Effective Date **2/1/2024**
Coverage Policy Number **1701**

Unassigned Drug or Biologic Code Medical Precertification

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INSTRUCTIONS FOR USE
The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

Overview

This policy supports medical necessity review for Drugs or Biologics with an unassigned Healthcare Common Procedure Code System (HCPCS) code.

This list may not be all inclusive. Cigna maintains individual and/or group topic Coverage Policies describing criteria for other products requiring precertification. Use the Pharmacy (Drugs, Vaccines & Biologics) A-Z Index search box with a specific product name to locate additional coverage policies. Refer to the Oncology Medications related coverage resource for "J9999, Not otherwise classified, antineoplastic drugs."

Medical Necessity Criteria

Absent specific coverage policies, Drugs or Biologics with an unassigned Healthcare Common Procedure Code System (HCPCS) code are considered medically necessary, in accordance with benefit plan specifications, when ONE of the following is met:

1. **ONE of the following:**
   A. Use is approved and listed in the FDA product information (Label)

B. Use is supported by standard medical reference compendia [for example, American Hospital Formulary Service-Drug Information (AHFS-DI)], and not contraindicated or otherwise not recommended in the FDA product information (Label)

2. **Product-specific criteria [Product-Specific Medical Necessity Criteria]**

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Dose, duration of therapy, frequency or quantity exceeding generally accepted medical practice standards is considered not medically necessary.

Receipt of sample product does not satisfy any criteria requirements for coverage.

Documentation: When documentation is required, the prescriber must provide written documentation supporting the trials of these other agents. Documentation may include, but is not limited to, chart notes, prescription claims records, and/or prescription receipts.

Authorization Duration

Initial and reauthorization is up to 12 months unless otherwise stated.

Product-Specific Criteria

HCPCS Code	Drug	Medical Necessity Criteria (dosing limitations, if specified)	Conditions Not Covered
J3490	**DefenCath®** (heparin-taurolidine) catheter lock solution	**Catheter-Related Bloodstream Infection, Prevention.** DefenCath is considered medically necessary when **ALL** of the following criteria are met: 1. 18 years of age or greater 2. Has kidney failure receiving chronic hemodialysis (HD) 3. Has central venous catheter (CVC) 4. Has history of catheter-related bloodstream infections (CRBSI)	**ANY** other use is considered experimental, investigational, or unproven, including the following: 1. For use in populations other than adult patients with kidney failure receiving chronic HD through a CVC
J3490	**Defitelio®** (defibrotide sodium)	Treatment of individuals with hepatic veno-occlusive disease (VOD) (sinusoidal obstruction syndrome [SOS]), with renal or pulmonary dysfunction following hematopoietic stem-cell transplantation (HSCT).	**ANY** other use is considered experimental, investigational, or unproven.
J3490	**Dsuvia®** (sufentanil)	**For the management of acute pain severe enough to require an opioid analgesic**. **ALL** of the following: 1. Individual is 18 years of age and older 2. To be administered by a health care provider in a certified medically supervised healthcare setting (for example, hospitals, surgical centers, and emergency departments) 3. Documented failure / inadequate response, contraindication per FDA label, intolerance, or not a candidate (for example, have not tolerated, or not	**ANY** other use is considered experimental, investigational, or unproven.

HCPCS Code	Drug	Medical Necessity Criteria (dosing limitations, if specified)	Conditions Not Covered
		expected to tolerate) for non-opioid analgesics **OR** opioid combination products Authorization is limited to 36 tablets per 72 hours.	
J3490	**Isuprel** (isoproterenol)	**ANY** of the following: 1. Mild or transient episodes of heart block that do not require electric shock or pacemaker therapy. 2. Serious episodes of heart block and Adams-Stokes attacks (except when caused by ventricular tachycardia or fibrillation). 3. Cardiac arrest until electric shock or pacemaker therapy, the treatments of choice, is available. 4. Bronchospasm occurring during anesthesia. 5. As adjunct to fluid and electrolyte replacement therapy and the use of other drugs and procedures in the treatment of hypovolemic and septic shock, low cardiac output (hypoperfusion) states, CHF, cardiogenic shock. 6. Bradycardia (significant hemodynamic compromise). 7. Management of cardiogenic shock due to bradycardia. 8. Restore sinus rhythm short QT-syndrome and ventricular tachycardia/ventricular fibrillation storm. 9. Management of Torsades de pointes. 10. Provocation during tilt table testing for syncope 11. Provocation of arrhythmia during electrophysiologic testing, includes pre- and post-ablation <u>Dosing Limitations:</u> <u>Adult</u> Max dose: There are no well-established maximum doses for the approved indications according to the prescribing information. Usual dose: • Bradyarrhythmias, AV nodal block o 2 to 10 mcg/minute IV infusion; titrate to patient response • Cardiogenic shock due to bradycardia o 2 to 20 mcg/minute IV infusion • Torsade de pointes (refractory) o 2 to 10 mcg/minute by continuous IV infusion; titrate to patient response. <u>Pediatric</u> Safety and efficacy of isoproterenol in pediatric patients have not been established. However, maximum doses have been established for Other Supported Uses.	**ANY** other use is considered experimental, investigational, or unproven.

HCPCS Code	Drug	Medical Necessity Criteria (dosing limitations, if specified)	Conditions Not Covered
		Max / Usual dose: • Bradycardia, severe; AV nodal block (other supported use) - Infants, children, and adolescents ○ Limited data available: 0.05 to 0.5 mcg/kg/minute IV infusion; titrate to effect; doses as high as 2 mcg/kg/minute may be needed in some patients	
J3490	Ketalar® (ketamine intravenous)	**ANY** of the following: 1. As anesthesia for diagnostic and surgical procedures that do not require skeletal muscle relaxation. 2. Induction of anesthesia prior to administration of other anesthesia agents. 3. As supplemental anesthesia for low-potency agents, such as nitrous oxide.	**ANY** other use is considered experimental, investigational, or unproven, including the following: 1. Bipolar Disorder 2. Major Depressive Disorder 3. Chronic Pain 4. Complex Regional Pain Syndrome
J3490	**Macrilen®** (macimorelin)	**For use to diagnosis adult growth hormone deficiency (AGHD). ALL** of the following: 1. 18 years of age and older 2. Body mass index (BMI) less than or equal to 40 kg/m^2	**ANY** other use is considered experimental, investigational, or unproven.
J3490	**Regiocit**	Individual meets **BOTH** of the following: 1. Used as a replacement solution only in adult patients being treated with Continuous Renal Replacement Therapy (CRRT) and for whom regional citrate anticoagulation (RCA) is appropriate 2. Administered in a critical care setting	**ANY** other use is considered experimental, investigational or unproven.

Background

Drugs intended for human use are evaluated by FDA's Center for Drug Evaluation and Research (CDER) to ensure that drugs marketed in the United States are safe and effective. Biological products are evaluated by FDA's Center for Biologics Evaluation and Research (CBER). Federal law generally requires that prescription drugs in the U.S. be shown to be both safe and effective prior to marketing for all indications or uses. FDA's review of the applicant's labeling insures that health care professionals and patients have the information necessary to understand a drug product's risks and its safe and effective use. (U.S. FDA, 2020a, 2020b)

Good medical practice and the best interests of the patient require that physicians use legally available drugs, biologics and devices according to their best knowledge and judgment. If physicians use a product for an indication not in the approved labeling, they have the responsibility to be well informed about the product, to base its use on firm scientific rationale and on sound medical evidence. This use is called "off-label," and the FDA generally allows an FDA-approved, marketed product used in this manner when the intent is the "practice of medicine". (U.S. FDA, 2020c)

Employers and health care organizations have an interest in promoting positive patient outcomes. One resource employed to achieve this goal is the medication precertification, process. This process takes into consideration evidence of a particular medication's efficacy and safety to promote appropriate utilization and thereby minimize waste and error.

Where medical precertification is a part of a benefit plan, specific criteria must be met to promote appropriate use:

- Benefit plan coverage parameters
- Medical necessity, including appropriate clinical use

Standard Medical Reference Compendia
Standard medical reference compendia utilized to establish medical necessity include, but not limited to: American Hospital Formulary Service-Drug Information (AHFS), Elsevier/Gold Standard Clinical Pharmacology, Truven Health Analytics Micromedex DrugDEX® (DrugDEX), and Facts & Comparisons®.

Ketalar (ketamine IV) Conditions Not Covered

Major Depressive Disorder and Bipolar Disorder

Ketamine injection has been investigated for the treatment of depression over the past two decades. A number of randomized, controlled trials in patients with treatment-resistant depression have been published. There have also been a number of open-label ketamine injection studies and case studies in patients with treatment-resistant MDD and treatment-resistant BPD.[11-18] In general, the studies had small sample sizes, were conducted in a single center, and were short-term.

Two Cochrane reviews on ketamine use for depression were published in 2015.[17,18] One reviewed the use of ketamine and other glutamate receptor modulators for the treatment of MDD in adults (nine studies of ketamine included), and the second reviewed the use of glutamate receptor modulators for the treatment of depression in adults with BPD (two studies of ketamine included). In the MDD review, only ketamine IV demonstrated greater efficacy than placebo, noting the quality of evidence was limited by risk of bias and small sample sizes.[17] Low quality evidence found that ketamine increased the likelihood of response after 24 hours, 72 hours, and one week; however, the antidepressant effect of ketamine was shown at two weeks in only one trial. Adverse events (AEs) with ketamine included confusion and emotional blunting vs. placebo. The review concluded that additional randomized, controlled trials (with adequate blinding) are needed to evaluate different modes of ketamine administration, efficacy of repeated administrations, longer-term follow-up, and the efficacy of ketamine vs. active comparators.

For the treatment of depression in patients with BPD, ketamine appeared to be more efficacious than placebo 24 hours after the infusion for the primary outcome of response rate (from two studies with 33 participants).[18] The statistically significant difference disappeared at 3 days, but the mean estimate still favored ketamine. However, at 1 week, there was no difference in response between ketamine and placebo. Limited evidence favored a single IV dose of ketamine as add-on therapy to mood stabilizers vs. placebo for response rate at ≤ 24 hours. Ketamine has the potential to have a rapid and transient antidepressant effect, but the efficacy of a single IV dose may be limited. This evidence was considered very low quality, and the potential bias introduced by inadequate blinding procedures cannot be ruled out. The authors concluded that additional randomized, controlled trials (with adequate blinding) are needed to evaluate different modes of administration of ketamine and different methods of sustaining antidepressant response, which could include repeated administrations.

Chronic Pain

Ketamine is not FDA-approved for this use, and clinical evidence is insufficient to determine efficacy and safety of ketamine for the treatment of chronic pain. Evidence is generally limited to small randomized controlled studies, observational studies, and case reports utilizing a wide range of dosages and administration protocols. Additional study is needed to establish the role of ketamine in patients with chronic pain and to determine optimum dosages, durability of response, and long-term efficacy and safety of ketamine. [19-25]

Complex Regional Pain Syndrome

Ketamine is not FDA-approved for this use, and clinical evidence is insufficient to determine efficacy and safety of ketamine for the treatment of complex regional pain syndrome. Evidence is generally limited to small randomized controlled studies, observational studies, and case reports utilizing a wide range of dosages and administration protocols. Additional study is needed to establish the role of ketamine in patients with chronic pain and to determine optimum dosages, durability of response, and long-term efficacy and safety of ketamine. [19-25]

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