome or other condition which may cause nocturnal arterial oxyhemoglobin desaturation

II. Surgical Management

- **Uvulopalatopharyngoplasty (UPPP)**
  - UPPP may be considered **MEDICALLY NECESSARY AND APPROPRIATE** when all the following criteria are met:
    - Presence of significant, unexplained cor pulmonale or cardiac arrhythmia resulting from documented OSA; **OR**
    - An AHI or RDI of 15 events per hour or greater; **AND**
      - BMI less than 40; AND
      - A trial of oral appliance therapy has failed or the patient is not a candidate for an oral appliance; AND
      - Patient has not responded to or does not tolerate CPAP, BiPAP, or APAP following a minimum of 4 hours per night for three (3) months of PAP usage; **OR**
    - An AHI or RDI between 5 and 14 and all of the following:
      - Documented hypertension, ischemic heart disease, or history of stroke; AND
      - BMI less than 40; AND
      - A trial of oral appliance therapy has failed or the patient is not a candidate for an oral appliance; AND
      - Patient has not responded to or does not tolerate CPAP, BiPAP, or APAP following a minimum of 4 hours per night for three (3) months of PAP usage.
- **Maxillofacial Procedures**
  - Maxillofacial surgical procedures, such as inferior sagittal mandibular osteotomy and genioglossal advancement with or without hyoid myotomy and suspension or mandibular-maxillary advancement (MMA) may be considered **MEDICALLY NECESSARY AND APPROPRIATE** when the following criteria are met:
    - The patient has reached skeletal maturity; **AND**
    - Presence of significant, unexplained cor pulmonale or cardiac arrhythmia resulting from documented OSA; **OR**
    - An AHI or RDI of 15 events per hour or greater; **AND**
      - Objective evidence of hypopharyngeal obstruction documented by either fiberoptic examination or cephalometric radiographs; AND
      - Patient has not responded to or does not tolerate CPAP, BiPAP, or APAP following a minimum of 4 hours per night for three (3) months of PAP usage; **OR**
    - An AHI or RDI between 5 and 14 and all of the following:
      - Documented hypertension, ischemic heart disease, or history of stroke; **AND**
      - Objective evidence of hypopharyngeal obstruction documented by either fiberoptic examination or cephalometric radiographs; **AND**

- Patient has not responded to or does not tolerate CPAP, BiPAP, or APAP following a minimum of 4 hours per night for three (3) months of PAP usage.

III. Treatment of Snoring

- Treatment of snoring is considered **NOT MEDICALLY NECESSARY AND APPROPRIATE** because simple snoring in the absence of documented obstructive sleep apnea is not considered a medical condition. Therefore, all procedures for the sole or adjunctive treatment of snoring are considered **NOT MEDICALLY NECESSARY AND APPROPRIATE**, including but not limited to:
  - Uvulopalatopharyngoplasty (UPPP)
  - Uvulectomy
  - Laser-assisted uvulopalatoplasty (LAUP)
  - Radiofrequency volumetric tissue reduction of the palatal tissues
  - Radiofrequency volumetric tissue reduction of the tongue, with or without radiofrequency reduction of the palatal tissues
  - Palatal stiffening procedures, including but not limited to, cautery-assisted palatal stiffening operation, and the implantation of palatal implants
  - Tongue base suspension (e.g.Encore™, AIRvance™)

IV. Investigative Indications

- The following treatments are considered **EXPERIMENTAL/INVESTIGATIVE** due to a lack of evidence demonstrating improved health outcomes:
  - UPPP for any condition other than obstructive sleep apnea or snoring
  - Expiratory Positive Airway Pressure (EPAP) including the Provent® device
  - Oral pressure therapy devices, including but not limited to the Winx™ system
  - Atrial pacing
  - Oral devices (e.g., Morning Repositioner, ProSomnus) purported to prevent temporomandibular joint (TMJ) disorders
  - Palate and mandible expansion devices, including but not limited to, the Daytime Nighttime Appliance (DNA Appliance, Biomodeling Solutions) and the mandibular Repositioning Nighttime Appliance (mRNA Appliance Biomodeling Solutions)
  - Positional sleep therapy devices (e.g., NightBalance)
  - Biomimetic oral appliance therapy (BOAT)
  - All other surgical procedures for the sole or adjunctive treatment of obstructive sleep apnea/upper airway resistance syndrome, including but not limited to:
    - Uvulectomy
    - Laser-assisted uvulopalatoplasty (LAUP)
    - Radiofrequency volumetric reduction of the palatal tissues
    - Radiofrequency volumetric tissue reduction of the tongue, with or without radiofrequency reduction of the palatal tissues
    - Palatal stiffening procedures including but not limited to, cautery-assisted palatal stiffening operation, and the implantation of palatal implants
    - Tongue base suspension (e.g.Encore™, AIRvance™)

Documentation Submission:

Documentation supporting the medical necessity criteria described in the policy must be included in the prior authorization, when prior authorization is required. In addition, the following documentation must also be submitted with prior authorization requests for UPPP:

- A summary of the most recent sleep study including AHI or RDI; AND
- Clinical notes from within the previous 60 days describing:

1. Comorbidities that may indicate medical necessity of UPPP if AHI or RDI equals 5 or more events per hour (i.e. cor pulmonale, cardiac arrhythmia) OR
2. If AHI or RDI is between 5 and 14 events per hour information must include:
    - BMI; AND
    - Comorbidities (i.e., hypertension, ischemic heart disease or stroke); AND
    - A description of all trials of an oral appliance, CPAP, BiPAP, APAP or other noninvasive treatments including the length and results of the trials.

- **Luspatercept, II-237**

I. Initial Review of Luspatercept (Reblozyl®) for Beta Thalassemia

Luspatercept may be considered **MEDICALLY NECESSARY AND APPROPRIATE** when **ALL** of the following criteria are met:

- Age 18 years or older; **AND**
- Diagnosis of beta thalassemia (including beta^{+} thalassemia, beta^{0} thalassemia, and hemoglobin E beta thalassemia); **AND**
- Absence of sickle beta thalassemia or alpha thalassemia; **AND**
- Required transfusion of 6-20 RBC units in the 24 weeks prior; **AND**
- No transfusion-free period for ≥35 days in the 24 weeks prior; **AND**
- Prescribed by or in consultation with a hematologist or other specialist with expertise in the diagnosis and management of beta thalassemia; **AND**
- No FDA labeled contraindications to luspatercept (see table 1 below); **AND**
- Dose is within the FDA labeled dose for the indication (see table 2 below).

II. Renewal Review of Luspatercept (Reblozyl®) for Beta Thalassemia

Luspatercept may be considered **MEDICALLY NECESSARY AND APPROPRIATE** when **ALL** of the following criteria are met:

- Previously approved for luspatercept through the initial review process; **AND**
- Demonstrated a minimum one-third reduction in RBC transfusions in response to luspatercept; **AND**
- Prescribed by or in consultation with a hematologist or other specialist with expertise in the diagnosis and management of beta thalassemia; **AND**
- No FDA labeled contraindications to luspatercept (see table 1 below); **AND**
- Dose is within the FDA labeled dose for the indication (see table 2 below).

III. Initial Review of Luspatercept (Reblozyl®) for Myelodysplastic Syndromes or Myelodysplastic/ Myeloproliferative Neoplasm

Luspatercept may be considered **MEDICALLY NECESSARY AND APPROPRIATE** when **ALL** of the following criteria are met:

- Age 18 years or older; **AND**
- Diagnosis of ONE of the following:
    - Myelodysplastic syndromes; or
    - Myelodysplastic/myeloproliferative neoplasm;

  AND
- Documented lower risk disease defined by one of the following:
    - Revised International Prognostic Scoring System (IPSS-R): very low, low, intermediate (Score 0 to ≤ 4.5); or
    - IPSS: low/intermediate-1 (Score 0 to 1); or
    - World Health Organization-Based Prognostic Scoring System (WPSS): very low, low, Intermediate (Score 0 to 2)

  AND

- ONE of the following:
  - Ring sideroblasts ≥ 15%; or
  - Ring sideroblasts ≥ 5% with an *SF3B1* mutation;

  AND
- **BOTH** of the following:
  - Hemoglobin <10 g/dL; and
  - Required transfusion of at least 2 units of packed red blood cells (pRBCs) in the prior 8 weeks;

  AND
- **ONE** of the following:
  - Patient is ineligible for erythropoiesis stimulating agent (ESA) therapy (e.g. serum erythropoietin >200 U/L); OR
  - Disease not responsive to prior treatment with (ESA) therapy; OR
  - Prior ESA therapy discontinued due to adverse event;

  AND
- Other causes of anemia (e.g., gastrointestinal bleeding, hemolysis, renal disease, nutritional deficiency, etc.) have been ruled out and/or addressed; **AND**
- Prescribed by or in consultation with a hematologist, oncologist, or other specialist with expertise in the diagnosis and management of myelodysplastic syndromes; **AND**
- No FDA labeled contraindications to luspatercept (see table 1 below); **AND**
- Dose is within the FDA labeled dose for the indication (see table 2 below).

IV. Renewal Review of Luspatercept (Reblozyl®) for Myelodysplastic Syndromes or Myelodysplastic/Myeloproliferative Neoplasm

Luspatercept may be considered **MEDICALLY NECESSARY AND APPROPRIATE** when **ALL** of the following criteria are met:

- Previously approved for luspatercept through the initial review process; **AND**
- Demonstrated transfusion independence for a minimum of 8 weeks since starting treatment with luspatercept; **AND**
- Prescribed by or in consultation with a hematologist, oncologist, or other specialist with expertise in the diagnosis and management of myelodysplastic syndromes; **AND**
- No FDA labeled contraindications to luspatercept (see table 1 below); **AND**
- Dose is within the FDA labeled dose for the indication (see table 2 below).

V. Experimental/Investigative Uses

All other uses of luspatercept, including but not limited to non-transfusion-dependent beta-thalassemia and treatment of patients not meeting the criteria above, are considered **EXPERIMENTAL/INVESTIGATIVE** due to the lack of clinical evidence demonstrating an impact on improved health outcomes.

Table 1. FDA Labeled Contraindications

Agent	FDA Labeled Contraindications
Luspatercept (Reblozyl®)	None

Table 2. Dosing
NOTE: See documentation submission requirements below if the requested dose is higher or more frequent than the dosing criteria provided in this table.

FDA Labeled Indications	Dosing
Anemia in adult patients with beta thalassemia who require regular RBC transfusions	1mg/kg once every 3 weeks by subcutaneous injection administered by a healthcare professional, with maximum dose of 1.25 mg/kg every 3 weeks. Discontinue treatment if no reduction in RBC transfusion burden after 3 consecutive doses (9 weeks) at 1.25 mg/kg.
Anemia failing an erythropoiesis stimulating agent and requiring 2 or more RBC units over 8 weeks in adult patients with very low- to intermediate-risk myelodysplastic syndromes with ring sideroblasts (MDS-RS) or with myelodysplastic/myeloproliferative neoplasm with ring sideroblasts and thrombocytosis (MDS/MPN-RS-T).	1 mg/kg once every 3 weeks by subcutaneous injection administered by a healthcare professional, with maximum dose of 1.75 mg/kg every 3 weeks. Discontinue treatment if no reduction in RBC transfusion burden after 3 consecutive doses (9 weeks) at 1.75 mg/kg.

Documentation Submission:
Documentation supporting the medical necessity criteria described in the policy must be included in the prior authorization, when prior authorization is required. In addition, the following documentation must also be submitted:

Initial Review
1. Clinical notes describing the diagnosis and clinical features of the diagnosis, including the frequency of RBC transfusions.
2. The dose being requested. If the requested dose is higher or more frequent than the dosing guidelines provided in the table above, a clear explanation for the medical necessity of the requested dose must be submitted, including prior dosing (strength and frequency) associated with inadequate response.

Renewal Review
1. Documentation of prior approval for luspatercept through the initial review process.
2. Documentation demonstrating positive clinical response:
   - For anemia in patients with beta thalassemia: ≥ 33% reduction from baseline in RBC transfusion frequency or
   - For anemia in patients with myelodysplastic syndromes or myelodysplastic/myeloproliferative neoplasms: transfusion independence for a minimum of 8 weeks since starting treatment with luspatercept;
3. The dose being requested. If the requested dose is higher or more frequent than the dosing guidelines provided in the table above, a clear explanation for the medical necessity of the requested dose must be submitted, including prior dosing (strength and frequency) associated with inadequate response.

- **Nusinersen, II-171**

I. Initial Review for Nusinersen (Spinraza®)

Nusinersen may be considered **MEDICALLY NECESSARY AND APPROPRIATE** when **ALL** of the following criteria are met:

- Diagnosis of spinal muscular atrophy (SMA); **AND**
- Genetic testing confirms diagnosis of classic (5q) SMA, including loss of, or defect in, the *SMN1* gene (NOTE: laboratory documentation must be provided); **AND**
- ONE of the following:
  - Genetic testing confirms no more than 2 copies of the *SMN2* gene (NOTE: laboratory documentation must be provided); OR
  - SMA type I, type II, or type III with onset of SMA-associated symptoms before 21 months of age;

  AND
- Patient does not have advanced SMA (e.g. complete paralysis of limbs, permanent ventilator dependence [defined as invasive ventilation (tracheostomy), or respiratory assistance for 16 or more hours per day (including noninvasive ventilatory support) continuously for 14 or more days in absence of an acute reversible illness, excluding perioperative ventilation]); **AND**
- No serious concomitant illness (e.g. severe liver or kidney disease, symptomatic cardiomyopathy, active viral infection); **AND**
- Nusinersen will not be used in combination with onasemnogene abeparvovec (Zolgensma®); **AND**
- For patients previously treated with onasemnogene abeparvovec (Zolgensma®), has not achieved the expected benefit from gene therapy, as demonstrated by the inability to achieve and sustain a CHOP INTEND score of more than 40 points within 3 months of gene therapy; **AND**
- Nusinersen is prescribed by or in consultation with a neurologist; **AND**
- No FDA labeled contraindications to therapy (see table 1 below); **AND**
- The dose is within the FDA labeled dose (see table 2 below).

II. Renewal Review for Nusinersen (Spinraza®)

Nusinersen may be considered **MEDICALLY NECESSARY AND APPROPRIATE** when **ALL** of the following criteria are met:

- Previously approved for nusinersen through the initial review process; **AND**
- Demonstrated positive clinical response to nusinersen therapy (e.g., improvement in motor function or stabilization of motor function loss); **AND**
- Patient does not have advanced SMA (e.g. complete paralysis of limbs, permanent ventilator dependence [defined as invasive ventilation (tracheostomy), or respiratory assistance for 16 or more hours per day (including noninvasive ventilatory support) continuously for 14 or more days in absence of an acute reversible illness, excluding perioperative ventilation]); **AND**
- No serious concomitant illness (e.g. severe liver or kidney disease, symptomatic cardiomyopathy, active viral infection); **AND**
- Nusinersen will not be used in combination with onasemnogene abeparvovec (Zolgensma®); **AND**
- For patients previously treated with onasemnogene abeparvovec (Zolgensma®), has not achieved the expected benefit from gene therapy, as demonstrated by the inability to achieve and sustain a CHOP INTEND score of more than 40 points within 3 months of gene therapy; **AND**
- Nusinersen is prescribed by or in consultation with a neurologist; **AND**
- No FDA labeled contraindications to therapy (see table 1 below); **AND**
- The dose is within the FDA labeled dose (see table 2 below).

III. Experimental/Investigative Uses

All other uses of nusinersen are considered **EXPERIMENTAL/INVESTIGATIVE**, including but not limited to treatment of non-5q SMA or any other types of SMA not meeting the criteria above, due to the lack of clinical evidence demonstrating an impact on improved health outcomes.

Table 1. FDA Labeled Contraindications

Agent	FDA Labeled Contraindications
Nusinersen	None

Table 2. Dosing

FDA Labeled Indication	Dosing
Spinal muscular atrophy (SMA)	12 mg (5 mL) per intrathecal administration Initiate treatment with 4 loading doses. The first 3 loading doses should be administered at 14-day intervals. The 4th loading dose should be administered 30 days after the 3rd dose. A maintenance dose should be administered once every 4 months thereafter.

Documentation Submission:

Documentation supporting the medical necessity criteria described in the policy must be included in the prior authorization. In addition, the following documentation must also be submitted:

Initial Review

1. Clinical notes describing the diagnosis and clinical features of the diagnosis.
2. Laboratory documentation confirming genetic diagnosis of SMA, including loss of, or defect in, the SMN1 gene.
3. The dose being requested. If the requested dose is higher or more frequent than the dosing guidelines provided in the table above, a clear explanation for the medical necessity of the requested dose MUST be submitted, including prior dosing (strength and frequency) associated with inadequate response.

Renewal Review

1. Documentation of prior approval for nusinersen through the initial review process.
2. Documentation supporting positive clinical response (e.g., improvement in motor function or stabilization of motor function loss).
3. The dose being requested. If the requested dose is higher or more frequent than the dosing guidelines provided in the table above, a clear explanation for the medical necessity of the requested dose MUST be submitted, including prior dosing (strength and frequency) associated with inadequate response.

- **Extended Hours Skilled Nursing in the Home for Patients with Medically Complex Conditions, IX-01**

I. Extended Hours Skilled Nursing

Extended Hours Skilled Nursing in the home may be considered **MEDICALLY NECESSARY AND APPROPRIATE** when **ALL** of the following criteria are met:

- Member has a condition that requires the skills, expertise, judgement, and decision making of a registered nurse (RN) or licensed practical nurse (LPN) working under the supervision of an RN; **AND**
- A written plan of care has been completed, which includes **ALL** of the following requirements:
  - Clinical summary, including the expected course of the member's medical conditions;
  - Current functional level, current functional limitations;
  - Current medication doses, routes, and frequency of administration;
  - Current treatments, including the frequency of each treatment;
  - Vital signs, including the frequency of each vital sign;
  - Long term and short term goals of care based on individualized needs of the member;
  - Current disciplines providing care, including the hours per day for each discipline; (RN, LPN, physical therapist [PT], occupational therapist [OT], speech therapist [ST], home health aide [HHA] personal care assistant [PCA], certified medical assistant [CMA],]etc.);
  - Demonstration of the need for services supported by all pertinent diagnoses.

  AND
- A professional practitioner (e.g., MD, DO, Advanced Practice Registered Nurse [APRN] or Physician Assistant [PA]) working within the scope of their practice has approved the written plan of care; **AND**
- The requested services are appropriate for the treatment of the member's illnesses or injuries; **AND**
- The member's treatment plan requires changes to the member's treatment at least daily, or the member requires invasive mechanical ventilation at least 6 hours daily; **AND**
- Documentation stating reasons the member's care needs cannot be met through intermittent skilled nursing visits; **AND**
- Documentation stating the specific reasons that the member's care needs cannot be met by a trained family caregiver; **Note:** Extended hours of home skilled nurse services provided to train the family caregiver(s) is covered for a period of up to 90 days; **AND**
- The services are not provided in an inpatient facility or skilled nursing facility.

II. Ongoing Authorization

Continued Extended Hours Skilled Nursing in the home may be considered **MEDICALLY NECESSARY AND APPROPRIATE** when **ALL** of the following are met:

- The member has a condition that requires the skills, expertise, judgement, and decision making of an RN or LPN working under the supervision of an RN; **AND**
- Home care records include **ALL** of the following:
  - Flowsheets that document the following **over the past 60 days**
    - Vital signs
    - Patient care treatments and rationales for changes to treatments including ventilator settings if applicable
    - Current symptoms and physical findings
    - When the home nurse is on duty, documentation of who specifically is providing care and for what hours and in what location(s)
    - When the home nurse is not on duty, documentation of who specifically is providing care and for what hours
  - Identification of specific barriers to the caregivers' ability to implement the plan of treatment with identification of specific strategies to overcome these barriers, implementation of these strategies, and ongoing assessment of the results of these strategies;

- Documentation that the ordered services were provided as prescribed in the written plan of care (described below);

AND

- Written plan of care updated at least each 60 days, which includes a clinical summary of member's current health status **over the past 60 days** with **ALL** of the following:
  - Expected course of the member's medical conditions ;
  - Functional level and functional limitations;
  - Medication doses, routes, and frequency of administration;
  - Treatments, including the type and frequency of each treatment;
  - Vital signs, including the frequency that each vital sign must be measured;
  - Long term and short term goals of care based on individualized needs of the member;
  - Hours per day / week for each discipline providing care (RN, LPN, PT, OT, ST, HHA, PCA, CMA, etc.);
  - Specific barriers to the member's caregivers' ability to implement the plan of care, the identification of specific strategies for this member's caregivers to overcome these barriers, and the assessment of the results of these strategies;
  - Demonstration of the need for the frequency and hours per day of all services supported by the submitted medical records;

AND

- A professional practitioner (e.g., MD, DO, Advanced Practice Registered Nurse [APRN]) or Physician Assistant [PA]) working within the scope of their practice has approved the written plan of care: **AND**
- The requested services are appropriate for the treatment of the member's illnesses or injuries; **AND**
- One or both of the following:
  - The member's treatment plan requires ongoing and daily assessment of the plan of care; OR
  - The member requires invasive mechanical ventilation at least 6 hours daily;

AND

- Documentation stating the specific reasons that the member's care needs cannot be met by a trained family caregiver;
  Note: Extended hours of home skilled nurse services provided to train the family caregiver(s) is covered for a period of up to 90 days. **AND**
- Documentation stating reasons the member's care needs cannot be met through Intermittent skilled nursing visits; **AND**
- The medical need for the hours per day of home RN/LPN services is supported in the submitted medical records, including specific documentation of the severity of the medical conditions, the intensity of the home nurse services provided, and the reason(s) that these services could not have been provided by a trained family caregiver; **AND**
- The services are not provided in an inpatient facility or skilled nursing facility.

III. Ineligible for Coverage as Extended Hours Skilled Nursing in the Home

- Care that can be provided by a trained family caregiver
- Caregiver is not available for training, or unable or unwilling to comply with the plan of care
- Care provided for the convenience of, or respite for, the family caregiver
- Care provided by the member's spouse, natural or adoptive child, parent, foster parent, brother, sister, grandparent or grandchild. This includes any person with an equivalent step or in-law relationship to the member
- Help with daily living activities, such as walking, grooming, bathing, dressing, getting in or out of bed, toileting, eating, or preparing foods
- Routine patient care such as changing dressings, periodic turning and positioning in bed, administering oral medication
- Care of a stable tracheostomy (including intermittent suctioning)

- Care of a stable nasogastric tube/gastrostomy/jejunostomy - including intermittent or continuous feedings
- Care of a stable colostomy/ileostomy
- Care of a stable indwelling bladder catheter (including emptying/changing containers and clamping tubing)
- Falls prevention
- Watching or protecting a member
- Care provided outside the home including but not limited to medical care in a clinic, outpatient facility, hospital, skilled nursing or intermediate care facility, licensed residential care facility, adult or child day care facility, or school, except as stated in the benefit chart.
- The member's care needs cannot be adequately and/or safely met in the home

Documentation Submission

Written documentation by the practitioner specifying the medical necessity, according to the criteria above, is required. Requested documentation may include, but is not limited to:

- A completed Form CMS-485 - Home Health Certification and plan of care;
- Current practitioner's order for the requested services;
- Daily home skilled nursing services log with the specific location and specific time of day;
  Example: 05/05/2020 7:00 AM – 8:15 AM home, 8:15 AM – 8:45 AM transport to Smith School, 8:45 AM – 3:15 PM Smith School, 3:15 PM – 3:45 PM transport to home, 3:45 PM – 5:30 PM home;
- All home care records for the past 60 days, and for all days with a significant medical event from the time of the previous request to the current request, which include **ALL** of the following:
  1. Current flowsheets that document vital signs, ventilator settings including the rationale for changes to the ventilator settings, and treatments including the rationale for changes to the treatments;
  2. Current symptoms and physical findings;
  3. Who specifically is providing cares and for what hours and in what location(s) when the extended hours nurse is on duty;
  4. Who specifically is providing cares and for what hours when the extended hours nurse is not on duty;
  5. The ongoing identification of specific barriers to the caregivers' ability to implement the plan of treatment, the identification of specific strategies to overcome these barriers, the implementation of these strategies, and the ongoing assessment of the results of these strategies.
- All professional practitioner (e.g., MD, DO, Advanced Practice Registered Nurse [APRN] or Physician Assistant [PA])) visit notes from the time of the previous request to the current request, with a current medication list;
- Emergency room provider notes from all emergency room visits that have occurred from the time of the previous request to the current request;
- Hospital history and physicals, hospital discharge summaries, and hospital progress notes from the final 7 days of all hospitalizations that have occurred from the time of the previous request to the current request.

- **Pharmacologic Therapies for Hereditary Angioedema, II-102**

NOTE:

- **C1 esterase inhibitor (Haegarda®), lanadelumab (Takhzyro™), and icatibant (Firazyr®) are self-administered agents; please refer to the applicable pharmacy benefit plans.**
- **When C1 esterase inhibitor (Berinert®, Ruconest®) will be self-administered, please refer to applicable pharmacy benefit plan.**

I. Initial Review for Berinert®, Ruconest®, or Kalbitor®

C1 esterase inhibitor (Berinert®, Ruconest®) or ecallantide (Kalbitor®) may be considered **MEDICALLY NECESSARY AND APPROPRIATE** when **ALL** of the following criteria are met:

- Diagnosis of hereditary angioedema (HAE), as evidenced by:
  - **BOTH** of the following for patients with HAE with C1 inhibitor deficiency/dysfunction (HAE type I or II):

1. C4 level below the lower limit of normal as defined by the laboratory performing the test; AND
2. ONE of the following:
   - C1 inhibitor antigenic level below the lower limit of normal as defined by the laboratory performing the test; or
   - C1 inhibitor functional level below the lower limit of normal as defined by the laboratory performing the test;

OR

- **ONE** of the following for patients with HAE with normal C1 inhibitor (previously HAE type III):
  1. Mutation in the coagulation factor XII gene associated with HAE; OR
  2. Family history or personal history of angioedema AND failure to respond to chronic, high-dose antihistamine therapy;

AND

- Used for treatment of acute HAE attacks; **AND**
- Not used in combination with other treatments for acute HAE attacks (e.g. Berinert®, Kalbitor®, Ruconest®); **AND**
- Medications known to cause angioedema (i.e., ACE-inhibitors, estrogens, angiotensin II receptor blockers) have been evaluated and discontinued when appropriate; **AND**
- Prescribed by or in consultation with an HAE specialist, such as a hematologist, allergist, or immunologist; **AND**
- No FDA labeled contraindications to therapy (see table 1 below); **AND**
- The dose is within the program quantity limit (see table 2 below).

II. Renewal Review for Berinert®, Ruconest®, or Kalbitor®

C1 esterase inhibitor (Berinert®, Ruconest®), or ecallantide (Kalbitor®) may be considered **MEDICALLY NECESSARY AND APPROPRIATE** when **ALL** of the following criteria are met:

- Previously approved for therapy through the initial review process; **AND**
- Used for treatment of acute HAE attacks; **AND**
- Patient continues to have acute HAE attacks; **AND**
- Not used in combination with other treatments for acute HAE attacks (e.g. Berinert®, Firazyr®, Kalbitor®, Ruconest®); **AND**
- Prescribed by or in consultation with an HAE specialist, such as a hematologist, allergist, or immunologist; **AND**
- No FDA labeled contraindications to therapy (see table 1 below); AND
- The dose is within the program quantity limit (see table 2 below).

III. Initial Review for Cinryze®

C1 esterase inhibitor (Cinryze®) may be considered **MEDICALLY NECESSARY AND APPROPRIATE** when **ALL** of the following criteria are met:

- Diagnosis of hereditary angioedema (HAE) as evidenced by:
  - BOTH of the following for patients with HAE with C1 inhibitor deficiency/dysfunction (HAE type I or II):
    1. C4 level below the lower limit of normal as defined by the laboratory performing the test; AND
    2. ONE of the following:
       - C1 inhibitor antigenic level below the lower limit of normal as defined by the laboratory performing the test; or
       - C1 inhibitor functional level below the lower limit of normal as defined by the laboratory performing the test;

    OR
  - ONE of the following for patients with HAE with normal C1 inhibitor (previously HAE type III):
    1. Mutation in the coagulation factor XII gene associated with HAE; OR
    2. Family history or personal history of angioedema AND failure to respond to chronic, high-dose antihistamine therapy;

    AND

- Medications known to cause angioedema (i.e., ACE-inhibitors, estrogens, angiotensin II receptor blockers) have been evaluated and discontinued when appropriate; **AND**
- Prescribed by or in consultation with an HAE specialist, such as a hematologist, allergist, or immunologist; **AND**
- No FDA labeled contraindications to therapy (see table 1 below); **AND**
- The dose is within the program quantity limit (see table 2 below).

IV. Renewal Review for Cinryze®

C1 esterase inhibitor (Cinryze®) may be considered **MEDICALLY NECESSARY AND APPROPRIATE** when **ALL** of the following criteria are met:

- Previously approved for therapy through the initial review process; AND
- ONE of the following:
  - Used for treatment of acute HAE attacks AND ALL of the following:
    1. Patient continues to have acute HAE attacks; AND
    2. Not used in combination with other treatments for acute HAE attacks (e.g. Berinert®, Firazyr®, Kalbitor®, Ruconest®); OR
  - Used for prophylaxis against HAE attacks AND ALL of the following:
    1. Patient has had a decrease in the frequency of acute attacks from baseline (prior to treatment); AND
    2. Not used in combination with other agents against HAE attacks (e.g., Haegarda®, Takhzyro™);

  AND
- Prescribed by or in consultation with an HAE specialist, such as a hematologist, allergist, or immunologist; AND
- No FDA labeled contraindications to therapy (see table 1 below); AND
- The dose is within the program quantity limit (see table 2 below).

V. Experimental/Investigative Uses

All other uses of C1 esterase inhibitor (Berinert®, Cinryze®, Ruconest®) or ecallantide (Kalbitor®), are considered **EXPERIMENTAL/INVESTIGATIVE** due to the lack of clinical evidence demonstrating an impact on improved health outcomes.

Table 1. FDA Labeled Contraindications

Agent	FDA Labeled Contraindications
C1 esterase inhibitor (Berinert®)	History of life-threatening immediate hypersensitivity reactions, including anaphylaxis, to C1 esterase inhibitor preparations
C1 esterase inhibitor (Cinryze®)	History of life-threatening immediate hypersensitivity reactions, including anaphylaxis, to C1 esterase inhibitor preparations
C1 esterase inhibitor (Ruconest®)	History of allergy to rabbits and rabbit-derived products History of life-threatening immediate hypersensitivity reactions, including anaphylaxis, to C1 esterase inhibitor preparations
Ecallantide (Kalbitor®)	Known clinical hypersensitivity to ecallantide

Table 2. Quantity Limits

NOTE: See documentation submission requirements below if the requested quantity (dose) is greater than the program quantity limit provided in this table.

Agent	Packaging	Dose	Maximum Quantity Limit	Maximum Billable Unit
C1 esterase inhibitor (Berinert®) 10 Units = 1 billable unit	500 Unit single-use vial	20 Units/kg IV	5,000 Units (10 vials) per 30 days*	500 billable units per 30 days*
C1 esterase inhibitor (Cinryze®) 10 Units = 1 billable unit	500 Unit single-use vial	Initial dose: 1,000 Units IV every 3 to 4 days Inadequate response to initial dose: Maximum 2,500 Units (not exceeding 100 Units/kg) IV every 3 to 4 days	10,000 Units (20 vials) per 30 days Maximum 25,000 Units (50 vials) per 30 days if inadequate response to initial dosing	1,000 billable units per 30 days Maximum 2,500 billable units per 30 days if inadequate response to initial dosing
C1 esterase inhibitor (Ruconest) 10 Units = 1 billable unit	2,100 Unit single-use vial	<185 lbs (<84 kg): 50 Units/kg IV ≥185 lbs (≥84 kg) or inadequate response to initial dose: Maximum 4,200 Units IV (2 doses in 24 hours)	16,800 Units (8 vials) per 30 days	1,680 billable units per 30 days
Ecallantide (Kalbitor) 1 mg = 1 billable unit	Three 10 mg/mL single-use vials per kit	30 mg SC in three 10 mg injections Inadequate response to initial dose: Maximum 60 mg SC (2 doses in 24 hours)	120 mg (4 kits) per 30 days	120 billable units per 30 days

IV (intravenous); SC (subcutaneous)
* Maximum quantity limit calculation based on CDC 90 percentile for weight in adults and averaged for men and women to 238 lbs (108 kg).

Documentation Submission:
Documentation supporting the medical necessity criteria described in the policy must be included in the prior authorization, when prior authorization is required. In addition, the following documentation must also be submitted:

Initial Review
1. Clinical notes and laboratory results describing confirmation of hereditary angioedema (HAE).
2. Intended use (treatment or prophylaxis) of the requested HAE agent.
3. The quantity (dose) being requested, including the patient's weight if needed. If the requested quantity is greater than the quantity limits provided in the table above, a clear explanation for the medical necessity of the requested quantity MUST be submitted.

Renewal Review
1. Documentation of prior approval for the requested HAE agent through the initial review process.
2. Documentation supporting ONE of the following:
   - For treatment of acute HAE attacks, patient continues to have acute HAE attacks.
   - For prophylaxis against HAE attacks, patient has had a decrease in the frequency of acute attacks from baseline (prior to treatment).
3. The quantity (dose) being requested, including the patient's weight if needed. If the requested quantity is greater than the quantity limits provided in the table above, a clear explanation for the medical necessity of the requested quantity MUST be submitted.

Policies Inactivated

- **Positron Emission Tomography (PET), V-27**

Policies Delegated to eviCore

- **Spinal Fusion: Lumbar, IV-87**
  For applicable clinical criteria, see the following eviCore clinical guideline(s):
  - Spine Surgery
    - CMM-609 Lumbar Fusion (Arthrodesis)

- **Percutaneous Facet Joint Denervation, IV-95**
  For applicable clinical criteria, see the following eviCore guideline(s):
  - CMM-208: Radiofrequency Joint Ablations/Denervations

- **Sacroiliac Joint Fusion, IV-126**
  For applicable clinical criteria, see the following eviCore clinical guideline(s):
  - Spine Surgery: CMM-611: Sacroiliac Joint Fusion or Stabilization

- **Spinal Cord Stimulation, IV-74**
  For applicable clinical criteria, see the following eviCore clinical guideline(s):
  - CMM-211: Spinal Cord Stimulators

- **Genetic Testing to Evaluate Patients with Developmental Delay/Intellectual Disability, Autism Spectrum Disorder, or Congenital Anomalies, VI-48**
  For applicable clinical criteria, see the following eviCore clinical guidelines:
  - Lab Management Program:
    - MOL.TS.150.A. Chromosomal Microarray Testing For Developmental Disorders
    - MOL.TS.269.A. Genetic Testing for Autism
    - MOL.CU.117.A Investigational and Experimental Molecular and Genomic Testing

- **Computed Tomography Angiography (CTA) for Evaluation of Coronary Arteries, V-14**
  For applicable clinical criteria, see the following eviCore clinical guidelines:
  - Cardiac Imaging
    - CD-4: Cardiac CT, Coronary CTA, and CT for Coronary Calcium (CAC)