**LUCENTIS® (RANIBIZUMAB)**

**Guideline Number:** MPG193.03  
**Approval Date:** June 14, 2017

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### INSTRUCTIONS FOR USE

This Policy Guideline is applicable to UnitedHealthcare Medicare Advantage Plans offered by UnitedHealthcare and its affiliates for health care services submitted on CMS 1500 forms and, when specified, to those billed on UB04 forms (CMS 1450), or their electronic comparative. The information presented in this Policy Guideline is believed to be accurate and current as of the date of publication.

This Policy Guideline provides assistance in administering health benefits. All reviewers must first identify member eligibility, any federal or state regulatory requirements, Centers for Medicare and Medicaid Services (CMS) policy, the member specific benefit plan coverage, and individual provider contracts prior to use of this Policy Guideline. When deciding coverage, the member specific benefit plan document must be referenced. The terms of the member specific benefit plan document may differ greatly from the standard benefit plan upon which this Policy Guideline is based. In the event of a conflict, the member specific benefit plan document supersedes this Policy Guideline. Other Policies and Guidelines may apply. UnitedHealthcare reserves the right, in its sole discretion, to modify its Policies and Guidelines as necessary.

UnitedHealthcare follows Medicare coverage guidelines and regularly updates its Medicare Advantage Policy Guidelines to comply with changes in CMS policy. UnitedHealthcare encourages physicians and other healthcare professionals to keep current with any CMS policy changes and/or billing requirements by referring to the CMS or your local carrier website regularly. Physicians and other healthcare professionals can sign up for regular distributions for policy or regulatory changes directly from CMS and/or your local carrier. This Policy Guideline is provided for informational purposes. It does not constitute medical advice.

### POLICY SUMMARY

#### Overview

Ranibizumab (Lucentis), is a recombinant humanized immunoglobulin G1 kappa (IgG1 kappa) monoclonal antibody fragment designed for intravitreal use, is a vascular endothelial growth factor A (VEGF-A) antagonist. Ranibizumab binds to active forms of human VEGF-A, including the cleaved form (VEGF 110), and inhibits their biologic activity.

VEGF-A induces neovascularization (angiogenesis) and increases vascular permeability, which appears to play a role in the pathogenesis and progression of the neovascular (wet) form of age-related macular degeneration (AMD), a leading cause of blindness in adults older than 60 years of age in developed countries. Binding of ranibizumab to VEGF-A prevents VEGF-A from binding to VEGF receptors (i.e., VEGFR-1, VEGFR-2) on the surface of endothelial cells, reducing endothelial cell proliferation, angiogenesis, and vascular permeability.

Ranibizumab was approved by the Food and Drug Administration (FDA) on June 30, 2006 for the treatment of patients with exudative senile macular degeneration. Effective June 22, 2010, the Food and Drug Administration (FDA) approved ranibizumab for macular edema following retinal vein occlusion (RVO). Effective August 10, 2012, the Food and Drug Administration (FDA) approved ranibizumab for diabetic macular edema.

#### Guidelines

This policy defines coding and coverage for Ranibizumab including off-label indications. The recommended dosage and frequency of treatment is 0.3mg/0.3 ml or 0.5 mg/0.05 mL (10mg/mL) administered by intravitreal injection once a month (approximately 28 days). Treatment may be continued monthly or reduced to one injection every three months after the first four injections, if monthly treatments are not feasible. Compared to monthly dosing, however, it is...
expected that quarterly dosing may be less effective, and as such, patients should be evaluated at regular regimens. The administration for ranibizumab must be billed on the same claim as the drug, with CPT code 67028 (intravitreal injection of a pharmacologic agent).

As published in CMS IOM CMS Program Integrity Manual, 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) Drugs and Biologicals,

The term “drugs” and the term “biologicals”, except for purposes of subsection (m)(5) and paragraph (2), include only such drugs (including contrast agents) and biologicals, respectively, as are included (or approved for inclusion) in the United States Pharmacopoeia, the National Formulary, or the United States Homeopathic Pharmacopoeia, or in New Drugs or Accepted Dental Remedies (except for any drugs and biologicals unfavorably evaluated therein), or as are approved by the pharmacy and drug therapeutics committee (or equivalent committee) of the medical staff of the hospital furnishing such drugs and biologicals for use in such hospital.

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 by UHC if we determine 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

Lucentis® (Ranibizumab)
UnitedHealthcare Medicare Advantage Policy Guideline
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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

**Drug Wastage**

Medicare 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 – Chapter 17 - Drugs and Biologicals, § 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. Chapter 17 - Drugs and Biologicals, § 100.2.9

**Documentation Requirements**

Documentation is expected to be maintained in the patient’s medical record and to be available to UHC upon request. Every page of the record is expected to be legible and include both the appropriate patient identification information (e.g., complete name dates of service(s), and information identifying the physician or non-physician practitioner responsible for and providing the care of the patient. The patient's medical record must contain documentation that fully supports the medical necessity for services. This documentation includes, but is not limited to, relevant medical history, physical examination, and results of pertinent diagnostic tests or procedures.

The medical record must include the following information:

- A physician's order
- The name of the drug or biological administered;
- The route of administration;
- The dosage (e.g., mgs, mcgs, cc's or IU's);

When a portion of the drug or biological is discarded, the medical record must clearly document the amount administered and the amount wasted or discarded.

**APPLICABLE CODES**

The following list(s) of codes is provided for reference purposes only and may not be all inclusive. Listing of a code in this guideline does not imply that the service described by the code is a covered or non-covered health service. Benefit coverage for health services is determined by the member specific benefit plan document and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Guidelines may apply.

<table>
<thead>
<tr>
<th>CPT Code</th>
<th>Description</th>
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<tbody>
<tr>
<td>67028</td>
<td>Intravitreal injection of a pharmacologic agent (separate procedure)</td>
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*CPT® is a registered trademark of the American Medical Association*

<table>
<thead>
<tr>
<th>HCPCS Code</th>
<th>Description</th>
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<tbody>
<tr>
<td>J2778</td>
<td>Injection, Ranibizumab, 0.1 mg</td>
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<tr>
<th>Modifier</th>
<th>Description</th>
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<tr>
<td>LT</td>
<td>Left side (used to identify procedures performed on the left side of the body)</td>
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<tr>
<td>RT</td>
<td>Right side (used to identify procedures performed on the right side of the body)</td>
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<tr>
<td>50</td>
<td>Bilateral procedure</td>
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<tr>
<td>JW</td>
<td>Drug amount discarded/not administered to any patient</td>
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<tr>
<td>EJ</td>
<td>Subsequent doses in a series</td>
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DEFINITIONS

Drug Wastage: The CMS encourages physicians, hospitals and other providers to schedule patients in such a way that they can use drugs or biologicals most efficiently, in a clinically appropriate manner. However, if a physician, hospital or other provider must discard the remainder of a single use vial or other single use package after administering a dose/quantity of the drug or biological to a Medicare patient, the program provides payment for the amount of drug or biological discarded along with the amount administered, up to the amount of the drug or biological as indicated on the vial or package label. Medical record documentation must clearly indicate the amount of drug administered and the amount wasted. When billing drugs, units of service must be billed in multiples of the dosage specified in the full HCPCS descriptor. This descriptor does not always match the dose given. The units billed must correspond with the smallest dose (vial) available for purchase from the manufacturer(s) that could provide the appropriate dose for the patient. The following examples will help illustrate some of these points:

Example of choice of vial size
1. HCPCS for drug A indicates 1 unit = 30 mg
2. Drug A doses available from the manufacturer: 60 mg vial and 90 mg vial
3. The amount prescribed for the patient is 48 mg. If the provider uses a 90 mg vial to administer the dose, the provider may only bill only 2 units (rather than 3 units) as the doses available from the manufacturer allow the prescribed amount to be administered with a 60 mg vial.

Additionally, if after administering the prescribed dosage of any given drug, the provider must discard the remainder of a single-use vial or other package, Medicare may cover the amount of the drug discarded along with the amount administered.

Off-Label Drug Use: An off-label/unlabeled use of a drug is defined as a use for a non-FDA approved indication, that is, one that is not listed on the drug's official label/prescribing information. An indication is defined as a diagnosis, illness, injury, syndrome, condition, or other clinical parameter for which a drug may be given. Off-label use is further defined as giving the drug in a way that deviates significantly from the labeled prescribing information for a particular indication. This includes but is not necessarily limited to, dosage, route of administration, duration and frequency of administration, and population to whom the drug would be administered. Drugs used for indications other than those in the approved labeling may be covered under Medicare if it is determined that the use is medically accepted, taking into consideration the major drug compendia, authoritative medical literatures and/or accepted standards of medical practice. Determinations as to whether medication is reasonable and necessary for an individual patient are made on appeal on the same basis as all other such determinations (i.e., with support from the peer-reviewed literature, with the advice of medical consultants, with reference to accepted standards of medical practice, and in consideration of the medical circumstance of the individual case).

REFERENCES

CMS Local Coverage Determinations (LCDs)

<table>
<thead>
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<th>LCD</th>
<th>Medicare Part A</th>
<th>Medicare Part B</th>
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<td>L34741 (Drugs and Biologics (Non-chemotherapy) WPS)</td>
<td>AK, AL, AR, AZ, CT, FL, GA, IA, ID, IL, IN, KS, KY, LA, MA, ME, MI, MN, MO, MS, MT, ND, NE, NH, NJ, OH, OR, RI, SC, SD, TN, UT, VA, VI, VT, WA, WI, WV, WY</td>
<td>IA, IN, KS, MI, MO, NE</td>
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<td>L33407 (Ranibizumab (Lucentis®)) First Coast</td>
<td>FL, PR, VI</td>
<td>FL, PR, VI</td>
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<tr>
<td>L33394 (Drugs and Biologicals, Coverage of, for Label and Off-Label Uses) NGS</td>
<td>CT, IL, MA, ME, MN, NH, NY (Entire State), RI, VT, WI</td>
<td>CT, IL, MA, ME, MN, NH, NY (Down State), NY (Upstate), NY (Queens), RI, VT, WI</td>
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<tr>
<td>L34252 (Drugs and Biologicals: Antiangiogenic Therapy for Ophthalmic Conditions) Cahaba Retired 09/30/2016</td>
<td>AL, GA, TN</td>
<td>AL, GA, TN</td>
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CMS Articles

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<td>A53121 (Billing and Coding Information Regarding Uses, Including Off-Label Uses, of Bevacizumab and Ranibizumab, for The Treatment of Ophthalmological Diseases) Novitas</td>
<td>DC, DE, MD, NJ, PA</td>
<td>DC, DE, MD, NJ, PA</td>
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<td>A52451 (Ranibizumab (e.g., Lucentis™) and Aflibercept (e.g., Eylea™) – Related to LCD L33394) NGS</td>
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CMS Benefit Policy Manual
Chapter 15; § 50 Drugs and Biologicals

CMS Claims Processing Manual
Chapter 17; § 40 Discarded Drugs and Biologicals, § 100.2.9 Submission of Claims with the Modifier JW, “Drug Amount Discarded/Not Administered to Any Patient”

CMS Transmittals
Transmittal 1419, Change Request 5865, Dated 01/18/2008 (January 2008 Integrated Outpatient Code Editor (I/OCE) Specifications Version 9.0)

UnitedHealthcare Commercial Policies
Macular Degeneration Treatment Procedures
Ophthalmologic Policy: Vascular Endothelial Growth Factor (VEGF) Inhibitors
Proton Beam Radiation Therapy

Others
CMS Medicare Program Integrity Manual 100-08, § 13.5.1 Reasonable and Necessary Provisions in LCDs, CMS Website
FDA News Release, FDA approves Lucentis to treat diabetic macular edema, FDA Website
XVIII of the Social Security Act (SSA): §1861(t)(1), Social Security Website

GUIDELINE HISTORY/REVISION INFORMATION

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<th>Action/Description</th>
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<tr>
<td>06/14/2017</td>
<td>• Annual review, new FDA approved ICDs added</td>
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