UnitedHealthcare®

Reimbursement Policy

Xgeva, Prolia (Denosmab)

Policy Number	XGE02282012RP	Approved By	UnitedHealthcare Medicare Reimbursement Policy Committee	Current Approval Date	09/10/2014

IMPORTANT NOTE ABOUT THIS REIMBURSEMENT POLICY

This policy is applicable to UnitedHealthcare Medicare Advantage Plans offered by UnitedHealthcare and its affiliates.

You are responsible for submission of accurate claims. This reimbursement policy is intended to ensure that you are reimbursed based on the code or codes that correctly describe the health care services provided. UnitedHealthcare reimbursement policies use Current Procedural Terminology (CPT®*), Centers for Medicare and Medicaid Services (CMS), or other coding guidelines. References to CPT or other sources are for definitional purposes only and do not imply any right to reimbursement.

This reimbursement policy applies to all health care services billed on CMS 1500 forms and, when specified, to those billed on UB04 forms (CMS 1450). Coding methodology, industry-standard reimbursement logic, regulatory requirements, benefits design and other factors are considered in developing reimbursement policy.

This information is intended to serve only as a general resource regarding UnitedHealthcare's reimbursement policy for the services described and is not intended to address every aspect of a reimbursement situation. Accordingly, UnitedHealthcare may use reasonable discretion in interpreting and applying this policy to health care services provided in a particular case. Further, the policy does not address all issues related to reimbursement for health care services provided to UnitedHealthcare enrollees. Other factors affecting reimbursement may supplement, modify or, in some cases, supersede this policy. These factors may include, but are not limited to: legislative mandates, the physician or other provider contracts, and/or the enrollee's benefit coverage documents. Finally, this policy may not be implemented exactly the same way on the different electronic claims processing systems used by UnitedHealthcare due to programming or other constraints; however, UnitedHealthcare strives to minimize these variations.

UnitedHealthcare may modify this reimbursement policy at any time by publishing a new version of the policy on this Website. However, the information presented in this policy is accurate and current as of the date of publication.

Table of Contents

Application

This reimbursement policy applies to services reported using the Health Insurance Claim Form CMS-1500 or its electronic equivalent or its successor form, and services reported using facility claim form CMS-1450 or its electronic equivalent or its successor form. This policy applies to all products, all network and non-network physicians, and other health care professionals.

The HCPCS/CPT code(s) may be subject to Correct Coding Initiative (CCI) edits. This policy does not take precedence over CCI edits. Please refer to the CCI for correct coding guidelines and specific applicable code combinations prior to billing UnitedHealthcare. It is not enough to link the procedure code to a correct, payable ICD-9-CM diagnosis code. The diagnosis must be present for the procedure to be paid. Compliance with the provisions in this policy is subject to monitoring by pre-payment review and/or post-payment data analysis and subsequent medical review. The effective date of changes/additions/deletions to this policy is the committee meeting date unless otherwise indicated.

Summary

Overview

Denosumab is a monoclonal antibody used for the treatment of osteoporosis in postmenopausal women with a high risk of bone fractures that were not successful with other osteoporosis therapies. Denosumab reduces the possibility of fractures of the hip and vertebral and non-vertebral fractures because it is a RANK Ligand inhibitor. It works by binding to the Rank Ligand inhibiting osteoclast formation, function, and survival, therefore preventing the osteoclasts from resorbing bone.

The FDA has approved the use of denosumab (Prolia™). Medicare has determined under Section 1861(t) that this drug may be paid when it is administered incident to a physician's service and is determined to be reasonable and necessary.

This reimbursement policy supplements but does not replace, modify or supersede existing Medicare applicable National Coverage Determinations (NCDs) or payment policy rules and regulations for chemotherapeutic drug and biological services. Federal statute and subsequent Medicare regulations regarding provision and payment for medical services are lengthy. They are not repeated in this policy. All providers who report services for UHC payment must fully understand and follow all existing laws, regulations and rules for Medicare payment for chemotherapeutic drug and biological services and must properly submit only valid claims for them. Please review and understand them and apply the medical necessity provisions in the policy within the context of the manual rules. Relevant CMS manual instructions and policies regarding chemotherapeutic drug and biological services are found in the following Internet-Only Manuals (IOMs) published on the CMS Web site:

- *Medicare Benefit Policy Manual* - Pub. 100-02, Chapter 15, Section 50.
- *National Coverage Determinations (NCD) Manual - Pub. 100-03* **...**
- *Medicare Claims Processing Manual* – Pub. 100-04, Chapter 17, Section 40.
- Correct Coding Initiative - *Medicare Contractor Beneficiary and Provider Communications Manual* - Pub. 100-09, Chapter 5.
- Social Security Act (Title XVIII) Standard References, Sections:
  - 1862(a)(1)(A) Medically Reasonable & Necessary
  - 1862(a)(1)(D) Investigational or Experimental
  - 1833(e) Incomplete Claim

Generally, drugs and biologicals are covered only if all of the following requirements are met:

They meet the definition of drugs or biologicals;

- They are of the type that are not usually self-administered by the patients who take them;
- They meet all the general requirements for coverage of items as incident to a physician's services;
- They are reasonable and necessary for the diagnosis or treatment of the illness or injury for which they are administered according to accepted standards of medical practice;
- They are not excluded as immunizations; and
- They have not been determined by the FDA to be less than effective.

In reading this document, please note that there is a difference between the section of the statute which defines the overall Medicare benefit for coverage of drugs and biologicals, and the section of the statute which states that no Medicare payment shall be made for items or services which are not reasonable and necessary for the diagnosis or treatment of illness or injury. This policy gives information about the overall Medicare benefit for coverage of drugs and biologicals.

Reimbursement Guidelines

Note: This policy does not describe drug and biological coverage under the Medicare Part D benefit.

Indications:

- For the treatment of postmenopausal women with osteoporosis at high risk for fracture, defined as a history of osteoporotic fracture, or multiple risk factors for fractures;
- For the treatment of postmenopausal women with osteoporosis who have failed or are intolerant to other available osteoporosis therapy.
- For patients with significant renal failure where treatment with biphosphonate is not indicated, CrCl less than 35 ml/min.
- Effective 11/18/2010, the FDA approved a second indication for denosumab (Xgeva™). Xgeva™ is approved for the treatment of patients with bone metastases from solid tumors.
- Effective 09/16/2011, the FDA approved denosumab (Prolia®) as a treatment to increase bone mass in men at high risk for fracture receiving androgen deprivation therapy for nonmetastatic prostate cancer. In these patients Prolia® also reduced the incidence of vertebral fractures.
- Prolia® is also indicated as a treatment to increase bone mass in women at high risk for fracture receiving adjuvant aromatase inhibitor therapy for breast cancer.
- Effective 09/02/2012, the FDA approved denosumab (Prolia®) as a treatment to increase bone mass in men with osteoporosis at high risk for fracture defined as a history of osteoporotic fracture, or multiple risk factors for fracture; or patients who have failed or are intolerant to other available osteoporosis therapy.
- Effective June 13, 2013, the FDA approved denosumab (XGEVA®) for the treatment of adults and skeletally mature adolescents with giant cell tumor of bone that is unresectable or where surgical resection is likely to result in severe morbidity.

Supplemental calcium and vitamin D are required. Hypocalcemia must be corrected prior to initiation of denosumab therapy.

Limitations

- Denosumab (Prolia™) is contraindicated in patients with hypocalcemia.
- Denosumab (Xgeva™) is not approved for patients with multiple myeloma or other cancer of the blood.

The recommended dose for the treatment of osteoporosis in postmenopausal women is 60 milligrams (mg) subcutaneously once every 6 months, plus calcium 1000 mg orally once daily and at least vitamin D 400 international units orally once daily. Denosumab (Xgeva™) is administered at a dose of 120mg every four weeks as a subcutaneous injection.

It is not appropriate to bill UHC for services that are not covered (as described by this entire reimbursement policy) as if they are covered. When billing for non-covered services, use the appropriate modifier (see "Coding Guidelines" section in this policy). Unless certain specified conditions are met, UHC will not reimburse for unlabeled use of non-self-administered drugs, since unlabeled use of the drug is considered an investigational use. UHC is not allowed to pay for investigational treatments. However, FDA-approved drugs used for indications other than what is indicated on the official label may be covered by UHC when Medicare determines the use to be medically accepted, taking into consideration the major drug compendia, authoritative medical literature and/or accepted standards of medical practice. In the case of unlabeled use for anti-cancer drugs, the conditions for Medicare coverage and reimbursement have been especially well outlined.

Xgeva, Prolia (Denosmab)

Notice: This reimbursement policy imposes diagnosis limitations that support diagnosis to procedure code automated denials. However, services performed for any given diagnosis must meet all of the indications and limitations stated in this policy, the general requirements for medical necessity as stated in CMS payment policy manuals, any and all existing CMS national coverage determinations, and all Medicare payment rules.

As published in CMS IOM 100-08, Section 13.5.1, in order to be covered under Medicare, a service shall be reasonable and necessary. UHC shall consider a service to be reasonable and necessary if we determine that the service is:

- Safe and effective.
- Not experimental or investigational (exception: routine costs of qualifying clinical trial services with dates of service on or after September 19, 2000, that meet the requirements of the Clinical Trials NCD are considered reasonable and necessary).
- Appropriate, including the duration and frequency that is considered appropriate for the service, in terms of whether it is:
  - Furnished in accordance with accepted standards of medical practice for the diagnosis or treatment of the patient's condition or to improve the function of a malformed body member.
  - Furnished in a setting appropriate to the patient's medical needs and condition.
  - Ordered and furnished by qualified personnel.
  - One that meets, but does not exceed, the patient's medical needs.
  - At least as beneficial as an existing and available medically appropriate alternative.

Drugs and biologicals must be determined to meet the statutory definition. Under the statute §1861(t) (1), payment may be made for a drug or biological only where it is included, or approved for inclusion, in the latest official edition of the United States Pharmacopoeia National Formulary (USP-NF), the United States Pharmacopoeia-Drug Information (USD-DI), or the American Dental Association (ADA) Guide to Dental Therapeutics, except for those drugs and biologicals unfavorably evaluated in the ADA Guide to Dental Therapeutics. The inclusion of an item in the USP DI does not necessarily mean that the item is a drug or biological. The USP DI is a database of drug information developed by the U.S. Pharmacopoeia but maintained by Micromedex, which contains medically accepted uses for generic and brand name drug products. Inclusion in such reference (or approval by a hospital committee) is a necessary condition for a product to be considered a drug or biological under the Medicare program, however, it is not enough. Rather, the product must also meet all other program requirements to be determined to be a drug or biological. Combination drugs are also included in the definition of drugs if the combination itself or all of the therapeutic ingredients of the combination are included, or approved for inclusion, in any of the above drug compendia.

Drugs and biologicals are considered approved for inclusion in a compendium if approved under the established procedure by the professional organization responsible for revision of the compendium.
Drugs that are usually self-administered by the patient, such as those in pill form, or are used for self-injection, are generally not covered by Part B. However, there are a limited number of self-administered drugs that are covered because the Medicare statute explicitly provides coverage. Examples of drugs that are usually self-administered by the patient and are covered include: blood clotting factors, drugs used in immunosuppressive therapy, erythropoietin for dialysis patients, and osteoporosis drugs for certain homebound patients. (See Self Administered Drug(s)) Generally, when a physician gives a patient pills or other oral medication, these drugs are excluded from coverage since the form of the drug is self-administered. Similarly, if a physician gives a patient an injection that is usually self-injected this drug is excluded from coverage, unless administered to the patient in an emergency situation.

In order to meet all the general requirements for coverage under the incident-to provision, an FDA approved drug or biological must be of a form that cannot be self-administered and must be administered by a physician or by auxiliary personnel employed by him/her under his/her personal supervision. To be covered, drugs and biologicals must be an expense to the physician billing for the service. For example, if a patient purchases a drug and the physician administers it, the drug is not covered. However, the administration of the drug, regardless of the source, is a service that represents an expense to the physician. Therefore, administration of the drug is payable if the drug would have been covered if the physician purchased it.

Use of the drug or biological must be safe and effective and otherwise reasonable and necessary. Drugs or biologicals and cancer chemotherapeutic agents approved for marketing by the Food and Drug Administration (FDA) are considered safe and effective for purposes of this requirement when used for indications specified on

the labeling.

Therefore, payment may be made for an FDA-approved chemotherapeutic drug or biological, if:

- It was injected on or after the date of the FDA's approval;
- It is reasonable and necessary for the individual patient; and
- All other applicable coverage requirements are met.

An unlabeled use of a drug is a use that is not included as an indication on the drug's label as approved by the FDA. FDA approved drugs used for indications other than what is indicated on the official label may be covered under Medicare if the contractor determines the use to be medically accepted, taking into consideration the major drug compendia, authoritative medical literature and/or accepted standards of medical practice. The following guidelines identify three categories in which medications would not be reasonable and necessary according to accepted standards of medical practice.

- Not for Particular Illness – – Medications given for a purpose other than the treatment of a particular condition, illness, or injury are not covered (except for certain immunizations).
- Injection Method Not Indicated – – Medication given by injection (parenterally) is not covered if standard medical practice indicates that the administration of the medication by mouth (orally) is effective and is an accepted or preferred method of administration.
- Excessive Medications – – Medications administered for treatment of a disease which exceed the frequency or duration of injections indicated by accepted standards of medical practice are not covered.

If a medication is determined not to be reasonable and necessary for diagnosis or treatment of an illness or injury according to these guidelines, the entire charge will be excluded (i.e., for both the drug and its administration). Also excluded from payment is any charge for other services (such as office visits) which are primarily for the purpose of administering a non–covered injection (i.e., an injection that is not reasonable and necessary for the diagnosis or treatment of an illness or injury).

- A drug that is less than effective is not eligible for reimbursement, i.e., one that the Food and Drug Administration has determined to lack substantial evidence of effectiveness for all labeled indications. Any other drug product that is identical, similar, or related, will also be ineligible.
- If a use is identified as not indicated by CMS or the FDA or if a use is specifically identified as not indicated (in one or more of the three compendia mentioned) or if it is determined (based on peer reviewed medical literature) that a particular use of a drug is not safe and effective, the off-label usage is not supported and, therefore, **the drug is not covered**. In this instance, the administration is also not covered.

Medicare Benefit Policy Manual - Pub. 100-02, Chapter 15, Section 50, describes national policy regarding Medicare guidelines for coverage of drugs and biologicals.

Coverage for medication is based on the patient's condition, the appropriateness of the dose and route of administration, based on the clinical condition and the standard of medical practice regarding the effectiveness of the drug for the diagnosis and condition. The drug must be used according to the indication and protocol listed in the accepted compendia ratings listed below.

- National Comprehensive Cancer Network (NCCN) Drugs and Biologies Compendium
- Thomson Micromedex DrugDex
- American Hospital Formulary Service-Drug Information (AHFS-DI)
- Clinical Pharmacology

The compendia employ various rating and recommendation systems that may not be readily cross-walked from compendium to compendium. In general, a use is identified by a compendium as medically accepted if the:

- Indication is a Category 1 or 2A in NCCN
- Class I, Class IIa, or Class IIb in DrugDex; or,
- Narrative text in AHFS or Clinical Pharmacology is supportive.

Self-administered drugs are not covered and should not be submitted to UHC unless requested to do so by the beneficiary. (See Self Administered Drug(s) Reimbursement Policy)

Drug Wastage

UHC provides payment for the discarded drug/biological remaining in a single-use drug product after administering what is reasonable and necessary for the patient's condition. If the physician has made good faith efforts to minimize the unused portion of the drug/biological in how patients are scheduled and how he

ordered, accepted, stored and used the drug, and made good faith efforts to minimize the unused portion of the drug in how it is supplied, the program will cover the amount of drug discarded along with the amount administered. Documentation requirements are given below. Refer to national policy: Medicare Claims Processing Manual – Pub. 100-04, Chapter 17, Section 40.

Note: The JW modifier is not used on claims for drugs or biologicals provided under the Competitive Acquisition Program (CAP). Reference to national policy: Medicare Claims Processing Manual, Pub. 100-04, Chapter 17, Section 100.2.9.

Documentation Requirements

The patient's medical record should contain documentation that fully supports the medical necessity for the administration of the denosumab(Prolia™). For postmenopausal osteoporosis at high risk for fracture such documentation should include 1 through 5 and for men the documentation should include 2 through 5, but is not limited to:

- Patient's age, sex and menopausal status.
- Documentation supporting the diagnosis of osteoporosis.
- Previous treatment of osteoporosis, agents used, outcomes and adverse reactions if any.
- History of previous fractures, including type of fracture, cause and time since occurrence.
- Risk factors for future fracture including preventive measures.

For the treatment of cancer treatment-induced bone loss (CTIBL) due to hormone ablation such documentation should include, but is not limited to:

- Documentation supporting the diagnosis of breast cancer (in women) or nonmetastatic prostate cancer.
- Use of adjuvant aromatase inhibitor (AI) therapy (in women) or androgen deprivation therapy (ADT).
- Additional diagnoses for risk factors, if any.

The patient's medical record should contain documentation that fully supports the medical necessity for the administration of the denosumab (Xgeva™). Such documentation should include, but is not limited to:

- Documentation of bone metastasis from a solid tumor and adequate calcium levels as well as the use of Vitamin D if indicated.

Utilization

The recommended dose for the treatment of osteoporosis is 60 milligrams (mg) subcutaneously once every 6 months, plus calcium 1000 mg orally once daily and at least vitamin D 400 international units orally once daily.

Denosumab (Xgeva™) is administered at a dose of 120 mg every four weeks as a subcutaneous injection.

Coding Requirements

1) Effective for dates of service on or after 01/01/2012, HCPCS code J0897 should be used to report denosumab (Prolia™, Xgeva™) for claims submitted to the Part A MAC and Part B MAC.
2) For dates of service prior to 01/01/2012, claims submitted to the Part B MAC, denosumab (Prolia™, Xgeva™) should be billed using HCPCS code J3590, Unclassified biologics. Include the name of the product and the dosage administered in item 19 of the CMS-1500 form or the electronic equivalent.
3) For claims submitted to the Part A MAC, denosumab (Prolia™, Xgeva™) should be coded using HCPCS code C9399. Effective for dates of service on or after 11/01/2010 through 12/31/2011, HCPCS code C9272 should be used to report denosumab (Prolia™, Xgeva™) for claims submitted to the FI or Part A MAC.
4) Administration of Denosumab may be billed using the chemotherapy administration code 96401 (Chemotherapy administration, subcutaneous or intramuscular; non-hormonal anti-neoplastic).
5) Correct coding requires that a bone metastasis diagnosis (ICD-9-CM code 198.5) be present on the claim as the primary diagnosis and the original cancer or history of cancer be included as the secondary diagnosis. This policy does not limit the primary cancer (as long as it is a solid tumor and not a myeloma or other cancer of the blood).
6) Any *significant and separately identifiable* E&M service billed should accurately reflect the level of the components documented. Observation of the patient by the physician post-injection may be included in the E&M service. Only face-to-face time with the physician may be considered. Observation and treatment time by the office or hospital staff may not be billed separately or counted towards a physician E&M service.

Xgeva, Prolia (Denosmab)

CPT / HCPCS Codes	
Code	**Description**
J0897	Injection, denosumab, 1 mg (effective 01/01/2012)
J3590	Unclassified biologics
96372	Therapeutic, prophylactic, or diagnostic injection (specify substance or drug); subcutaneous or intramuscular
96401	Chemotherapy administration, subcutaneous or intramuscular; non-hormonal anti-neoplastic

Modifiers	
Code	**Description**
GY	Item or service statutorily excluded, does not meet the definition of any Medicare benefit or for non-Medicare insurers, is not a contract benefit
GZ	Item or service expected to be denied as not reasonable and necessary
JW	Drug amount discarded/not administered to any patient
EJ	Subsequent claims for a defined course of therapy, e.g., EPO, sodium hyaluronate, infliximab

References Included (but not limited to):

CMS LCD(s)

Numerous LCDs

CMS Article(s)

Numerous Articles

CMS Benefit Policy Manual

Chapter 15; § 50 Drugs and Biologicals

CMS Claims Processing Manual

Chapter 17; § 40 Discarded Drugs and Biologicals

Chapter 32 Billing Requirements for Special Services

CMS Transmittals

Transmittal 2378, Change Request 7682, Dated 12/29/2011 (January 2012 Update of the Ambulatory Surgery Center Payment System (ASC))

UnitedHealthcare Medicare Advantage Coverage Summaries

Chemotherapy, and Associated Drugs and Treatments

Medications/Drugs (Outpatient/Part B)

UnitedHealthcare Reimbursement Policies

Lucentis (Ranibizumab)

Self Administered Drug(s)

MLN Matters

Article MM7672, January 2012 Update of the Hospital Outpatient Prospective Payment System (OPPS)

Others

CGS Coding, Drugs and Biological Drug Chart, CMS Website

NCCN Drugs & Biologics Compendium, National Comprehensive Cancer Network Website

Medicare Program Integrity Manual, Chapter 13 Local Coverage Determinations; § 13.5.1 Reasonable and Necessary Provisions in LCDs

Social Security Act (Title XVIII) Standard References, Sections:

- 1862(a)(1)(A) Medically Reasonable & Necessary
- 1862(a)(1)(D) Investigational or Experimental
- 1833(e) Incomplete Claim
- 1861(t) (1) Drugs and Biologicals

Xgeva, Prolia (Denosmab)

History	
Date	**Revisions**
09/10/2014	Administrative updates
06/27/2014	Administrative updates
04/02/2014	Policy updated
10/11/2013	Administrative updates
09/25/2013	Administrative updates
12/20/2012	Administrative updates
12/19/2012	Reimbursement Policy Re-review was presented to MRP committee and recommended changes were approved
11/15/2012	RP re-reviewed and updated
07/18/2012	Administrative updates
05/30/2012	Administrative updates
02/29/2012	Policy Implemented
02/08/2012	Policy Developed