



**Healthcare Common Procedure Coding
System (HCPCS) Level II Drug and
Biological Product Coding
Development Manual**

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1. Purpose

The purpose of this document is to serve as a technical reference guide describing the methodology and decision-making framework used by the Centers for Medicare & Medicaid Services (CMS) when developing HCPCS Level II codes for drugs and biological products. CMS establishes and maintains the HCPCS Level II code set under its authority to adopt standard code sets for health care transactions, consistent with the Health Insurance Portability and Accountability Act. This authority supports a uniform coding system used by all payers. HCPCS Level I is comprised of Current Procedural Terminology®, a numeric coding system maintained by the American Medical Association.

This manual is intended to help manufacturers, applicants, and other external stakeholders understand HCPCS Level II drug and biological coding considerations and process prior to the submission of an application to either establish, revise, or discontinue a HCPCS Level II code.

HCPCS Level II codes are alpha-numeric codes used primarily to identify drugs, biologicals and non-biological items, supplies, and services for submitting healthcare claims. This manual is organized to walk applicants through the sequential decision-making process that CMS applies when evaluating a HCPCS Level II coding application for drug and biological products, beginning with product classification and Food and Drug Administration (FDA) approval pathway determination and proceeding through dosage calculation, descriptor language construction, and final code assignment.

While CMS has made every effort to describe the most common HCPCS Level II coding scenarios and considerations applicable to drugs and biological products, this manual does not represent an exhaustive description of all HCPCS Level II coding scenarios, product-specific factors, or circumstances that CMS may encounter during the HCPCS Level II coding review process. The methodology described in this manual reflects changes in policy, regulation, coding conventions, and product complexity over time. As a result, existing HCPCS Level II codes established prior to the adoption of the current methodology may not fully reflect the descriptor language, dosage conventions, or coding structure outlined in this manual. Applicants and stakeholders should not rely on legacy code language as a model for new or revised code applications.

CMS may update this manual periodically to reflect changes in policy, regulation, or coding conventions. Applicants are encouraged to consult the CMS HCPCS Level II homepage at <https://www.cms.gov/medicare/coding-billing/healthcare-common-procedure-system> for the most current information.

Important Note: This manual is not a substitute for a formal HCPCS Level II code application submitted through the Medicare Electronic Application Request Information System™ (MEARIS™). Applicants seeking an official HCPCS Level II coding determination must submit a complete application through MEARIS™ at <https://mearis.cms.gov/public/home>. CMS will review each application on its own merits and in accordance with applicable policies, regulations, and coding conventions in effect at the time of the review.

Additionally, a HCPCS Level II code assignment does not constitute a coverage determination. Coding, coverage, and payment are separate processes, and the assignment of a HCPCS Level II code does not guarantee that a payer, including Medicare, will cover or pay for the product associated with that HCPCS Level II code.

2. General Framework

2.1 Guiding Principles

This document is intended as a technical reference guide. For HCPCS Level II coding determinations, applicants should submit a formal HCPCS Level II code application through MEARIS™. CMS reserves the right to make final HCPCS Level II coding determinations based on all available clinical, regulatory, and administrative information and reserves the right to adjust determinations accordingly.

Determinations may reflect circumstances or product-specific factors that fall outside the scope of the guidance provided here.

Note on Code Alpha Designations: There is a common misconception that certain letter-prefixed HCPCS Level II codes are “temporary” while others are “permanent.” For example, HCPCS Level II Q codes are sometimes described as temporary and HCPCS Level II J codes as permanent. This distinction no longer exists within the HCPCS Level II coding system. All HCPCS Level II codes assigned through the HCPCS Level II coding process are subject to the standard code maintenance processes and are active unless otherwise announced.

2.2 HCPCS Level II Coding Schedule

HCPCS Level II coding applications for drugs and biological products are reviewed on a quarterly basis. Table 1 below outlines the HCPCS Level II quarterly coding schedule, including HCPCS Level II application deadlines, publication of final determinations, and effective dates.

Table 1: HCPCS Level II drug and biologicals coding schedule.

Quarter	Application Deadline (first business day by 11:59 PM ET)	Publication of Final Determinations (approximate)	Effective Date (calendar day)
First	January	April	July 1 st
Second	April	July	October 1 st
Third	July	October	January 1 st (following year)
Fourth	October	January (following year)	April 1 st (following year)

Applications that are received and determined by CMS to be complete by the deadline will be considered for inclusion in that HCPCS Level II quarterly coding cycle. Applications received after the deadline will be considered for the subsequent coding cycle. Applications received by the deadline that are determined to be incomplete will be declined, and the applicant should submit a completed application in a subsequent coding cycle.

2.3 Off-Cycle HCPCS Level II Coding

During special circumstances and for specific products, CMS may permit the submission and consideration of HCPCS Level II applications outside of the established quarterly and biannual coding cycles. CMS may allow off-cycle coding applications related to products needed in a National Emergency or a Public Health Emergency. CMS may also allow off-cycle coding applications related to anti-infective agents that address urgent infectious or respiratory illness or disease. CMS would be informed by resources such as the Centers for Disease Control and Prevention’s National Respiratory and Enteric Virus Surveillance System to guide those determinations. CMS may also consider other circumstances that warrant flexibility in the timing of a coding determination, evaluated on a case by case basis.

These HCPCS Level II codes will not circumvent the FDA approval or authorization date. Off-cycle coding is not a pathway to establish a HCPCS Level II code before an FDA approval has been granted. On rare occasions, CMS may consider a product's Emergency Use Authorization (EUA) issued by the FDA as an alternative to full FDA approval when evaluating eligibility for off-cycle HCPCS Level II coding. This consideration is limited to extraordinary circumstances, such as a declared Public Health Emergency or National Emergency, where a product authorized under an EUA is critical to the public health response. The availability of this pathway does not guarantee a HCPCS Level II coding determination, and CMS retains full discretion in evaluating such requests on a case-by-case basis.

2.4 Submission Requirements

Applicants requesting a modification to the HCPCS Level II code set must submit a complete application package through MEARIS™. Applications for the establishment of or revision to an existing HCPCS Level II code must include the FDA approval documentation and this information must be noted within the appropriate question in the MEARIS™ application.

The submission must also include product labeling, specifically the prescribing information, which is used to determine dosage information and billing unit conventions. As part of the application, the applicant should also submit any descriptive material, including the manufacturer's product literature and any other information that the applicant believes would be helpful in furthering CMS' understanding of the medical features of the product for which a HCPCS Level II code revision is requested. When applicable, applicants must supply the National Drug Code (NDC) number or numbers associated with the product, a proposed HCPCS Level II code descriptor, and a clinical rationale explaining why a distinct HCPCS Level II code is warranted.

CMS will consider all available clinical, regulatory, and administrative information, including the product's prescribing information and the implications for Medicare discarded drug policy, to determine the most appropriate dose description for the HCPCS Level II code. Applicants are encouraged to provide complete and accurate dosage information in the MEARIS™ application to assist CMS in making this determination.

A manufacturer is also requested to share whether the manufacturer has a Medicaid National Drug Rebate Agreement in effect or intends to pursue such an Agreement. The Agreement is not a requirement for the application process, nor a condition of a HCPCS Level II code, but informs CMS in regard to whether the drug is payable by Medicare.

3. Pre-Application Guidance for Applicants

This section describes what type of HCPCS Level II code the applicant should request and ensure that complete information is provided at the time of submission. The guide walks applicants through a sequential series of questions beginning with product classification and FDA approval pathway identification. Each step corresponds to a specific question or data field within the MEARIS™ application, and applicants are expected to document their responses accordingly.

3.1 Definitions of Single Source Drug or Biological and Multiple Source Drug

Applicants must identify and clearly state whether they believe their product is a single source drug or biological product (as defined at section 1847A(c)(6)(D) of the Social Security Act (the Act)) or a multiple source drug (as defined at section 1847A(c)(6)(C) of the Act), since this classification may affect CMS' HCPCS Level II coding determination.

Applicants should consult the most recent edition of the FDA’s Approved Drug Products with Therapeutic Equivalence Evaluations (commonly known as the “Orange Book”) before applying. This publication is updated regularly, and a product's classification can change over time. For example, a product that is launched as a single source drug may become a multiple source drug following the approval of a therapeutic equivalence (TE) generic. When this occurs, CMS will evaluate whether a revision to the existing HCPCS Level II code or another coding action is appropriate. Applicants who are aware of pending TE determinations or who plan to petition the FDA for a TE rating should disclose this information in the MEARIST™ application, as it may affect the coding outcome.

3.2 Product Classification: FDA Approval Pathway

The applicant must identify the FDA approval pathway for their product, as this information governs which HCPCS Level II coding cycle and process applies.

3.2.1 Pending FDA Approval

If the product is pending FDA approval or has not yet been approved, the application will be deemed incomplete. All FDA documentation is required by the application deadline, and CMS will not process applications for products that have not yet received FDA marketing authorization.

3.2.2 Biologics License Application (BLA)

If the product was approved through a BLA, the applicant must note whether the approval was under section 351(a) or section 351(k) of the Public Health Service (PHS) Act within the appropriate question in the MEARIST™ application, and CMS will consider these requests within the quarterly HCPCS Level II coding cycle for drug and biological products. If the product has a BLA approval number that is associated with an existing HCPCS Level II code, the product will typically not receive its own HCPCS Level II code. In such circumstances, a revision of the existing HCPCS Level II code describing the products under the BLA approval number may be appropriate.

If a biosimilar was approved under the section 351(k) pathway, the applicant must provide clear information about the reference biological product(s), including the reference product’s BLA approval number. If the biosimilar references multiple BLA approval numbers, the applicant must include all associated reference BLA approval numbers in the MEARIST™ application.

3.2.3 Supplemental Biologics License Application (sBLA)

If the product was approved through an sBLA, the applicant must note whether the supplemental approval was under section 351(a) or section 351(k) of the PHS Act within the appropriate question in the MEARIST™ application, and CMS will consider these requests within the quarterly HCPCS Level II coding cycle for drug and biological products. If the sBLA has the same BLA approval number as the original BLA number, the product will typically not receive its own HCPCS Level II code; however, in certain circumstances, an existing HCPCS Level II code may be revised.

3.2.4 New Drug Application (NDA)

If the drug was approved through an NDA under section 505 of the Food, Drug, and Cosmetic Act (FD&C Act), including NDAs approved through section 505(b)(2) of the FD&C Act (hereinafter referred to as a 505(b)(2) NDA), this information must be noted within the appropriate question in the MEARIST™ application, and CMS will consider these requests within the quarterly HCPCS Level II coding cycle for drug and biological products. If the product has an NDA approval number that is associated with an

existing HCPCS Level II code, the product will typically not receive its own HCPCS Level II code. In such circumstances, a revision of the existing HCPCS Level II code describing the products under the NDA approval number may be appropriate.

In certain cases, if a product approved under a 505(b)(2) NDA has a TE rating published in the FDA's most recent edition of the Orange Book, it may not receive its own HCPCS Level II code. Applicants should disclose in the MEARIS™ application whether the product has any TE rating published in the Orange Book. Additionally, if the applicant plans to petition the FDA for a TE rating relative to other marketed products, this information should also be disclosed, as a TE designation will generally affect whether a unique HCPCS Level II code is assigned.

3.2.5 Supplemental New Drug Application (sNDA)

If the product was approved through an sNDA and received a unique NDA approval number, this information must be noted within the appropriate question in the MEARIS™ application, and CMS will consider these requests within the quarterly HCPCS Level II coding cycle for drug and biological products. If the sNDA has the same NDA approval number as the original NDA approval number, the product will typically not receive its own HCPCS Level II code; however, in certain circumstances, an existing HCPCS Level II code may be revised.

3.2.6 Abbreviated New Drug Application (ANDA)

If the product was approved through an ANDA under section 505(j) of the FD&C Act, the product does not typically receive its own HCPCS Level II code. Usually, drugs approved through an ANDA are described by an existing HCPCS Level II code for other products that are rated as TE according to the Orange Book. In cases where a drug approved through an ANDA is not described by an existing HCPCS Level II code or the NDA approved drug and any other ANDA TE drugs are no longer manufactured, CMS may consider these requests within the quarterly HCPCS Level II coding cycle for drug and biological products.

3.2.7 Premarket Approval (PMA)

If the product was approved under a PMA, CMS typically reviews these applications in the biannual HCPCS Level II coding cycles for non-drug and non-biological products. However, there are certain circumstances where CMS will review these applications in the quarterly coding cycles for drug and biological products, such as when Medicare pays for the product under section 1847A of the Act (e.g., certain hyaluronic acid joint injections).

3.2.8 Skin Substitute

If the product is a skin substitute regulated by the FDA as a human cell, tissue, or cellular or tissue-based product solely under section 361 of the PHS Act and 21 Code of Federal Regulations (CFR) Part 1271, cleared through the 510(k) regulatory pathway, or approved under a PMA, effective January 1, 2026, CMS reviews complete HCPCS Level II coding applications for these products in the biannual non-drug and non-biological products coding cycles (see the Calendar Year 2026 Physician Fee Schedule final rule at [90 FR 49508](#)). The applicant should submit their application accordingly, as the submission deadline for non-drug and non-biological products is the first business day of January and July at 11:59 PM ET. In addition, these products will be subject to the public meeting process established for the biannual HCPCS Level II coding applications for non-drug and non-biological products.

3.3 *Existing HCPCS Level II Code*

Prior to submitting an application for a new HCPCS Level II code, the applicant should review the most recently updated HCPCS Level II code set at <https://www.cms.gov/medicare/coding-billing/healthcare-common-procedure-system/quarterly-update> and assess if a HCPCS Level II code already describes the product.

If there is an existing HCPCS Level II code that the applicant thinks may describe the product, the applicant should assess whether the drug or biological product is approved under the same FDA approval (e.g., the same BLA approval number) as a product with an existing HCPCS Level II code or if it is TE to a product with an existing HCPCS Level II code (e.g., an NDA approval that is TE to the reference listed drug). If the applicant's product meets those conditions, CMS will typically not establish a new HCPCS Level II code, regardless of the route of administration or if two products under the same approval number are not interchangeable. If there is an existing HCPCS Level II code that the applicant thinks may describe the product, and drug or biological product is approved under separate FDA approvals, CMS may consider revising existing HCPCS Level II code(s) to account for multiple routes of administration.

If the applicant believes that the existing HCPCS Level II code needs to be revised, CMS may consider these requests within the quarterly HCPCS Level II coding cycle for drug and biological products.

If the applicant believes that no existing HCPCS Level II code describes the product, the applicant should note this information in the MEARIS™ application.

3.3.1 **Existing HCPCS Level II C Code**

HCPCS Level II C codes are a category of HCPCS Level II codes generally used to identify certain drugs, biologicals, and devices for billing under the Hospital Outpatient Prospective Payment System (OPPS). When the existing HCPCS Level II code is a C code, the applicant should assess whether the drug or biological product can be used in multiple settings of care other than settings paid under the OPPS where a HCPCS Level II code is used for billing and payment. If so, CMS will consider discontinuing the existing HCPCS Level II C code and establishing a new HCPCS Level II code, and this information should be noted within the appropriate question in the MEARIS™ application. If the drug or biological product is only used in settings paid under the OPPS, CMS will typically not establish a new HCPCS Level II code, and the HCPCS Level II C code will remain active until otherwise announced.

3.4 *Administration Setting*

The applicant must identify where the product is or is expected to be administered, including any combination of settings, within the MEARIS™ application; while there may be other administration settings not described below, the following represent certain key settings and their associated HCPCS Level II code implications.

- **Settings paid under the Inpatient Prospective Payment System (IPPS) only:** If the product is only administered in settings paid under the IPPS, CMS considers whether a distinct HCPCS Level II code is needed to identify the product for billing purposes. Applicants should be aware that, for Medicare, payment for such products is generally included in the Medicare Severity Diagnosis Related Group (MS-DRG) payment.
- **Physician office only:** If the drug is only administered in a physician office setting, the applicant should note this information in the MEARIS™ application.

3.5 *Self-Administration*

When the applicant believes that the drug is usually self-administered and is administered via a Medicare-covered item of durable medical equipment (DME), the applicant should note this information in the MEARIS™ application.

If the applicant believes that the drug is self-administered but is not administered via a DME, the applicant should check the self-administered drug (SAD) exclusion list at the applicable Medicare Administrative Contractor (MAC) webpage. If the product is on the SAD list, the applicant should note this information in the MEARIS™ application. The information may vary based on geographical area and MAC jurisdiction. While the SAD exclusion list can serve as a useful reference, it is not determinative of Medicare coverage or payment status, nor is it determinative of coverage or payment decisions made by other payers. Coverage by Medicare or another payer is not determinative of whether a product will receive a HCPCS Level II code.

If the drug can be self-administered, but the applicant believes that the drug is payable under Medicare Part B (e.g., an immunosuppressive drug described in section 1861(s)(2)(J) of the Act), the applicant should note this information in the MEARIS™ application.

Note Regarding Products with Multiple Administration Pathways: Some products may be administered through more than one pathway. For example, a product may be administered as a non-self-administered drug furnished in a physician's office or other clinical setting, as a drug furnished through a covered item of DME, or as a product self-administered by the individual at home. If more than one administration pathway applies to the product, the applicant should clearly identify all applicable administration routes in the MEARIS™ application. If a product is approved for multiple routes of administration, including a self-administered route, under a single FDA approval, CMS will typically add the following parenthetical language to the HCPCS Level II code description: "(code may be used for Medicare when drug administered under the direct supervision of a physician, not for use when drug is self administered)." This additional language clarifies the circumstances under which the HCPCS Level II code may be used for Medicare billing purposes.

4. Drug and Biological Product HCPCS Level II Code Specifics

If a new HCPCS Level II code is warranted, applicants should understand what to expect from CMS in relation to the HCPCS Level II long and short descriptions. The following conventions govern how CMS constructs HCPCS Level II code description language for drug and biological products.

4.1 *Symbols and Characters Used in HCPCS Level II Code Descriptions*

HCPCS Level II codes are alpha-numeric codes consisting of five characters. The first character is always a single upper-case letter, followed by the four remaining characters, which are always numeric digits ranging from zero to nine. No other characters, symbols, punctuation marks, or lowercase letters appear within the five-character alpha-numeric code itself.

Historically, CMS did reassign HCPCS Level II alpha-numeric codes that had not been used for an extended period. However, CMS' current practice is that each alpha-numeric code is unique and, once assigned, is not reassigned. A previously used HCPCS Level II code will not be reassigned to a different drug, biological product, billing unit or service, ensuring the integrity and historical accuracy of the HCPCS Level II coding system. While CMS makes every effort to group similar products and services together within the HCPCS Level II coding structure, the assignment of a specific alpha-numeric code is

determined by CMS based on a variety of factors, and CMS cannot guarantee that a new HCPCS Level II code will be placed in any category, section, or alpha-numeric range.

4.1.1 HCPCS Level II Short Description

The short description is limited to 28 characters or less. This constraint means that only the most essential alpha-numeric characters, spaces, standard abbreviations, and minimal punctuation are used in the short description. The short description serves as a concise identifier for the drug, biological product, or other item or service associated with the HCPCS Level II code.

4.1.2 HCPCS Level II Long Description

The long description is the full written description associated with each HCPCS Level II code. Table 2 below shows the characters and symbols that can be used within long descriptions:

Table 2: Symbols or characters that can be used within the long descriptions of a HCPCS Level II code.

Symbol or Character	Common Purpose and Example
Uppercase and lowercase letters (A–Z, a–z)	Used to spell out ingredient names, routes of administration, and billing units (e.g., “Injection, adalimumab”). Due to Medicare claims processing system limitations, the first letter of the long description is the only letter that is uppercase.
Numerals (0–9)	Used to express dosage quantities and billing units of measure (e.g., “10 mg,” “0.5 micrograms”).
Comma (,)	Used to separate key descriptor elements such as the route of administration, active ingredient, and unit of measure (e.g., “Injection, adalimumab, 1 mg”).
Decimal point (.)	Used in dosage quantities when a fractional amount must be expressed (e.g., “0.5 mg”).
Hyphen (-)	Used in compound chemical names or multi-word ingredient names (e.g., “factor viii, anti-hemophilic”).
Parentheses ()	Used to include manufacturer, brand names or clarifying information within the descriptor (e.g., “Injection, carboplatin (avyxa), 1 mg”).
Semicolon (;)	Used in select codes to separate distinct descriptor elements when a comma alone would be insufficient for clarity.
Forward slash (/)	Used in units of measure when expressing a ratio or concentration (e.g., “mg/mL”) or to separate multiple manufacturer or brand names (e.g., “Injection, bendamustine hydrochloride, (belrapzo/bendamustine), 1 mg”).
Space	Used as standard word separation between all descriptor elements.
Caret (^)	Used in select codes when expressing “to the power of” (e.g., “containing nominal 2×10^{13} vector genomes”).

Several additional special characters are used less frequently in HCPCS Level II descriptor language for drug and biological product codes. These include the ampersand (&), brackets ([]), quotation marks (" or '), the plus sign (+), the equals sign (=), the greater-than sign (>), the less-than sign (<), and the pound or hash sign (#). Other special characters and symbols, such as trademarks (™), registration marks (®), at sign (@), do not appear in HCPCS Level II long descriptions, as they fall outside the standardized descriptor format established by CMS.

4.2 HCPCS Level II Drug and Biological Long Description Components

A typical HCPCS Level II code description for a drug and biological product follows a standardized format consisting of the route of administration, the nonproprietary name, and the dose description. In such cases, the HCPCS Level II code descriptor will follow the format:

HCPCS Level II code XXXXX, “route of administration, nonproprietary name, dose description”

Each HCPCS Level II code long descriptor is composed of key elements that serve a specific purpose.

- **Route of administration:** Specifies how the drug is delivered, including, but not limited to, injection, inhalation, oral, or topical.
- **Nonproprietary name:** Identifies the drug or biological product. Typically, CMS uses the nonproprietary name from the FDA-approved labeling to ensure consistency and clarity. For products approved under a BLA, the nonproprietary name (also called the proper name) consists of a core name (e.g., denosumab) and a distinguishing four-letter suffix (e.g., denosumab-kyqq). Most products approved under a BLA prior to implementation of the [FDA’s 2017 Guidance for Industry](#) do not have the four-letter suffix.
- **Dose description:** Defines the quantity of the product represented in one billing unit for claims processing. This can be expressed per milligram (mg), per microgram (mcg), per milliliter (mL), per therapeutic dose, per vial, or in another unit appropriate to the product. CMS has a long-standing convention to assign dose descriptors to the smallest amount of the product that could be billed in multiple units to accommodate a variety of doses and support streamlined billing. This structure allows providers to bill the appropriate number of units to reflect the amount of the product.

4.2.1 Drug and Biological Long Description – Single Product (No Other Products Marketed with the Same Nonproprietary Name)

A typical HCPCS Level II code description for a drug or biological product approved under section 351(k) of the PHS Act follows a standardized format consisting of the route of administration, the nonproprietary name, and the dose description. In such cases, the HCPCS Level II code descriptor will follow the format:

HCPCS Level II code XXXXX, “route of administration, nonproprietary name, dose description”

4.2.2 Drug Product Long Description – Multiple Products (Other Products Marketed with the Same Nonproprietary Name)

When there are multiple drugs approved and marketed with the same nonproprietary name, CMS will further distinguish a new HCPCS Level II code by using the manufacturer or brand name, when deemed appropriate (e.g., separate NDA approval numbers). This additional specificity ensures that each product can be accurately identified and prevents confusion between products that share the same nonproprietary name but cannot share the same HCPCS Level II code for billing purposes (e.g., when two products with the same nonproprietary name are approved under different NDAs and are not rated as TE). In such cases, the typical HCPCS Level II code descriptor will follow the format:

HCPCS Level II code XXXXX, “route of administration, nonproprietary name (manufacturer/brand name), dose description”

CMS aims to mitigate marketing biases within the HCPCS Level II code set. When determining whether to include the manufacturer or brand name in a new HCPCS Level II code descriptor, CMS typically applies the following conventions. If the other existing HCPCS Level II codes with nonproprietary name or active ingredient already utilizes the manufacturer name, CMS will follow the same convention. However, this determination depends on whether the manufacturer also manufactures a generic or TE product, in which CMS will typically then use the brand name. If the other existing HCPCS Level II codes do not specify the manufacturer or brand name, CMS will move forward with including the manufacturer or labeler name in the new HCPCS Level II code first, unless circumstances exist that prevent that option from appropriately distinguishing the drug.

In some situations, the manufacturer who received the FDA approval is not the same name that is used on the product's package, otherwise known as a labeler name. In these situations, CMS will use the labeler's or the distributor's name that appears on the product's package, and not the company that received the FDA approval.

4.2.3 Biosimilar Long Description

For biosimilar biological products approved under section 351(k) of the PHS Act, a new HCPCS Level II code long description will include the word "biosimilar." Many biosimilar products include a unique four-letter suffix assigned by the FDA, in addition to the nonproprietary name, to distinguish the biosimilar from the reference biological product and from other biosimilars. In this case, the unique suffix serves as the distinguishing identifier in the HCPCS Level II code long descriptor. In such cases, the typical HCPCS Level II code descriptor will follow the format:

HCPCS Level II code XXXXX, "route of administration, nonproprietary name-suffix, biosimilar, dose description"

The reference biological product retains its existing HCPCS Level II code upon the approval of a biosimilar, so long as the two products are approved under separate BLA approval numbers.

4.2.4 Drug Long Description – Not Therapeutically Equivalent

CMS considers TE status when evaluating whether a new HCPCS Level II code is warranted for a product that shares a nonproprietary name with a product that already has an existing code. Specifically, if a product is determined to be TE in the FDA's Orange Book to a product that already has an existing HCPCS Level II code, CMS will typically not establish a new HCPCS Level II code for the product. Instead, the TE product will be grouped under the existing HCPCS Level II code as the reference listed drug.

When a product is approved under an NDA and shares a nonproprietary name with a product that has an existing code, and the manufacturer holds both TE and not-TE approvals, CMS will typically include "not therapeutically equivalent to" followed by the existing HCPCS Level II code to which it is being compared. The typical HCPCS Level II code descriptor will follow the format:

HCPCS Level II code XXXXX, "route of administration, nonproprietary name (manufacturer/brand name), not therapeutically equivalent to XXXXX, dose description"

When a drug has one or more TE products on the market, the applicant must identify and document all related products in the MEARIST[™] application, as this information is used by CMS to determine the appropriate HCPCS Level II coding outcome.

4.2.5 Unique Long Description – Radiopharmaceuticals

There may be circumstances that fall outside of the code description scenarios described in the preceding sections of this manual, such as radiopharmaceuticals. Radiopharmaceuticals contain a radioactive component (radionuclide) and are used for diagnostic imaging or therapeutic purposes. These products present unique HCPCS Level II coding considerations due to their short half-lives. In the HCPCS Level II code description, CMS may include the route of administration, the nonproprietary name, the radionuclide (e.g., technetium Tc 99m, fluorine F-18, iodine I-131), and the dose description. Because radiopharmaceuticals are commonly dosed in units of radioactivity (millicuries or megabecquerels) rather than mass, the dosage description in the HCPCS Level II code will reflect the appropriate unit of radioactivity or is user specific. In addition, within the HCPCS Level II code description, CMS may distinguish diagnostic radiopharmaceuticals (used for imaging) and therapeutic radiopharmaceuticals (used for treatment). Given the short half-life of many radiopharmaceuticals, CMS may also consider a product's approximate window of clinical usability, for example a period of approximately six hours from calibration, when evaluating dose description and billing conventions for these products. The applicant should note all relative information pertaining to radiopharmaceuticals within the MEARIS™ application.

4.3 Route of Administration

HCPCS Level II code descriptors include the route of administration as a standard element of the code description. The route of administration identifies how a drug or biological product is delivered to an individual. CMS generally reflects the route of administration as described in the title of the FDA-approved labeling for the product.

CMS will typically use the general term “injection” in the HCPCS Level II code descriptor to describe the route of administration for drugs and biological products administered parenterally, even when the product is approved for only a single route of administration. When the term “injection” appears without qualification, it encompasses multiple routes of administration, such as, intravenous (IV), intramuscular, subcutaneous, intradermal, or intravitreal. This approach is consistent with CMS’ practice of creating HCPCS Level II codes for products themselves and it accommodates the possibility that a product's approved routes of administration may expand over time.

When a product has multiple FDA-approved routes of administration that are approved under two unique FDA approval numbers, CMS will consider specifying the route of administration in the HCPCS Level II code description to ensure that each distinct product can be accurately identified. In cases where a single HCPCS Level II code covers a product that may be administered by more than one parenteral route, claims should be billed with either the JA modifier to indicate IV infusion of the drug or the JB modifier to indicate subcutaneous (SC/SQ) injection of the drug, so that the route of administration is captured at the claim level.

4.4 Dose Description Determination

CMS follows a general framework, described below, to determine an appropriate dose description for a new or revised HCPCS Level II code. This framework is intended to promote consistency and support efficient claims processing. CMS may deviate from this general approach based on product-specific clinical, regulatory, or administrative factors. As a general matter, CMS aims to assign dose descriptors to the smallest amount of the product that could be billed in multiple units, allowing providers to accommodate a variety of doses and supporting streamlined billing.

This general approach reflects practical limits within the Medicare claims processing system, which generally permits no more than 999 units to be reported on a single claim line per date of service for

Medicare fee-for-service claims submitted on the CMS-1500 form. Although multiple claim lines may be used to accommodate billing amounts that exceed 999 units, CMS generally aims to determine a dose description that allows a single claim line to be used in most circumstances. As a result, the HCPCS Level II code descriptor generally focuses on the drug or biological product dosage itself rather than the form in which it is supplied, such as powder or solution. Dosage information must be drawn from the prescribing information and must be noted within the appropriate question in the MEARIS™ application.

Product specific factors may support the use of an alternative methodology to calculate the dose descriptor. In certain situations, an applicant may believe that a dose descriptor lower or higher than what CMS would otherwise assign is more appropriate for the product. If an applicant believes a different dose description is most appropriate, the applicant must provide a clear and detailed rationale within the MEARIS™ application explaining why the requested dose descriptor is warranted.

4.4.1 Required Dosage Information

Applicants must provide the prescribing information that allows CMS to calculate the minimum and maximum daily dosage for the product. When selecting a dose description, CMS prefers to use whole numbers, such as 1 mg. Fractions should generally only be used if the product's recommended doses are also expressed as a fraction, such as 0.05 mg or 2.5 mg. The use of a fractional dose descriptor does not necessarily reflect the minimum or maximum daily dosage for the product. Rather, a fractional dose descriptor may be appropriate when one of the recognized administration doses for the product is expressed as a fraction, even if other doses are administered in whole number amounts.

4.4.2 Discarded Drug Policy and Dose Description Determination

The dose description methodology described in this section applies to drugs and biological products that are subject to the Medicare discarded drug policy. Under that policy, when a drug or biological product is supplied in a single-use vial or package and a portion of the drug must be discarded because it is not administered to the individual, the discarded amount may be separately billed on a claim. Because providers may bill for both the administered dose and discarded amounts from a single-use vial or container, CMS calculates the lowest common dose description based on the minimum and maximum daily doses as documented in the product's FDA-approved prescribing information, rather than on the vial size or package configuration in which the product is supplied.

4.4.3 General Methodology for Calculating the Dose Description

The dose description is the specific quantity of a drug or biological product that equals one reportable billing unit on a claim. CMS follows the following general methodology to identify the lowest common dose description based on the product's minimum and maximum daily doses, as described in the product's prescribing information. Product-specific clinical, regulatory, or administrative factors may result in variations from the general methodology described in this document. The examples provided below are intended to be illustrative; dose description calculations for individual products may vary.

4.4.3.1 Step 1: Identify the Maximum Daily Dose from the Prescribing Information

CMS begins by reviewing the prescribing information to identify the recommended drugs or biological products minimum and maximum daily doses. These values establish the dose boundaries that will be used throughout the dose description calculation process.

4.4.3.2 Step 2: Determine Whether the Dose Is Weight-Based or Body Surface Area-Based

If the product's recommended dose is based on an adult's weight, CMS generally uses a standard weight of 70 kg for calculation purposes. If the dose is based on an adult's body surface area, CMS generally uses a standard body surface area of 1.81 m². When a pediatric dose must be considered, the applicant should consult the prescribing information and reputable clinical guidelines to determine the appropriate weight in kilograms or body surface area in square meters according to the relevant age group. This approach is intended to promote consistency and is not intended to reflect individual dosing or clinical decision-making. CMS may use a different approach when appropriate based on product-specific factors.

Table 3 below illustrates a calculation of the minimum and maximum doses for a drug whose recommended dosage is based on an individual's body weight (expressed in mg/kg). To use this table, multiply the recommended dose (in mg/kg) by the standard adult reference weight of 70 kg. In this example, a drug with a recommended daily dose range of 3 mg/kg to 30 mg/kg results in a minimum dose of 210 mg and a maximum dose of 2,100 mg. These two values, 210 mg and 2,100 mg, will be carried forward into the subsequent dose description calculation steps.

Table 3: For a drug with a recommended daily dose range of 3 mg/kg to 30 mg/kg.

	Calculation	Result
Minimum dose	3 mg/kg × 70 kg	210 mg
Maximum dose	30 mg/kg × 70 kg	2,100 mg

Table 4 below illustrates a calculation of a daily dose for a drug that is dosed based on body surface area, expressed in grams per square meter (g/m²). To use this table, multiply the recommended daily dose (in g/m²) by the standard reference body surface area for an adult of 1.81 m². In this example, a drug with a recommended daily dose of 10 g/m² results in a daily dose of 18.1 g. This approach is common for chemotherapy and other specialty drugs where dosing is tied to an individual's body surface area rather than body weight alone.

Table 4: For a drug with a recommended daily dose of 10 grams/m².

	Calculation	Result
Daily dose	10 g/m ² × 1.81 m ²	18.1 g

4.4.3.3 Step 3: Account for Dosing Frequency (If the Drug Is Administered More Than Once Per Day)

If the product is administered more than once per day, CMS calculates the total minimum and maximum daily dose by multiplying the single dose amount by the number of administrations per day. When prescribing information specifies a dosing interval (e.g., every 12 hours) rather than an explicit daily frequency, CMS may calculate the daily dose by dividing 24 hours by the dosing interval to determine the number of doses per day, if appropriate for the product specific dose. This approach may vary for products with complex administration schedules or based on product-specific factors.

Table 5 below illustrates the calculation of a daily dose for a drug that is administered more than once per day. To use this table, first determine the number of doses per day by dividing 24 hours by the dosing interval specified in the prescribing information. In this example, a dosing interval of every 12 hours results in 2 doses per day (24 hours / 12 hours = 2 doses). That frequency is then applied to both the minimum and maximum single doses to calculate the total daily dose range. A minimum single dose of 210 mg becomes 420 mg per day, and a maximum single dose of 2,100 mg becomes 4,200 mg per day.

This step ensures that the billing unit reflects the full daily drug utilization rather than just a single administration.

Table 5: For a drug with a recommended dose range of 210 mg every 12 hours.

	Calculation	Result
Frequency per day	24 hours / 12 hours	2
Minimum dose	210 mg $\times$ 2	420 mg
Maximum dose	2,100 mg $\times$ 2	4,200 mg

4.4.3.4 Step 4: Test Whole Number Dose Descriptions

CMS then tests incrementally whole-number dose descriptions, beginning with the smallest possible whole number, to identify the lowest amount of drug represented by one billing unit at which both the minimum and maximum daily doses result in 999 units or fewer. The 999-unit threshold is a claims processing constraint, and both the minimum and maximum daily doses must fall within this limit for a billing unit to be considered acceptable. CMS generally calculates the amount of drug represented by one billing unit based on the weighted amount of the drug (e.g., mg or g), not the volume of the solution (e.g., mL). This approach may vary based on product-specific factors.

Table 6 below illustrates the process of identifying the smallest whole number dose description that keeps the number of billing units at or below 999 for both the minimum and maximum daily doses. To use this table, divide both the minimum and maximum daily doses by the dose description being tested, beginning with 1 mg, and checking whether both results fall at or below 999 units. If either result exceeds 999 billing units, proceed to the next whole number and repeat the test.

Table 6: For a drug with a minimum daily dose of 210 mg and a maximum daily dose of 2,100 mg. Continue to try the next whole number until both the minimum and maximum doses result in 999 units or fewer. In this example, the appropriate billing unit is 3 mg.

Dose Description Test		Calculation	Units	Within 999 Units?
1 mg	Minimum dose	210 mg / 1 mg	210 units	Yes
	Maximum dose	2,100 mg / 1 mg	2,100 units	No
2 mg	Minimum dose	210 mg / 2 mg	105 units	Yes
	Maximum dose	2,100 mg / 2 mg	1,050 units	No
3 mg	Minimum dose	210 mg / 3 mg	70 units	Yes
	Maximum dose	2,100 mg / 3 mg	700 units	Yes
4 mg	Minimum dose	210 mg / 4 mg	52.5 units	Yes, but not a whole number
	Maximum dose	2,100 mg / 4 mg	525 units	Yes
5 mg	Minimum dose	210 mg / 5 mg	42 units	Yes
	Maximum dose	2,100 mg / 5 mg	420 units	Yes

In this example, at 1 mg per billing unit, the minimum dose yields 210 billing units, which is acceptable, however, the maximum dose yields 2,100 billing units, which exceeds 999 and may present billing challenges, as it generally cannot be captured on a single claim line. At 2 mg per unit, the minimum dose

yields 105 billing units, which also falls within a billable range; however, the maximum dose yields 1,050 billing units, which similarly exceeds 999 and may present the same billing limitations. At 3 mg per unit, the minimum dose yields 70 billing units, and the maximum dose yields 700 billing units, and both results are at or below 999 units. Therefore, 3 mg is the appropriate dose description per billing unit, as it is the smallest whole number at which both the minimum and maximum daily doses fall within the 999-unit claims processing limit. Although dose descriptions of 4 mg and 5 mg also result in billing units at or below 999 for both the minimum and maximum daily doses, 3 mg is the preferred dose description because it is the smallest whole number dose description at which both the minimum and maximum daily doses yield whole number billing units that fall within the 999-unit claims processing limit. However, product specific factors may result in the selection of a different dose descriptor.

4.4.3.5 Step 4a: Test Whole Number Dose Descriptions – Single-Dose Containers

If the product is supplied in a single-dose container, CMS will ensure that the amount of drug specified on the label is divisible by the amount of drug represented in one billing unit. In this situation, CMS may adjust the dose description such the amount of drug on the label divided by the dose description equals a whole number. For example, if the product from Table 6 is supplied in a 100 mg single-dose vial, a dose description of 3 mg would not result in a whole number of billing units per vial ($100 \text{ mg} / 3 \text{ mg} = 33.33$ units). Since claims cannot accept fractional billing units, the provider would have to round up to 34 billing units per vial, which would lead to inaccurate billing. Similarly, 4 mg would not be applicable. Though a dose description of 4 mg would result in a whole number of billing units per vial ($100 \text{ mg} / 4 \text{ mg} = 25$ units), it produces a fractional billing unit for the minimum daily dose and therefore cannot be used. The amount of drug represented by one billing unit could be adjusted to 5 mg so that each single-dose vial would contain 20 billing units ($100 \text{ mg} / 5 \text{ mg} = 20$ units) while also satisfying the 999-unit threshold for both minimum and maximum daily doses. CMS' determinations on the appropriate dose descriptor may vary based on product-specific factors.

4.4.3.6 Step 5: Test Fractional Dose Descriptions

CMS will consider using a fractional dose description only if the drug's recommended doses are also expressed as a fraction in the prescribing information. A fraction is not used simply for convenience; it must be supported by the way the drug is dosed in clinical practice as documented in the prescribing information.

Table 7 below walks through the process of identifying the smallest fractional dose description that keeps the number of billing units at or below 999 for both the minimum and maximum daily doses. To use this table, divide both the minimum and maximum daily doses by the dose description being tested, beginning with 0.1 mg, and check whether both results fall at or below 999 units. If either result exceeds 999 billing units, proceed to the next fractional number and repeat the test.

Table 7: For a drug with a minimum daily dose of 84 mg (1.2 mg/kg * the average 70 kg adult) and a maximum daily dose of 175 mg (2.5 mg/kg * the average 70 kg adult). Continue to try the next whole number until both the minimum and maximum doses result in 999 units or fewer. In this example, the appropriate billing unit is 0.2 mg.

		Calculation	Units	Within 999 Units?
Test 0.1 mg per unit	Minimum dose	84 mg / 0.1 mg per unit	840 units	Yes
	Maximum dose	175 mg / 0.1 mg per unit	1,750 units	No
	Minimum dose	84 mg / 0.2 mg per unit	420 units	Yes

		Calculation	Units	Within 999 Units?
Test 0.2 mg per unit	Maximum dose	175 mg / 0.2 mg per unit	875 units	Yes

In this example, at 0.1 mg per billing unit, the minimum dose yields 840 billing units, which is acceptable, but the maximum dose yields 1,750 billing units, which exceeds 999 and generally would not be selected because the maximum dose would not be able to be billed on a single claim line. At 0.2 mg per unit, the minimum dose yields 420 billing units, which is acceptable, and the maximum dose yields 875 billing units, and both results are at or below 999 units. Therefore, 0.2 mg is the appropriate dose description per billing unit in this example, as it is the smallest whole number at which both the minimum and maximum daily doses fall within the 999-unit claims processing limit. Product-specific factors may lead to selection of different dose descriptors.

4.4.4 User-Specific Dosing

If the product's recommended dose is user-specific, such as in the case of autologous cellular and gene therapy treatments, CMS considers adding "per therapeutic dose" as the dose description to accurately reflect the individualized nature of the dosing. These products cannot be assigned a standardized billing unit because the dose is inherently individualized and is not measured in conventional weight-based or volume-based amounts. CMS may also consider a user specific dose description, such as per treatment or per course of therapy, for other categories of products with individualized dosing, where appropriate.

4.4.5 Unique Dose Description Scenarios

There may be circumstances that fall outside of the dose description scenarios described in the preceding sections of this manual. CMS may modify the above methodology based on product-specific factors. For example, there may be situations in which the lowest common dose description cannot be determined because both the minimum and/or maximum daily doses exceed the 999-unit claims processing limit. Another example is for multiple-dose containers (vials or packages designed for multiple users), for which the JW modifier is not appropriate for reporting discarded amounts. In such cases, CMS may not complete step 4a described above to establish a dose description.

With regard to clotting factors for which a furnishing fee is added (as described in section 1842(o)(5) of the Act), the furnishing fee is added per unit of clotting factor. To facilitate the addition of the furnishing fee, CMS generally does not apply the steps described above to determine the dose description. For example, when a provider bills for a clotting factor, such as HCPCS Level II code J7190, "Factor viii (antihemophilic factor, human) per i.u.," more than one claim line may be required because the amount billed exceeds 999 billing units, but the dose description of per i.u. is appropriate to facilitate the addition of the furnishing fee.

In addition, there may be times when the active ingredient used is not easily trackable or quantifiable by the end user. In these cases, the dose description may not be determined by the active ingredient itself, but rather by the finished product as it appears in the package. This distinction is important, since it clarifies how dosing is understood and reported for certain products.