Non-Injectable Drugs

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This section includes information, ‹‹sorted alphabetically,›› about billing for non-injectable drug services.

NDC Billing Requirement

The Federal Deficit Reduction Act of 2005 (DRA) requires collection of rebates from drug manufacturers for physician-administered drugs. This policy may affect the billing of non-injectable drugs. Before submitting claims for non-injectable drugs, providers should review important National Drug Code (NDC) billing instructions in the *Physician-Administered Drugs – NDC* section of this manual.

Albuterol

Claims for albuterol inhalation solution (HCPCS code J7611) billed in excess of 30 mg require documentation of continued airflow obstruction.

Aminolevulinic Acid 10% Gel

Aminolevulinic acid 10% gel, is a porphyrin precursor, used in combination with photodynamic therapy using BF-RhodoLED lamp. Photoactivation following topical application of Ameluz® occurs when aminolevulinic acid (prodrug) is metabolized to protoporphyrin IX (PpIX), a photoactive compound which accumulates in the skin. When exposed to red light of a suitable wavelength and energy, PpIX is activated resulting in an excited state of porphyrin molecules. In the presence of oxygen, reactive oxygen species are formed which causes damage to cellular components, and eventually destroys the cells.

Indication

Aminolevulinic acid 10% gel is indicated for the lesion-directed and field-directed treatment of actinic keratoses of mild-to-moderate severity on the face and scalp for patients 18 years of age and older.

Dosage

Administer Ameluz only by a health care provider.

- Ameluz is for topical use only
- Photodynamic therapy with Ameluz involves preparation of lesions, application of the product, occlusion and illumination with BF-RhodoLED.
- Retreat lesions that have not completely resolved 3 months after the initial treatment
- See BF-RhodoLED user manual for detailed lamp safety and operating instructions

Authorization

A *Treatment Authorization Request* (TAR) is required for reimbursement.

Required Codes

ICD-10-CM diagnosis code L57.0

Billing

HCPCS code J7345 (aminolevulinic acid HCl for topical administration, 10% gel, 10 mg)

Azithromycin for Chlamydia

Physicians, nurse practitioners or nurse midwives may be reimbursed for azithromycin when provided for the treatment of chlamydial infections of the cervix or urethra.

Required codes

Required ICD-10-CM codes are as follows:

- Chlamydial infection of lower genitourinary tract A56.01, A56.09

Billing

HCPCS code Q0144 (azithromycin dihydrate, oral, capsules/powder, 1 gram)

For the diagnoses above, providers may be reimbursed for a maximum of 1 gram of azithromycin per patient and date of service.

Beremagene geperpavec-svdt (VYJUVEK™)

Dystrophic epidermolysis bullosa (DEB) is caused by mutation(s) in the COL7A1 gene, which results in reduced or absent levels of biologically active COL7. Upon topical application to the wounds, VYJUVEK can transduce both keratinocytes and fibroblasts. Following entry of VYJUVEK into the cells, the vector genome is deposited in the nucleus. Once in the nucleus, 14 transcriptions of the encoded human COL7A1 are initiated. The resulting transcripts allow for production and secretion of COL7 by the cell in its mature form. These COL7 molecules arrange themselves into long, thin bundles that form anchoring fibrils. The anchoring fibrils hold the epidermis and dermis together and are essential for maintaining the integrity of the skin. Patients with autosomal dominant DEB (DDEB) have lower than normal functional anchoring fibrils, and patients with RDEB have no functional anchoring fibrils.

Indications

All FDA-approved indications.

Dosage

FDA-approved dosages.

TAR Requirement

An approved *Treatment Authorization Request* (TAR) is required for reimbursement.

TAR Criteria

Vyjuvek is medically necessary when all of the following criteria are met:

- Must be used for FDA-approved indications and dosages.
- Patient must be six months of age or older.
- Patient must have a confirmed diagnosis of dystrophic epidermolysis bullosa (DEB) (either autosomal dominant DEB [DDEB] or autosomal recessive DEB [RDEB]) by genetic testing, including collagen type VII alpha 1 chain (COL7A1) gene.
- ‹‹Patient has one or more cutaneous wounds meeting the following criteria››:
  - Location: similar in size, located in similar anatomical regions, and similar in appearance
  - Appearance: clean with adequate granulation tissue, excellent vascularization, and did not appear infected
- Must be prescribed by or in consultation with a dermatologist with expertise in the treatment of DEB.

- ‹‹Patient does not have any of the following:
  - Current evidence or a history of squamous cell carcinoma (SCC) in the area that would undergo treatment
  - Receipt of a skin graft in the last three months

Authorization is for six months.

Continued therapy:

- Patient continues to meet initial approval criteria.
- Patient has experienced positive response such as a clinically significant wound healing.

Reauthorization is for 12 months.

Billing

HCPCS code J3401, (beremagene geperpavec-svdt for topical administration, containing nominal 5 x 10^9 pfu/ml vector genomes, per 0.1 ml)

Required ICD-10-CM Diagnosis Codes

Q81.2

Prescribing Restrictions

Frequency of billing equals 1.6 ml/16 units weekly

Maximum billing units equals 1.6 ml/16 units››

Bupivacaine and Meloxicam (Zynrelef™)

Zynrelef is a fixed-dose combination of bupivacaine and meloxicam.

Bupivacaine

Local anesthetics block the generation and the conduction of nerve impulses presumably by increasing the threshold for electrical excitation in the nerve, by slowing the propagation of the nerve impulse, and by reducing the rate of rise of the action potential. In general, the progression of anesthesia is related to the diameter, myelination, and conduction velocity of affected nerve fibers. Clinically, the order of loss of nerve function is as follows: (1) pain, (2) temperature, (3) touch, (4) proprioception, and (5) skeletal muscle tone.

Meloxicam

The mechanism of action of meloxicam, like that of other Non-Steroidal Anti-Inflammatory Drugs (NSAIDs), is not completely understood but involves inhibition of cyclooxygenase (COX-1 and COX-2). Meloxicam is a potent inhibitor of prostaglandin synthesis in vitro. Prostaglandins sensitize afferent nerves and potentiate the action of bradykinin in inducing pain in animal models. Prostaglandins are mediators of inflammation. Because meloxicam is an inhibitor of prostaglandin synthesis, its mode of action may be due to a decrease of prostaglandins in peripheral tissues.

Indications

All FDA-approved indications

Dosage

FDA-approved dosages

TAR Requirement

An approved *Treatment Authorization Request* (TAR) is required for reimbursement.

TAR Criteria

Zynrelef is considered medically necessary when all of the following criteria are met:

- Must be used for FDA-approved indications and dosages
- Patient must be 18 years of age or older
- Medication is being used to produce postsurgical analgesia and it has not been more than 72 hours since surgery
- Patient had one of the following surgeries:
  - Bunionectomy
  - Open inguinal herniorrhaphy
  - Total knee arthroplasty
- Patient will not use local anesthetics within 96 hours of administration
- Patient does not have a known hypersensitivity (for example, anaphylactic reactions and serious skin reactions) to any amide local anesthetic
- Patient does not have a history of asthma, urticaria, or other allergic-type reactions after taking aspirin or other NSAIDs
- Patient is not undergoing obstetrical paracervical block anesthesia
- Patient is not undergoing coronary artery bypass graft (CABG) surgery

Authorization is for a single-dose administration.

Age Limits

Must be 18 years of age or older.

Billing

HCPCS code C9088 (instillation, bupivacaine and meloxicam, 1 mg/0.03 mg).

Prescribing Restriction(s)

Frequency of billing equals 400 mg/12 mg/400 units as a single dose.

Maximum billing units equals 400 mg/12 mg/400 units

Buprenorphine Implant

Buprenorphine implant is a partial opioid agonist for subdermal administration. Each implant is 26 mm in length and 2.5 mm in diameter and contains 74.2 mg of buprenorphine (equivalent to 80 mg of buprenorphine hydrochloride) and ethylene vinyl acetate (EVA).

Indications

Buprenorphine implant is reimbursable for the maintenance treatment of moderate or severe opioid dependence in patients who have already started buprenorphine therapy with dose titration and stabilization for greater than or equal to 7 days.

Buprenorphine implant is used as part of a comprehensive treatment program including psychosocial counseling, support and regular, frequent office visits to continually evaluate and monitor the patient's progress.

Comprehensive treatment program best-practice guidelines are described in, but are not limited to, the following references:

- *Federal Guidelines for Opioid Treatment Programs* by the Substance Abuse and Mental Health Services Administration (SAMHSA), U.S. Department of Health and Human Services, 2015;
- *ASAM National Practice Guideline for the Use of Medications in the Treatment of Addiction Involving Opioid Use* by the American Society of Medicine, 2015;
- *Practice Guideline for the Treatment of Patients with Substance Use Disorders, Second Edition* by the American Psychiatric Association (APA), 2010;
- *Model Policy on Data 2000 and Treatment of Opioid Addiction in the Medical* by the Federation of State Medical Boards, 2013.

A prescribing physician, nurse practitioner or physician assistant must hold a current state medical practitioner license number, a regular U.S. Drug Enforcement Agency (DEA) controlled substance registration number and a special SAHMSA waiver DEA identification number. Prescription use is limited under the Drug Addiction Treatment Act of 2000 (Public Law 106-310, Title XXXV, Sections 3501 and 3502) and the Comprehensive Addiction and Recovery Act of 2016 (Public Law 114-198, Title III, Section 303).

Due to the risk of migration, protrusion, expulsion and nerve damage associated with the insertion and removal of the implant, buprenorphine implant is only available through a restricted distribution program called the Probuphine® Risk Evaluation and Mitigation Strategy (REMS) Program. Healthcare providers who prescribe, insert and remove buprenorphine implant must be certified with the Probuphine® REMS Program.

Age

16 years and older

Dosage

After induction, titration and stabilization with a buprenorphine transmucosal formulation for greater than or equal to 7 days, the recommended dose of four buprenorphine implants is inserted sub-dermally into the inner side of an upper arm. The implants release up to six months of buprenorphine treatment until removal by the end of the sixth month. A subsequent dose may be administered in the contralateral arm, but buprenorphine implants should not be used beyond a single insertion per arm.

Authorization

An approved *Treatment Authorization Request* (TAR) is required for reimbursement.

The TAR must include clinical documentation that demonstrates medical necessity for maintenance treatment of moderate or severe opioid use disorder as defined in the Diagnostic and Statistical Manual of Mental Disorders – Version 5 (DSM-5) by the presence of 4 or more symptom criteria for opioid use disorder within a 12-month period:

- The diagnosis has been confirmed by a comprehensive assessment including but not limited to a medical history and physical examination, objective clinical scales that measure symptoms of withdrawal, psychosocial and functional impairment, laboratory testing data, etc.
- The service is part of a comprehensive treatment program including psychosocial treatment and regular, frequent office visits to continually evaluate and monitor the patient’s progress.
- The patient has voluntarily demonstrated the motivation and ability to participate in maintenance treatment for opioid use disorder.

- The patient is currently on a dose of 8 to 24 mg per day of a buprenorphine transmucosal formulation for seven or more days.
- The treating practitioner's completed order/treatment plan/procedure note for buprenorphine implant, including the practitioner's current CA medical license, regular U.S. Drug Enforcement Agency (DEA) registration control number and special Substance Abuse and Mental Health Services Administration (SAMHSA) waiver DEA identification number.

Required Codes

One of the following ICD-10-CM diagnosis codes is required for reimbursement:

- F11.20 (opioid dependence, uncomplicated)
- F11.21 (opioid dependence, in remission)
- F11.24 (opioid dependence with opioid-induced mood disorder)
- F11.250 (opioid dependence with opioid-induced psychotic disorder with delusions)
- F11.251 (opioid dependence with opioid-induced psychotic disorder with hallucinations)
- F11.259 (opioid dependence with opioid-induced psychotic disorder, unspecified)
- F11.281 (opioid dependence with opioid-induced sexual dysfunction)
- F11.282 (opioid dependence with opioid-induced sleep disorder)
- F11.288 (opioid dependence with other opioid-induced disorder)
- F11.29 (opioid dependence with unspecified opioid-induced disorder)

Billing

HCPCS code J0570 (buprenorphine implant, 74.2 mg)

One (1) unit of J0570 equals a single 74.2 mg buprenorphine implant

‹‹Cantharidin (YCANTH™)

Cantharidin is a topical vesicant.

Indications

All FDA-approved indications.

Dosage

FDA-approved dosages.››

TAR Requirement

An approved *Treatment Authorization Request* (TAR) is required for reimbursement.

TAR Criteria

The TAR must include clinical documentation that demonstrates the following:

- Must be used for FDA-approved indication and dosing regimen.
- Patient must be two years of age or older.
- Health care professional preparing and administering treatment received instruction and training on Ycanth.
- Inadequate response, intolerance, or contraindication to cryotherapy, curettage, podofilox, or salicylic acid.

Authorization is for six months.

Age Limits

Must be two years of age or older.

Billing

‹‹HCPCS code J7354 (cantharidin for topical administration, 0.7 percent, single unit dose applicator [3.2 mg]).››

Prescribing Restriction(s)

Frequency of billing equals two applicators/two units per treatment every three weeks.

Maximum billing unit(s) equals two applicators/two units.

Capsaicin Patch (QUTENZA®)

Capsaicin is an agonist for the transient receptor potential vanilloid 1 receptor (TRPV1), which is an ion channel-receptor complex expressed on nociceptive nerve fibers in the skin. Topical administration of capsaicin causes an initial enhanced stimulation of the TRPV1-expressing cutaneous nociceptors that may be associated with painful sensations. This is followed by pain relief thought to be mediated by a reduction in TRPV1- expressing nociceptive nerve endings. Over the course of several months, there may be a gradual re-emergence of painful neuropathy thought to be due to TRPV1 nerve fiber reinnervation of the treated area.

Indications

All FDA-approved indications.

Dosage

FDA-approved dosages.

TAR Requirement

No *Treatment Authorization Request* (TAR) is required for reimbursement.

Age Limits

Must be 18 years of age or older.

Billing

HCPCS code J7336 (capsaicin 8 percent patch, per square centimeter).

Required ICD-10-CM Diagnosis Codes

B02.22, B02.23, B02.29, E08.40, E08.42, E09.42, E10.40 thru E10.42, E11.40 thru E11.42, E13.40, E13.42

Cinacalcet Tablets (Sensipar®)

Sensipar is an oral calcimimetic medication that lowers the levels of parathyroid hormone (PTH), phosphorous and calcium in patients undergoing kidney dialysis or in patients with parathyroid cancer. The calcium-sending receptor on the surface of the chief cell of the parathyroid gland is the principal regulator of PTH synthesis and secretion. Cinacalcet, the active ingredient in Sensipar, directly lowers PTH levels by increasing the sensitivity of the calcium-sensing receptor to activation by extracellular calcium. The reduction in PTH is associated with a concomitant decrease in serum calcium levels.

Indications

All FDA-approved indications

Dosage

FDA-approved dosages

TAR Requirement

An approved *Treatment Authorization Request* (TAR) is required for reimbursement.

TAR Criteria

Initial Therapy

Sensipar will be considered medically necessary when the following criteria are met:

- Must be used for FDA-approved indications and dosages
- Patient must be 18 years of age or older
- Patient must have a diagnosis of one of the following
    1. Secondary hyperparathyroidism (HPT) with chronic kidney disease (CKD) and is on dialysis
        - Current lab results show intact parathyroid hormone (iPTH) and serum calcium levels above the normal range
    2. Hypercalcemia with parathyroid carcinoma (PC)
    3. Hypercalcemia with primary hyperparathyroidism (HPT) and unable to undergo parathyroidectomy
        - Calcium greater than 12.5 mg/dL
- Prescriber to monitor calcium levels periodically throughout therapy

Initial approval is for 6 months.

Continued therapy:

- Patient is responding positively to therapy as evidenced by a decrease in iPTH (for secondary HPT) or a decrease in serum calcium level (for PC or primary HPT); and
- Patient's serum calcium level is not less than the lower limit of normal

Reauthorization is for 12 months.

Age Limits

Must be 18 year of age or older

Billing

HCPCS code, J0604, Cinacalcet, oral, 1 mg, (for ESRD on dialysis)

Prescribing Restrictions

Frequency of billing equals every 24 hours

Maximum billing unit(s) equals 360 mg/360 units

Ciprofloxacin Otic Solution

Ciprofloxacin is a quinolone antimicrobial. Quinolones rapidly inhibit DNA synthesis by promoting cleavage of bacterial DNA in the DNA-enzyme complexes of DNA gyrase and type IV topoisomerase, resulting in rapid bacterial death.

Indications

Ciprofloxacin otic solution is a quinolone antimicrobial indicated for the treatment of acute otitis externa due to susceptible isolates of Pseudomonas aeruginosa or Staphylococcus aureus.

Authorization

An approved *Treatment Authorization Request* (TAR) is required for reimbursement. The TAR must state that the patient has otitis externus due to susceptible isolates of Pseudomonas aeruginosa or Staphylococcus aureus.

Dosage

Contents of one single-use container should be instilled into the affected ear twice daily (approximately 12 hours apart) for seven days.

Required Code

ICD-10-CM diagnosis code H60.20

Billing

HCPCS code J7342 (installation, ciprofloxacin otic suspension, 6 mg)

Cocaine Nasal Solution (Numbrino™)

Cocaine hydrochloride is a local anesthetic of the ester type. Cocaine hydrochloride prevents conduction in nerve fibers by reversibly blocking voltage-gated sodium channels and preventing the transient rise in sodium conductance necessary for generation of an action potential.

Indications

All FDA-approved indications.

Dosage

FDA-approved dosages.

TAR Requirement

An approved *Treatment Authorization Request* (TAR) is required for reimbursement.

TAR Criteria

Numbrino is considered medically necessary when all of the following criteria are met:

- Must be used for FDA approved indications and dosages.
- Patient mut be 18 years or older.
- Patient requires a diagnostic or surgical procedure on or through accessible mucous membranes of the nasal cavities.
- Patient does not have any of the following:
  - Coronary artery disease
  - Congestive heart failure
  - Irregular heart rhythm, abnormal screening ECG
  - Uncontrolled hypertension (defined as systolic blood pressure (BP) equals to or greater than 140 mm Hg or diastolic BP equals to or greater than 90mm Hg)
  - Recent or active history of myocardial infarction
  - Thyrotoxicosis
  - Epilepsy
  - Hereditary pseudocholinesterase deficiency
- Patient is not on any of the following:
  - Cholinesterase inhibitors
  - α-modifying drugs
  - Tricyclic antidepressants

Authorization is for three months

Age Limits

Must be 18 years of age or older.

Billing

HCPCS code C9143 (cocaine hydrochloride nasal solution [numbrino], 1 mg).

Prescribing Restriction(s)

Frequency of billing equals160 mg /160 units in both nasal cavities for one dose.

Maximum billing unit(s) equals160 mg /160 units.

Daprodustat (JESDUVROQ)

Jesduvroq is a reversible hypoxia-inducible factor prolyl hydroxylase (HIF PH) inhibitor of HIF-PH1, PH2 and PH3 (IC_{50} in the low nM range). This activity results in the stabilization and nuclear accumulation of HIF-1α and HIF-2α transcription factors, leading to increased transcription of the HIF-responsive genes, including erythropoietin.

Indications

All FDA-approved indications

Dosage

FDA-approved dosages

TAR Requirement

An approved *Treatment Authorization Request* (TAR) is required for reimbursement.

TAR Criteria

The TAR must include clinical documentation that demonstrates the following:

- Must be used for FDA-approved indications and dosages.
- Patient must be 18 years of age or older.
- Patient has been receiving dialysis for at least four months.
- Patient is iron replete.
- Documented assessment of serum alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase, and total bilirubin prior to initiation of JESDUVROQ.
- Patient does not have severe hepatic impairment (Child-Pugh Class C).
- Patient does not have a history of myocardial infarction, cerebrovascular event, or acute coronary syndrome within the past three months.
- Patient does not have a NYHA Class IV chronic heart failure.
- Patient does not have uncontrolled hypertension.
- Patient is not taking a strong cytochrome P450 2C8 (CYP2C8) inhibitors such as gemfibrozil.

- Patient does/did not have gastrointestinal bleeding or erosion within the past four weeks.
- Patient does not have an active malignancy.
- Patient has had an inadequate treatment response, intolerance or contraindication to epoetin alfa, epoetina alfa-epbx, or darbepoetin alfa.

Initial approval is for six months.

Treatment continuation:

- Patient continues to meet initial approval criteria.
- Patient has experience positive clinical response as evidenced by an improvement in hemoglobin levels.

Reauthorization is for 12 months.

Age Limits

Must be 18 years of age or older.

Billing

HCPCS code J0889 (Daprodustat, oral, 1 mg, [for esrd on dialysis])

Required ICD-10-CM Diagnosis Codes

D63.1, N18.4, N18.5, N18.9

Prescribing Restriction(s)

Frequency of billing equals 24 mg/24 units daily.

Maximum billing unit(s) equals 24 mg/24 units.

‹‹Dexmedetomidine Sublingual Film (IGALMI™)

Dexmedetomidine is an alpha-2 adrenergic receptor agonist. The mechanism of action of IGALMI in the acute treatment of agitation associated with schizophrenia or bipolar I or II disorder is thought to be due to activation of presynaptic alpha-2 adrenergic receptors.

Indications

All FDA-approved indications.

Dosage

FDA-approved dosages.››

‹‹TAR Requirement

An approved *Treatment Authorization Request* (TAR) is required for reimbursement.

TAR Criteria

The TAR must include clinical documentation that demonstrates all of the following:

- Must be used for all FDA-approved indications and dosages.
- Patient is 18 years of age or older.
- Documentation of a diagnosis of schizophrenia or bipolar I or II.
- Documentation that Igalmi will be used for the acute treatment of agitation.
- Documentation that Igalmi will be used under the supervision of a healthcare provider.
- Patient has not been treated with alpha-1 noradrenergic blockers, benzodiazepines, antipsychotic drugs, or other hypnotics four hours prior to drug administration.
- Patient does not have a history of syncope or syncopal attacks; systolic blood pressure (SBP) is not less than 110 mmHg; diastolic blood pressure (DBP) is not less than 70 mmHg; heart rate (HR) is not less than 55 beats per minute; does not have evidence of hypovolemia or orthostatic hypotension.

Approval is for 24 hours.

Age Limits

Must be 18 years of age or older.

Billing

HCPCS code J1105 (dexmedetomidine, oral, 1 mcg)

Required ICD-10-CM Diagnosis Codes

F20.0 thru F20.9, F25.0 thru F25.9 (Schizophrenia)

F31.0 through F31.31 (Bipolar Disorder)

Prescribing Restriction(s)

Frequency of billing equals 360 mcg/360 units per 24 hours.

Maximum billing unit(s) equals 360 mcg/360 units.››

Dornase Alfa

HCPCS code J7639 (dornase alfa, 1 mg, inhalation solution, FDA-approved final product, noncompounded, administered through DME, unit dose form, per mg) must be billed with ICD-10-CM codes E84.0 through E84.9. Maximum dosage is 2 mg.

Esketamine Nasal Spray (Spravato®)

Esketamine, the S-enantiomer of racemic ketamine, is a non-selective, non-competitive antagonist of the N-methyl-D-aspartate (NMDA) receptor, an ionotropic glutamate receptor. The mechanism by which esketamine exerts its antidepressant effect is unknown. The major circulating metabolite of esketamine (noresketamine) demonstrated activity at the same receptor with less affinity.

Indications

All FDA-approved indications

Dosage

FDA-approved dosages

TAR Requirement

An approved *Treatment Authorization Request* (TAR) is required for reimbursement.

TAR Criteria

Initial Therapy

The TAR must include clinical documentation that demonstrates all of the following:

- Must be used for FDA-approved indications and dosages.
- Patient must be 18 years of age or older.
- Patient must have a diagnosis of one of the following:
  - Treatment-resistant depression (TRD)
  - Major depressive disorder (MDD) with acute suicidal ideation or behavior
- Diagnosis must be confirmed by baseline depression assessment using any validated rating scale.
- Must be prescribed by or in consultation with a psychiatrist or other specialist in the treatment of the disease.

A. Treatment-Resistant Depression (TRD)
Must meet the following criteria:

1. Diagnosis of Major Depressive Disorder (MDD) by Diagnostic and Statistical Manual of Mental Disorders -Version 5 (DSM-5) diagnostic criteria.
2. Patient must meet the DSM-5 diagnostic criteria for single-episode major depressive disorder (MDD) (if single-episode MDD, the duration must be two years or more) or recurrent MDD, without psychotic features, based upon clinical assessment.
3. Must have a documentation of inadequate response with a therapeutic trial of two or more antidepressants from different classes, given at adequate dose and duration (at least six weeks), including in the current depressive episode, unless contraindicated or clinically significant adverse effects are experienced. Inadequate response is defined as less than or equal to 25 percent reduction on Montgomery-Asberg Depression Rating Scale [MADRS] with minimum score greater than or equal to 28 for adults, or greater than or equal to 24 for geriatrics).

4. Must have a documented therapeutic trial (duration of at least six weeks) of antidepressant augmentation therapy in the current depressive episode with one or more of the following, unless contraindicated, clinically significant adverse effects are experienced, or patient is at high risk for suicidality:
   I. Atypical antipsychotic
   II. Lithium
   III. Antidepressant from a different class used in the previous therapeutic trials
   IV. Electroconvulsive therapy
   V. Transcranial Magnetic Stimulation (TMS)

B. Depressive symptoms with major depressive disorder (MDD) with acute suicidal ideation or behavior.
Must meet the following criteria:

1. Patient has a severe depressive episode (cannot care for self, participate in life, has persistent thoughts of hopelessness, persistently sad, anxious or has an "empty" mood, thoughts of suicide, etc.)
2. Provider has attested that acute psychiatric hospitalization is clinically warranted due to patient's imminent risk of suicide.

As well as the following for both diagnoses (B1 and B2)

- Patient must have documentation of concurrent antidepressant therapy
- Prescriber must attest that:
  - An accessible treatment center certified in the Spravato Risk Evaluation and Mitigation Strategies (REMS) program has been identified
  - Dosing schedule has been reviewed with the patient
  - The patient understands and is committed to dosing schedule and requirements (for example, treatment visits, transportation)
- Patient does not have any of the following conditions:
  - Pregnancy
  - History of psychotic disorder (including MDD with psychotic symptoms), bipolar disorder, obsessive-compulsive disorder, intellectual disability, autism, borderline personality disorder, dementia or intellectual disability.
  - Other major medical conditions including coronary artery disease.

Initial approval is for three months

<u>Continued therapy</u>

- Patient continues to meet initial approval criteria

- Prescriber attestation of patient compliance with doses and treatment visits
- Attestation or documentation of clinical improvement as evidenced by improvement in the same validated rating scale used for baseline depression assessment
- Documentation of concurrent use of antidepressant

Reauthorization is for 12 months

REMS

Spravato is available through a Risk Evaluation and Mitigation Strategy (REMS) program to mitigate the risks of serious adverse outcomes resulting from sedation and dissociation caused by Spravato administration, and abuse and misuse of Spravato by ensuring that:

- Spravato is only dispensed and administered to patients in a medically supervised healthcare setting that monitors these patients.
- Ensuring pharmacies and healthcare settings that dispense Spravato are certified.
- Each patient is informed about the serious adverse outcomes resulting from sedation and dissociation and need for monitoring.
- All patients who receive treatment are enrolled in an outpatient healthcare setting in a registry to further characterize the risks and support safe use.

Age Limits

Must be 18 years of age or older

Billing

HCPCS code S0013 (esketamine, nasal spray, 1 mg)

Prescribing Restrictions

Frequency of billing equals 84 mg / 84 units twice weekly

Maximum billing unit(s) equals 84 mg/ 84 units

Fecal Microbiota, Live – jslm (Rebyota™)

The mechanism of action of Rebyota probably involves competitive exclusion of Clostridiodides difficile by donor microbes with reduced toxin production; other factors may include restoration of protective taxa and modulation of the recipient's microbiome by phage, donor microbes, or metabolites.

Indications

All FDA-approved indications.

Dosage

FDA-approved dosages.

TAR Requirement

An approved *Treatment Authorization Request* (TAR) is required for reimbursement.

TAR Criteria

Must submit clinical documentation to substantiate the following:

- May be used for FDA approved indications and dosages
- Patient is 18 years of age or older
- Patient has a diagnosis of recurrent clostridioides difficile infection (CDI) defined by one of the following:
  - Had at least 2 recurrences after a primary episode and had completed at least 1 round of standard-of-care oral antibiotic therapy (for example, vancomycin, metronidazole, fidaxomicin)
  - Had at least 2 episodes of severe CDI resulting in hospitalization within the last year
- The current episode of CDI was confirmed with a positive stool test for clostridiodes difficile toxin
- Rebyota will be administered 24 to 72 hours after the last dose of antibiotics for the current episode of CDI
- Patient has not received bezlotoxumab (Zinplava) within the last year

Authorization is for 6 months (up to 2 doses)

Age Limits

Must be 18 years of age or older.

Billing

HCPCS code: J1440 (Fecal microbiota, live - jslm, 1 ml)

Prescribing Restriction(s)

Frequency of billing equals 150 ml/150 units as a single dose (up to 2 doses in 6 months)

Maximum billing unit(s) equals 150 ml/150 units

Formoterol Fumarate

For HCPCS code J7606 (formoterol fumarate, inhalation solution, 20 mcg), when billing for a quantity greater than two (40 mcg), providers must document that either the recipient's weight requires a higher dose or that there is a continued airway obstruction.

Ganciclovir Long-Acting Implant

The ganciclovir, 4.5 mg, long-acting implant is billed with HCPCS code J7310 for the treatment of cytomegalovirus (CMV) retinitis in patients with AIDS.

The insertion of the implant should be performed by a board-certified ophthalmologist who is trained in this procedure. Each ganciclovir long-acting implant contains a minimum of 4.5 mg of ganciclovir and is designed to slowly release ganciclovir into the vitreous cavity over a period of five to eight months. The implants are usually replaced electively at seven to eight months. However, the implant may be replaced earlier if the depletion of ganciclovir from the implant occurs, as evidenced by progression of retinitis.

Billing

The ganciclovir long-acting implant is reimbursable when billed in conjunction with ICD-10-CM diagnosis codes B25.8, B25.9 (cytomegaloviral disease) or codes H30.001 through H31.099 (chorioretinal inflammation and other disorders of choroid). The implantation procedure is billed using CPT® code 67027 (implantation of intravitreal drug delivery system [e.g., ganciclovir implant], includes concomitant removal of vitreous) and is reimbursable to the ophthalmologic surgeon who performs the insertion or to the surgeon's employer, such as an eye clinic or hospital outpatient department. One ganciclovir long-acting implant is reimbursed per patient in any six-month period. Additional implants may be reimbursed if documented medical justification accompanies the claim such as, but not limited to, one of the following:

- The patient requires an implant in both eyes.
- The implant becomes depleted of ganciclovir and needs to be replaced.
- It is time for elective replacement of the implant.
- The patient has developed an infection and/or complication.

Patients with a ganciclovir long-lasting implant in one eye may still require systemic coverage with either ganciclovir or foscarnet to protect the contralateral, uninvolved eye. Ganciclovir administered intravenously will not be approved for longer than 30 days following the insertion of a ganciclovir implant unless documentation of medical justification is entered in the *Remarks* field (Box 80)/*Additional Claim Information* field (Box 19) of the claim or on an attachment. Patients with bilateral retinal disease and a ganciclovir long-lasting implant in both eyes may not require oral or intravenous therapy unless there is evidence of previous pulmonary, gastrointestinal or other systemic CMV disease.

Goserelin (Zoladex®)

Goserelin (a gonadotropin-releasing hormone [GnRH] analog) causes an initial increase in luteinizing hormone (LH) and follicle stimulating hormone (FSH). Chronic administration of goserelin results in a sustained suppression of pituitary gonadotropins. Serum testosterone falls to levels comparable to surgical castration. The exact mechanism of this effect is unknown but may be related to changes in the control of LH or down-regulation of LH receptors.

Indications

All FDA-approved indications.

Dosage

FDA-approved dosages.

TAR Requirement

An Approved *Treatment Authorization Request* (TAR) is required for reimbursement.

TAR Criteria

The TAR must include clinical documentation that demonstrates the following:

Universal Criteria

- Must be used for FDA-approved indications and dosages
- Patient must be 18 years of age or older.
- Zoladex is being used for one of the following diagnoses:
  - Advanced breast cancer
  - Endometrial thinning
  - Endometriosis
  - Prostatic carcinoma
  - Stage B2-C prostatic carcinoma
- The patient must meet the criteria described below for “Advanced Breast Cancer,” “Endometrial Thinning or Endometriosis” or “Prostatic Carcinoma.”

Advanced Breast Cancer (3.6 mg only):

- Patient is a pre- or perimenopausal woman with a diagnosis of advanced breast cancer.
- Disease is estrogen receptor positive or progesterone receptor positive.

- Drug is for palliative treatment of advanced disease.
- Must be prescribed by or in consultation with an oncologist.

Initial authorization is for 12 months.

Reauthorization:

- Documentation of continued clinical benefit from treatment.
- Reauthorization is for 12 months.

Endometrial Thinning or Endometriosis (3.6 mg only)

Patient has one of the following diagnoses: endometrial thinning or endometriosis.

Endometrial Thinning

- Patient is a premenopausal female with a diagnosis of dysfunctional uterine bleeding.
- Drug is being used as an endometrial-thinning agent prior to endometrial ablation for dysfunctional uterine bleeding.
- Must be prescribed by or in consultation with a gynecologist.

Initial authorization is two months (one treatment course).

Reauthorization:

- Documentation of the reason for delay in ablation surgery.
- Reauthorization is for two months (one additional treatment course, maximum of two courses total).

Endometriosis (3.6 mg only)

- Patient has a confirmed diagnosis of endometriosis.
- Must be prescribed by or in consultation with a gynecologist.
- Drug is for management of endometriosis, including pain relief and reduction of endometriotic lesions for the duration of therapy.
- Patient has tried and failed a three-month trial of NSAIDs and/or combined oral estrogen-progesterone contraceptive or danazol unless intolerance or contraindicated.

Authorization is for six months (1 treatment course) for endometriosis.

Reauthorization:

- Documentation of the justification for retreatment.
- Reauthorization is for six months (one additional treatment course, maximum of two courses total).

Prostatic Carcinoma 93.6 mg or 10.8 mg)

Patient has one of the following diagnoses: advanced prostatic carcinoma or stage B2-C prostatic carcinoma.

Advanced Prostatic Carcinoma (3.6 mg or 10.8 mg):

- Drug is being used for palliative treatment.
- It must be prescribed by or in consultation with an oncologist or urologist; or

Stage B2-C Prostatic Carcinoma (3.6 mg or 10.8 mg):

- Disease is locally confined Stage T2b-T4 (Stage B2-C).
- Drug is being used in combination with radiotherapy and an antiandrogen [eg, flutamide].
- Must be prescribed by or in consultation with an oncologist or urologist
- Therapy with Zoladex and antiandrogen therapy will begin eight weeks prior to initiating radiation therapy and continue during radiation therapy.

Initial authorization is six months with flutamide and radiation and 12 months for palliative.

Reauthorization is for 12 months and requires documentation of continued clinical benefit treatment.

Age Limits

Must be 18 years of age or older.

Billing

HCPCS code J9202 (goserelin acetate implant, per 3.6 mg)

Prescribing Restrictions

Frequency of billing equals 3.6 mg per 1 unit every 28 days or 10.6 mg per 3 units every 12 weeks.

Maximum billing equals 10.8 mg per 3 units.

Granisetron (Oral Tablets)

Granisetron hydrochloride is indicated for the prevention of:

- Nausea and vomiting associated with initial and repeat courses of emetogenic cancer therapy, including high-dose cisplatin
- Nausea and vomiting associated with radiation, including total body irradiation and fractionated abdominal radiation

Dosing

The recommended adult dosage of oral granisetron hydrochloride is 2 mg once daily or 1 mg twice daily. In the 2 mg once-daily regimen, the 2 mg dose is given up to 1 hour before chemotherapy. In the 1 mg twice-daily regimen, the first 1 mg dose is given up to 1 hour before chemotherapy, and the second dose is given 12 hours after the first. Either regimen is administered only on the day(s) chemotherapy is given.

Billing

HCPCS code Q0166 (granisetron hydrochloride, 1 mg, oral)

Histrelin Implant

HCPCS code J9225 (histrelin implant, 50 mg, Vantas®), for the treatment of males 30 years of age or older with prostate cancer, is reimbursable when billed with ICD-10-CM diagnosis code C61. Coverage is limited to one in 12 months.

HCPCS code J9226 (histrelin implant, 50 mg, Supprelin LA®), is used for the treatment of precocious puberty in children aged 2 through 15 years. Claims may be reimbursed when billed in conjunction with ICD-10-CM diagnosis code E30.1 or E30.8. Coverage is limited to one in 12 months.

Lidocaine and Tetracaine Patch

Claims for HCPCS code C9285 (lidocaine 70 mg/tetracaine 70 mg, per patch) billed in excess of 2 patches per day require an approved *Treatment Authorization Request* (TAR) for reimbursement.

Mannitol

Claims for HCPCS code J7665 (mannitol, administered through an inhaler, 5 mg) billed in excess of 635 mg (127 units) require authorization.

‹‹Miglustat (OPFOLDA)

Policy for miglustat (HCPCS code J1202) is located in the *Injections: Drugs E Policy* section in the appropriate Part 2 manual.››

Rolapitant

Rolapitant is a substance P/neurokinin 1 (NK1) receptor antagonist indicated in combination with other antiemetic agents in adults for the prevention of delayed nausea and vomiting associated with initial and repeat courses of emetogenic cancer chemotherapy, including, but not limited to, highly emetogenic chemotherapy.

Dosage

The recommended dosage is 180 mg rolapitant administered approximately one to two hours prior to the start of chemotherapy in patients 18 years of age and older. Administer dosage in combination with dexamethasone and a 5-hydroxytryptamine3 (5-HT3) receptor antagonist.

Required Code

ICD-10-CM diagnosis code R11.2

Billing

HCPCS code J8670 (rolapitant, oral, 1 mg)

Testosterone Pellet

HCPCS code S0189 (testosterone pellet, 75 mg), is used for replacement therapy in conditions associated with a deficiency or absence of endogenous testosterone. Code S0189 is restricted to males only.

Required Codes

Claims for code S0189 must be billed in conjunction with ICD-10-CM diagnosis codes E29.1, E29.8 or E29.9.

Dosage

Maximum dosage is 450 mg every 90 days.

Treatment Policy for the Management of Chronic Hepatitis C

This policy was developed by the Department of Health Care Services (DHCS) based on a review of the medical literature, the most recent guidelines and reports published by the American Association for the Study of Liver Diseases (AASLD)/ Infectious Diseases Society of America (IDSA). This policy may be revised as new information becomes available. This policy may be revised as new information becomes available.

Treatment Considerations and Choice of Regimen for Hepatitis C Virus (HCV) Infected Patients

Please refer to AASLD guidelines for recommended treatment regimens and durations.

Identifying Treatment Candidates

a. Treatment is recommended for all patients with chronic HCV infection, except those with a short life expectancy who cannot be remediated by HCV therapy, liver transplantation, or another directed therapy.

b. Patient readiness and adherence:

   i. Patients shall be evaluated for readiness to initiate treatment.

   ii. Patients selected for treatment shall be able and willing to strictly adhere to treatment protocols prescribed by their provider.

   iii. Caution shall be exercised with patients who have a history of treatment failure with prior HCV treatment due to non-adherence with treatment regimen and appointments.

   iv. Patients shall be educated regarding the potential risks and benefits of HCV therapy, as well as the potential for resistance and failed therapy if medication is not taken as prescribed.

Other considerations

Quantity limits:

i. Prescription of HCV therapy will be dispensed in quantities up to 28 days at a time.

Criteria for reauthorization/continuation of therapy:

i. Initial authorization criteria have been met.

ii. Evidence of lack of adherence may result in denial of treatment reauthorization.

iii. Missed medical appointments related to HCV may result in the denial of treatment authorization.

Laboratory testing:

i. Documentation of baseline HCV-RNA level.

ii. Laboratory testing and monitoring should be consistent with current AASLD/IDSA guidelines.

Populations Unlikely to Benefit from HCV Treatment

According to AASLD/IDSA HCV guidelines, “Patients with a limited life expectancy that cannot be remediated by HCV treatment, liver transplantation or another directed therapy do not require antiviral treatment. Patients with a short life expectancy owing to liver disease should be managed in consultation with an expert.” Please refer to AASLD guidelines for more information on populations unlikely to benefit from HCV treatment *(hcvguidelines.org)*.

Retreatment

Retreatment will be considered where there is evidence that such retreatment will improve patient outcomes. Please refer to AASLD guidelines for recommended retreatment regimens (*hcvguidelines.org*).

Criteria for Coverage of Investigational Services (Title 22 § 51303)

Investigational services are not covered except when it is clearly documented that all of the following apply:

- Conventional therapy will not adequately treat the intended patient's condition

- Conventional therapy will not prevent progressive disability or premature death
- The provider of the proposed service has a record of safety and success with it equivalent or superior to that of other providers of the investigational service
- The investigational service is the lowest cost item or service that meets the patient's medical needs and is less costly than all conventional alternatives
- The service is not being performed as a part of a research study protocol
- There is a reasonable expectation that the investigational service will significantly prolong the intended patient's life or will maintain or restore a range of physical and social function suited to activities of daily living

All investigational services require prior authorization. Payment will not be authorized for investigational services that do not meet the above criteria or for associated inpatient care when a beneficiary needs to be in the hospital primarily because she/he is receiving such non-approved investigational services.

Unlabeled Use of Medication

Authorization for unlabeled use of drugs shall not be granted unless the requested unlabeled use represents reasonable and current prescribing practices. The determination of reasonable and current prescribing practices shall be based on:

- Reference to current medical literature.
- Consultation with provider organizations, academic and professional specialists.

Age Requirements

As approved by FDA.

Quantity Limits

Up to 28 days at a time.

Tuberculosis (TB) Treatment Drugs

Drug-Resistant TB

Tuberculosis (TB) is a disease caused by Mycobacterium tuberculosis. It mainly affects the lungs, making pulmonary disease the most common presentation. However, it can affect other organ systems including, but not excluded to the respiratory system, the gastrointestinal (GI) system, the lymphoreticular system, the skin, the central nervous system, the musculoskeletal system, the reproductive system, and the liver.

Multidrug-resistant tuberculosis (MDR TB) is caused by Mycobacterium tuberculosis that is resistant to at least isoniazid and rifampin, the two most effective of the four first-line TB drugs (the other two drugs being ethambutol and pyrazinamide). MDR TB includes the subcategory of extensively drug-resistant TB (XDR TB), which is MDR TB with additional resistance to any fluoroquinolone and to at least one of three injectable anti-TB drugs (i.e., kanamycin, capreomycin, or amikacin), or MDR TB with additional resistance to any fluoroquinolone and bedaquiline or linezolid.

Treatment Guidelines

Below is a summary of Centers for Disease Control and Prevention (CDC) treatment guidelines for the treatment of drug-resistant tuberculosis, specific to the recent FDA approved regimen combining bedaquiline, pretomanid, and linezolid (BPaL)

- The use of pretomanid 200 mg in combination with bedaquiline and linezolid (BPaL) was approved by FDA in August 2019.
- CDC recommends the use of pretomanid 200 mg daily for 26 weeks in the treatment of adults with pulmonary extensively drug-resistant (XDR), pre-extensively drug-resistant (pre-XDR) (i.e., resistant to isoniazid, rifampin, and at least one fluoroquinolone or injectable medications [i.e., amikacin, kanamycin, capreomycin]) or treatment- intolerant (TI)/nonresponsive (NR) multidrug-resistant TB when a safe and effective treatment regimen cannot otherwise be provided and when administered in combination with bedaquiline and linezolid as the BPaL regimen.

Pretomanid:

- Can be extended to nine months (39 weeks) within the BPaL regimen based on delayed treatment response within the first eight weeks;
- Is approved for treatment of pulmonary TB only, and not yet approved for treatment of extrapulmonary TB;
- Is not indicated for use alone and has not been approved for use in combination with other anti-TB medications not included in the BPaL regimen.

For additional details, refer to Provisional CDC Guidance for the Use of Pretomanid as part of a Regimen [Bedaquiline, Pretomanid, and Linezolid (BPaL)] to Treat Drug-Resistant Tuberculosis Disease.

In addition to the above, there is more extensive guidance on the approach to treatment of drug-resistant TB using different agents and duration depending on the resistance pattern and tolerability of second- and third-line TB medications. These include:

- WHO consolidated guidelines on tuberculosis. Module 4: treatment - drug-resistant tuberculosis treatment, 2022 update
- ATS/CDC/ERS/IDSA Clinical Practice Guideline - Treatment of Drug-Resistant Tuberculosis (cdc.gov)

- Drug-Resistant Tuberculosis: A Survival Guide for Clinicians, 3rd edition / 2022 Updates | Curry International Tuberculosis Center (ucsf.edu)

Utilization and Treatment Policy

Bedaquiline (SIRTURO®)

Bedaquiline is an oral diarylquinoline antimycobacterial drug that inhibits mycobacterial ATP (adenosine 5'-triphosphate) synthase, by binding to subunit c of the enzyme that is essential for the generation of energy in Mycobacterium tuberculosis.

Indications

SIRTURO is a diarylquinoline antimycobacterial drug indicated as part of combination therapy in adult and pediatric patients with multi-drug resistant tuberculosis (MDR-TB). SIRTURO is strongly recommended as one of the medications to be used in the treatment of MDR TB (see ATS reference). Reserve SIRTURO for use when an effective treatment regimen cannot otherwise be provided. Although currently not being used for latent tuberculosis, this may change in the future as additional data becomes available.

TAR Requirement

No *Treatment Authorization Request* (TAR) is required for reimbursement.

Eligibility Criteria:

- Must be prescribed by or in consultation with an infectious disease specialist, a pulmonologist or tuberculosis expert.
- Bedaquiline will be administered by directly observed therapy (DOT) in the setting determined appropriate by the public health department.
- Patient meets criteria A or B below.

A. Drug Resistant Tuberculosis without Pretomanid

- Patient has a diagnosis of pulmonary multi-drug resistant tuberculosis
- (MDR-TB) with resistance to at least isoniazid and rifampin and possibly additional antituberculous agents.
- An effective treatment regimen cannot otherwise be provided.
- Bedaquiline must be used in combination with at least three other antituberculosis drugs to which the patient’s isolate is susceptible. This may differ slightly depending on the stage in treatment (initial, continuation) and if susceptibilities are known at the start of treatment.

Recommended Dosage

- Recommended dosage in adult patients: 400 mg (four of the 100 mg tablets or 20 of the 20 mg tablets) once daily for two weeks followed by 200 mg (two of the 100 mg tablets or 10 of the 20 mg tablets) three times per week (with at least 48 hours between doses) for 22 weeks.
- Recommended dosage in pediatric patients (five years and older and weighing at least 15 kg) is based on body weight.

Approval is for a total of 24 weeks.

May approve up to 48 weeks based on tolerability of other 2nd and 3rd line agents.

B. Drug Resistant Tuberculosis with Pretomanid

- Patient must be 14 years of age or older.
- Patient has a confirmed diagnosis of pulmonary multi-drug resistant tuberculosis (MDR-TB) with resistance to at least isoniazid and rifampin and possibly additional antituberculous agents; or a diagnosis of extensively drug resistant tuberculosis (XDR-TB) with confirmed resistance to isoniazid, rifampin, a fluoroquinolone (levofloxacin or moxifloxacin), and at least one second-line injectable agent (amikacin, capreomycin, kanamycin); or treatment-intolerant (TI)/nonresponsive (NR) multidrug-resistant TB.
- Or a safe and effective alternate regimen cannot otherwise be provided.

Recommended Dosage

- Bedaquiline 400 mg and 200 mg doses are being used in combination with linezolid starting at or less than 1200 mg and pretomanid 200mg (BPaL).
- Dose does not exceed 400 mg per day for the first two weeks, followed by 200 mg three times per week, for a total dose of 600 mg per week.

Approval is for a total of 26 weeks.

May approve for up to nine months (39 weeks) within the BPaL regimen (with delay in culture conversion).

Billing

Drug code:

Bill the following miscellaneous HCPCS code for drug reimbursement:

- S5000 (prescription drug, generic)
- S5001 (prescription drug, brand name)

Provide the following on each claim:

- Name and strength of drug administered
- NDC Amount given
- Actual acquisition cost
- Copy of the drug invoice

Administration code:

Directly Observed Therapy (DOT) billed using HCPCS code H0033 (oral medication administration, direct observation), in the setting determined appropriate by the public health department and may be in the community.

Suggested ICD-10 Diagnosis Codes

- Z16.24, Z16.342, Z16.35, A15 thru A19

Pretomanid

Pretomanid is an oral nitroimidazooxazine antimycobacterial drug. Pretomanid kills actively replicating M. tuberculosis by inhibiting mycolic acid biosynthesis, thereby blocking cell wall production. Under anaerobic conditions, against non-replicating bacteria, pretomanid acts as a respiratory poison following nitric oxide release. All of these activities require nitro-reduction of pretomanid within the mycobacterial cell by the deazaflavin-dependent nitroreductase, Ddn, which is dependent on the reduced form of the cofactor F420. Reduction of F420 is accomplished by the F420-dependent glucose-6-phosphate dehydrogenase, Fgd1.

Indications

Limited Population: Pretomanid Tablet is indicated, as part of a combination regimen with bedaquiline and linezolid for the treatment of adults with pulmonary extensively drug resistant (XDR) or treatment-intolerant or nonresponsive multidrug-resistant (MDR) tuberculosis (TB). Approval of this indication is based on limited clinical safety and efficacy data. This drug is indicated for use in a limited and specific population of patients. In addition, guidelines have also recommended the use of bedaquline, pretomanid, linezolid, and moxifloxacin for MDR TB, rifampin resistant TB, and pre-XDR TB (WHO, 2022) based on recently published clinical trial data, A 24-Week, All-Oral Regimen for Rifampin-Resistant Tuberculosis.

TAR Requirement

No *Treatment Authorization Request* (TAR) is required for reimbursement.

Eligibility Criteria:

- Patient has a diagnosis of pulmonary extensively drug-resistant (XDR), pre-extensively drug-resistant (pre-XDR) (i.e., resistant to isoniazid, rifampin, and at least one fluoroquinolone or injectable medications [i.e., amikacin, kanamycin, capreomycin]) or treatment-intolerant (TI)/nonresponsive (NR) multidrug-resistant TB.
- Must be prescribed by or in consultation with an infectious disease specialist, a pulmonologist or tuberculosis expert.
- May be considered in those with drug-susceptible or drug-resistant TB (non-MDR), in which a safe and effective treatment regimen cannot otherwise be provided.
- Pretomanid 200 mg must be used in combination with bedaquiline and linezolid (BPaL) by directly observed therapy (DOT), in the setting determined appropriate by the public health department and may be in the community.
- Note there may be situations where pretomanid is used off-label and combined with other TB medications for the treatment of drug-resistant or treatment intolerant TB.

Initial approval of BPaL regimen is 26 weeks.

Recommended Dosage

The recommended dosage and duration for bedaquiline and linezolid when used in the combination regimen with pretomanid tablet are as follows:

- Pretomanid tablet 200 mg orally (one tablet of 200 mg), once daily, for 26 weeks.
- Bedaquiline 400 mg orally once daily for two weeks followed by 200 mg three times per week, with at least 48 hours between doses, for 24 weeks for a total of 26 weeks
- Linezolid starting at or less than 1200 mg with dose adjustments to 600 mg daily and further reduction to 300 mg daily or interruption of dosing as necessary for known linezolid adverse reactions.
- Dosing of the combination regimen of pretomanid tablets, bedaquiline, and linezolid can be extended beyond 26 weeks, if necessary.

Continued treatment:

Pretomanid can be extended to nine months (39 weeks) within the BPaL regimen based on delayed treatment response within the first eight weeks.

Billing

Drug code:

Bill the following miscellaneous HCPCS code for drug reimbursement:

- S5000 (prescription drug, generic)
- S5001 (prescription drug, brand name)

Provide the following on each claim:

- Name and strength of drug administered
- NDC
- Amount given
- Actual acquisition cost
- Copy of the drug invoice

Administration code:

Directly Observed Therapy (DOT) billed using HCPCS code H0033 (oral medication administration, direct observation) DOT will be administered in the setting determined appropriate by the public health department and may be in the community.

Suggested ICD-10 Diagnosis Codes

- Z16.24, Z16.342, Z16.35, A15 thru A19

Linezolid (Zyvox®) (injection or oral drug)

Linezolid inhibits bacterial protein synthesis by binding to bacterial 23S ribosomal RNA of the 50S subunit. This prevents the formation of a functional 70S initiation complex that is essential for the bacterial translation process. Linezolid is bacteriostatic against enterococci and staphylococci and bactericidal against most strains of streptococci.

Indications

ZYVOX is an oxazolidinone-class antibacterial indicated in adults and children for the treatment of the following infections caused by susceptible Gram-positive bacteria: Nosocomial pneumonia; Community-acquired pneumonia; Complicated skin and skin structure infections, including diabetic foot infections, without concomitant osteomyelitis; Uncomplicated skin and skin structure infections; Vancomycin-resistant Enterococcus faecium infections.

TAR Requirement

No *Treatment Authorization Request* (TAR) is required for reimbursement.

Eligibility Criteria

Off-Label Use: Drug-Resistant Tuberculosis Disease
Linezolid is used as part of regimen consisting of bedaquiline, pretomanid, and linezolid (BPaL) as recommended by CDC. FDA approved the use of pretomanid 200 mg in combination with bedaquiline and linezolid (BPaL) in August 2019.

- Patient has a diagnosis of pulmonary drug-resistant, including extensively drug-resistant (XDR), preextensively drug-resistant (pre-XDR) (i.e., resistant to isoniazid, rifampin, and at least one fluoroquinolone or injectable medications (i.e., amikacin, kanamycin, capreomycin)) or treatment-intolerant (TI)/nonresponsive (NR) multidrug-resistant TB.
- Must be prescribed by or in consultation with an infectious disease specialist, a pulmonologist or tuberculosis expert.
- May be considered in those with drug-susceptible or drug-resistant TB (non-MDR), in which a safe and effective treatment regimen cannot otherwise be provided

Initial approval of BPaL regimen is 26 weeks.

Recommended Dosage

FDA-approved doses in the BPaL regimen in adults are as follows:

- Linezolid starting at or less than 1200 mg per day for 26 weeks, with dose adjustments to 600 mg daily and further reduction to 300 mg daily or interruption of dosing as necessary for known linezolid adverse reactions of myelosuppression, peripheral neuropathy, and optic neuropathy. Although the initial NIX trial and FDA approval recommended 1200 mg daily dosing, recent data (TB PRACTECAL and ZeNIX) suggest that lower starting doses of linezolid 600 mg daily can be used. In addition, linezolid can be used outside of the BPaL regimen for the treatment of TB and is dosed at 600 mg daily.
- Pretomanid 200 mg administered orally once daily for 26 weeks.

- Bedaquiline 400 mg administered orally once daily for two weeks, followed by 200 mg administered orally three times weekly, with at least 48 hours between doses, for 24 weeks for a total treatment duration of 26 weeks.

Continued treatment:

Treatment can be extended to nine months (39 weeks) within the BPaL regimen based on delayed treatment response within the first eight weeks.

Billing

Oral Drug Codes:

Bill the following miscellaneous HCPCS code for ORAL drug reimbursement:

- S5000 (prescription drug, generic)
- S5001 (prescription drug, brand name)

Provide the following on each claim:

- Name and strength of drug administered
- NDC
- Amount given
- Actual acquisition cost
- Copy of the drug invoice

Injection Drug Code

- J2020, Injection, linezolid, 200 mg

Oral Drug Administration Code:

Directly Observed Therapy (DOT) billed using HCPCS code H0033 (oral medication administration, direct observation), in the setting determined appropriate by the public health department and may be in the community.

Suggested ICD-10 Diagnosis Codes

- Z16.24, Z16.342, Z16.35, A15 thru A19

Resources

1. Provisional CDC Guidance for the Use of Pretomanid as part of a Regimen [Bedaquiline, Pretomanid, and Linezolid (BPaL)] to Treat Drug-Resistant Tuberculosis Disease
2. CDC: Treatment of Multidrug-Resistant TB: Bedaquiline Fact Sheet
3. Rapid communication: key changes to the treatment of drug-resistant tuberculosis (who.int)
4. Global tuberculosis report 2021. Geneva: World Health Organization; 2021
5. WHO consolidated guidelines on tuberculosis Module 4: Treatment – drug-resistant tuberculosis treatment. Geneva: World Health Organization; 2020
6. WHO consolidated guidelines on tuberculosis Module 4: Treatment – drug-resistant tuberculosis treatment, 2022 update. Geneva: World Health Organization; 2022
7. Treatment of Drug-Resistant Tuberculosis. An Official ATS/CDC/ERS/IDSA Clinical Practice Guideline | American Journal of Respiratory and Critical Care Medicine (atsjournals.org)
8. Provisional CDC Guidelines for the Use and Safety Monitoring of Bedaquiline Fumarate (Sirturo) for the Treatment of Multidrug-Resistant Tuberculosis
9. Drug-Resistant Tuberculosis: A Survival Guide for Clinicians, 3rd edition / 2022 Updates | Curry International Tuberculosis Center (ucsf.edu)
10. Management of Multidrug-Resistant Tuberculosis in Children: A Field Guide, Fifth Edition: March 2022

Pre-Exposure Prophylaxis (PrEP) Drugs

Pre-exposure prophylaxis (PrEP) involves taking antiretroviral medications to reduce the likelihood of getting human immunodeficiency virus (HIV). PrEP is for adults and adolescents who do not have HIV but are at increased risk of getting HIV through sexual exposures or injection drug use. PrEP is part of a comprehensive prevention plan to prevent such individuals from acquiring HIV and other sexually transmitted infections (STIs) through counselling regarding use of PrEP medication(s) as prescribed, risk-reduction methods and necessary testing. The United States Preventive Services Task Force (USPSTF) recommends offering PrEP with effective antiretroviral therapy (ART) to persons at high risk of HIV acquisition with a grade of A recommendation, as reasonable and necessary for the prevention or early detection of illness or disability under §1861(ddd) (1) of the Social Security Act (the Act).

Medi-Cal covers PrEP using antiretroviral drugs (whether oral or injectable) approved by the US Food and Drug Administration (FDA) to prevent HIV infection in individuals at high risk of HIV acquisition as determined by the health care provider. Any licensed prescriber can prescribe PrEP. PrEP is a primary care preventive service that can be offered by any prescriber who cares for people without HIV who are at higher risk for acquiring HIV. Providers must follow up with recommended laboratory tests, baseline and ongoing assessments and follow-up schedules for their patients who commence taking PrEP.

Eligibility Criteria for PrEP

Centers for Disease Control and Prevention (CDC) guidelines, and enrollment criteria for clinical trials provide guidance on identifying persons who may be at higher risk for acquiring HIV infection. These include men who have sex with men, persons at risk via heterosexual contact and persons who inject drugs.

The USPSTF and the CDC recommend that PrEP be considered for people who are HIV negative and who have had anal or vaginal sex in the past six months and:

- have a sexual partner with HIV (especially if the partner has an unknown or detectable viral load), or
- have not consistently used a condom, or
- have been diagnosed with a bacterial sexually transmitted disease (STD) in the past six months.

PrEP is also recommended for people without HIV who inject drugs and:

- have an injection partner with HIV, or
- share needles, syringes, or other equipment to inject drugs.

PrEP should also be considered for people without HIV who have been prescribed non-occupational post-exposure prophylaxis (PEP) and:

- report continued risk behavior, or
- have used multiple courses of PEP.

Providers may refer to CDC and USPSTF guidelines under “Resources” section for additional details on eligibility criteria, etc.

Approved Drugs

Of the three drugs that have been approved for use as PrEP by the FDA, two consist of a combination of drugs in a single oral tablet taken daily; the third is a medication given by injection every two months.

- Emtricitabine (F) 200 mg in combination with tenofovir disoproxil fumarate (TDF) 300 mg: (F/TDF: brand name Truvada® or generic equivalent).
- Emtricitabine (F) 200 mg in combination with tenofovir alafenamide (TAF) 25 mg (F/TAF: brand name Descovy®).
- Cabotegravir (CAB) 600 mg injection (brand name Apretude®).

Dosages

These medications are approved to prevent HIV in adults and adolescents weighing at least 77 lb. (35 kg) as follows:

- Daily oral PrEP with F/TDF is recommended to prevent HIV among all people at risk through sex or injection drug use.
- Daily oral PrEP with F/TAF is recommended to prevent HIV among people at risk through sex, **excluding people at risk through receptive vaginal sex**. F/TAF has not yet been studied for HIV prevention for people assigned female at birth who could get HIV through receptive vaginal sex.
- Injectable PrEP with CAB is recommended to prevent HIV among all people at risk through sex. CAB is given as an intramuscular injection. CAB for PrEP is started by administering the first injection followed by a second injection one month after the first. CAB injections are given every two months thereafter.

For additional details on each drug, providers may refer to the drug package inserts for Descovy, Truvada and Apretude.

Billing

HCPCS Codes:

J0750 (Emtricitabine 200mg and tenofovir disoproxil fumarate 300mg, oral, FDA approved prescription, only for use as HIV pre-exposure prophylaxis [not for use as treatment of HIV])

J0751 (Emtricitabine 200mg and tenofovir alafenamide 25mg, oral, FDA approved prescription, only for use as HIV pre-exposure prophylaxis [not for use as treatment of HIV])

J0799 (FDA approved prescription drug, only for use as HIV pre-exposure prophylaxis [not for use as treatment of HIV], not otherwise classified)

Note: Providers may bill Truvada and Descovy with J0750 and J0751, as applicable. J0799 is a miscellaneous code for billing other PrEP drugs with no specific HCPCS code. The policy and billing code for Apretude can be found in the injections section of the manual.

Resources

1. USPSTF Final Recommendation Statement on PrEP for HIV Prevention
2. US Public Health Service: Preexposure Prophylaxis for the Prevention of HIV Infection in the United States – 2021 Update, a Clinical Practice Guideline
3. CDC Resources for HIV Prevention
4. CDC Resources for PrEP

Legend

Symbols used in the document above are explained in the following table.

Symbol	Description
‹‹	This is a change mark symbol. It is used to indicate where on the page the most recent change begins.
››	This is a change mark symbol. It is used to indicate where on the page the most recent change ends.