Overview
Irinoctecan hydrochloride (HCL) is an antineoplastic drug that is a semisynthetic derivative of camptothecin, an alkaloid extract from plants. The drug works by causing strand breaks in DNA that the cell cannot repair leading to cell death.

Irinotecan is FDA approved for the following indications:

- As a component of first-line therapy in combination with 5-fluorouracil and leucovorin for patients with metastatic carcinoma of the colon or rectum.
- For patients with metastatic carcinoma of the colon or rectum whose disease has recurred or progressed following initial fluorouracil-based therapy.

Irinotecan will be covered for its FDA approved use, as well as for the treatment of the following off-labeled indications. Refer also to the NCCN Compendium® for additional off-label indications.

- Carcinoma of small intestine
- Non small-cell lung carcinoma (alone or in combination for the treatment of locally advanced and/or metastatic stage IIIB or IV NSCLC)
- Small-cell lung carcinoma, extensive-stage small-cell lung cancer, first line treatment, in combination with cisplatin
- Cervical carcinoma
- Pancreatic carcinoma
- Advanced esophageal carcinoma
- Metastatic gastric carcinoma
- Primary brain tumor
- Epithelial ovarian cancer for platinum-resistant or platinum-refractory patients
- Metastatic breast cancer, refractory

Guidelines
This policy guideline 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 Medicare 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.

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;
There are many reasons to consider an unlabeled use for a cancer chemotherapy agent. Some of these are: compendia, authoritative medical literature and/or accepted standards of medical practice.

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. In the case of unlabeled use for anti-cancer drugs, the conditions for Medicare coverage and reimbursement have been especially well outlined.

Note: This policy guideline 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 Program Integrity Manual, Section 13.5.1, in order to be covered under Medicare, a service shall be reasonable and necessary.

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 (USP), the National Formulary (NF), the United States Homeopathic Pharmacopoeia (HPUS), or in New Drugs or Accepted Dental Remedies (except for any drugs and biologicals unfavorably evaluated therein). The inclusion of an item in one of these publications does not necessarily mean that the item is a drug or biological. 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. [See the Medicare Advantage Policy Guideline titled Self-Administered Drug(s) (SAD).]

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.

There are many reasons to consider an unlabeled use for a cancer chemotherapy agent. Some of these are:

- Drugs may be effective for many other cancers in addition to the ones that were considered in the primary drug labeling.
• Many chemotherapeutic agents are given in combinations. Any one of the drugs in the combination may not have been approved in the initial labeling of the products. In addition the combination of effective chemotherapeutic agents changes over time.
• Cancer chemotherapeutic agents are always changing and improving over time.
• Oncologists are often left with few approved treatment options if initial treatment regimens have failed.

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.

Several cancer chemotherapeutic agents and regimes have been developed and approved by the Food and Drug Administration (FDA) to treat various types of cancer. The intended mechanism of action is to interfere with or prevent the growth of malignant (cancerous) cells.

Generally, cancer chemotherapeutic agents are covered only if all of the following requirements are met:
• Documentation is present to support that the drug is safe and effective and is being administered for an approved indication.
• Documentation in the patient’s medical record supports the medical necessity of administering the chemotherapy drug to that individual patient.
• Documentation in the patient’s medical record supports that the chemotherapy drug was administered as billed.

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
- American Hospital Formulary Service-Drug Information (AHFS-DI)
- Thomson Micromedex DrugDex
- Clinical Pharmacology
- Wolters Kluwer Lexi-Drugs

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;
• Narrative text in AHFS or Clinical Pharmacology is supportive; or
• Indication is listed in Lexi-Drugs as “Use: Off-Label” and rated as “evidence level A”

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. Self-administered drugs are not covered and should not be submitted to Medicare unless requested to do so by the beneficiary. [See the Medicare Advantage Policy Guideline titled Self-Administered Drug(s) (SAD).]

Chemotherapy Administration
Chemotherapy administration codes apply to parenteral administration of nonradionuclide anti-neoplastic drugs; and also to anti-neoplastic agents provided for treatment of noncancer diagnoses (e.g., cyclophosphamide for autoimmune conditions) or to substances such as: Monoclonal antibody agents and other biologic response modifiers. The following drugs are commonly considered to fall under the category of monoclonal antibodies: infliximab, rituximab, alemtuzumab, gemtuzumab, and trastuzumab. Drugs commonly considered to fall under the category of hormonal antineoplastics include leuprolide acetate and goserelin acetate. The drugs cited are not intended to be a complete list of drugs that may be administered using the chemotherapy administration codes. The administration of anti-anemia drugs and anti-emetic drugs by injection or infusion for cancer patients are not considered chemotherapy administration. If performed to facilitate the chemotherapy infusion or injection, the following services and items are included and are not separately billable:

Camptosar® (Irinotecan)
- Use of local anesthesia;
- IV access;
- Access to indwelling IV, subcutaneous catheter or port;
- Flush at conclusion of infusion;
- Standard tubing, syringes and supplies; and
- Preparation of chemotherapy agent(s).

Coding Guidelines
- Use the appropriate J code to report the drug being used.
- True codes reflect the dosage of the drug; the number of units should indicate the total number of units given in item 24G of the CMS 1500 form. If filing electronically, the total units should be placed in the NSF Format, Record FAO-18.0, ANSI 837 format Segment SV1-05 (3032) or Segment SV2-04 (3052).

Documentation Requirements
Medical record documentation maintained by the ordering/referring physician must substantiate the medical need for the use of these chemotherapy drugs by clearly indicating the condition for which these drugs are being used. This might include the type of cancer, staging, if applicable, prior therapy and the patient’s response to that therapy. This documentation is usually found in the history and physical or in the office/progress notes.

If the provider of the service is other than the ordering/referring physician, that provider must maintain copies of the ordering/referring physician’s order for the chemotherapy drug. The physician must state the clinical indication/medical need for using the chemotherapy drug in the order.

The medical record must include the following information:
- The name of the drug or biological administered;
- The route of administration;
- The dosage (e.g., mgs, mcgs, cc's or IU's); and
- The duration of the administration (for CPT codes that are time based).

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.

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ICD-10 Diagnosis Code | Description
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C79.61 | Secondary malignant neoplasm of right ovary
C79.62 | Secondary malignant neoplasm of left ovary
C79.71 | Secondary malignant neoplasm of right adrenal gland
C79.72 | Secondary malignant neoplasm of left adrenal gland
C79.81 | Secondary malignant neoplasm of breast
C79.82 | Secondary malignant neoplasm of genital organs
C79.89 | Secondary malignant neoplasm of other specified sites
C79.9 | Secondary malignant neoplasm of unspecified site
C7A.1 | Malignant poorly differentiated neuroendocrine tumors
C7A.8 | Other malignant neuroendocrine tumors
C7B.8 | Other secondary neuroendocrine tumors
C80.0 | Disseminated malignant neoplasm, unspecified
C80.1 | Malignant (primary) neoplasm, unspecified
C80.2 | Malignant neoplasm associated with transplanted organ
D37.1 | Neoplasm of uncertain behavior of stomach
D37.8 | Neoplasm of uncertain behavior of other specified digestive organs
D37.9 | Neoplasm of uncertain behavior of digestive organ, unspecified
Z80.49 | Family history of malignant neoplasm of other genital organs
Z85.00 | Personal history of malignant neoplasm of unspecified digestive organ
Z85.01 | Personal history of malignant neoplasm of esophagus
Z85.028 | Personal history of other malignant neoplasm of stomach
Z85.038 | Personal history of other malignant neoplasm of large intestine
Z85.068 | Personal history of other malignant neoplasm of small intestine
Z85.07 | Personal history of malignant neoplasm of pancreas
Z85.118 | Personal history of other malignant neoplasm of bronchus and lung
Z85.43 | Personal history of malignant neoplasm of ovary
Z85.830 | Personal history of malignant neoplasm of bone
Z85.831 | Personal history of malignant neoplasm of soft tissue
Z85.841 | Personal history of malignant neoplasm of brain
Z85.858 | Personal history of malignant neoplasm of other endocrine glands

**DEFINITIONS**

**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).

**PURPOSE**

The Medicare Advantage Policy Guideline documents are generally used to support UnitedHealthcare Medicare Advantage claims processing activities and facilitate providers’ submission of accurate claims for the specified services. The document can be used as a guide to help determine applicable:

- Medicare coding or billing requirements, and/or
- Medical necessity coverage guidelines; including documentation requirements.
UnitedHealthcare follows Medicare guidelines such as LCDs, NCDs, and other Medicare manuals for the purposes of determining coverage. It is expected providers retain or have access to appropriate documentation when requested to support coverage. Please utilize the links in the References section below to view the Medicare source materials used to develop this resource document. This document is not a replacement for the Medicare source materials that outline Medicare coverage requirements. Where there is a conflict between this document and Medicare source materials, the Medicare source materials will apply.

REFERENCES

CMS National Coverage Determination (NCD)
NCD 110.7 Anti-Cancer Chemotherapy for Colorectal Cancer

CMS Local Coverage Determinations (LCDs)

<table>
<thead>
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<th>LCD</th>
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<th>Medicare Part B</th>
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<td>L34093 (Chemotherapy and Biologicals) CGS</td>
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<td>L33727 (Irinotecan) First Coast</td>
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CMS Articles

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<td>A53049 (Approved Drugs and Biologicals; Includes Cancer Chemotherapeutic Agents) Novitas</td>
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<td>A52701 (Drugs and Biologicals - Chemotherapeutic Agents) Cahaba Retired 02/25/2018</td>
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CMS Benefit Policy Manual
Chapter 15; § 50 Drugs and Biologicals

UnitedHealthcare Commercial Policy
Oncology Medication Clinical Coverage Policy

Others

CMS Program Integrity Manual, § 13.5.1 Reasonable and Necessary Provisions in LCDs
Correct Coding Initiative - Medicare Contractor Beneficiary and Provider Communications Manual, Chapter 5.
Medicare Managed Care Manual Chapter 4; § 10.7 Clinical Trials
NCCN Drugs & Biologics Compendium
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

GUIDELINE HISTORY/REVISION INFORMATION

Revisions to this summary document do not in any way modify the requirement that services be provided and documented in accordance with the Medicare guidelines in effect on the date of service in question.

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<td>09/11/2019</td>
<td>• Annual review</td>
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<tr>
<td></td>
<td>• Added ICD-10 codes C48.0 and C79.9 effective 01/01/2019</td>
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TERMS AND CONDITIONS

The Medicare Advantage Policy Guidelines are applicable to UnitedHealthcare Medicare Advantage Plans offered by UnitedHealthcare and its affiliates.

These Policy Guidelines are provided for informational purposes, and do not constitute medical advice. Treating physicians and healthcare providers are solely responsible for determining what care to provide to their patients. Members should always consult their physician before making any decisions about medical care.
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 member specific benefit plan document identifies which services are covered, which are excluded, and which are subject to limitations. In the event of a conflict, the member specific benefit plan document supersedes the Medicare Advantage Policy Guidelines.

Medicare Advantage Policy Guidelines are developed as needed, are regularly reviewed and updated, and are subject to change. They represent a portion of the resources used to support UnitedHealthcare coverage decision making. UnitedHealthcare may modify these Policy Guidelines at any time by publishing a new version of the policy on this website. Medicare source materials used to develop these guidelines include, but are not limited to, CMS National Coverage Determinations (NCDs), Local Coverage Determinations (LCDs), Medicare Benefit Policy Manual, Medicare Claims Processing Manual, Medicare Program Integrity Manual, Medicare Managed Care Manual, etc. The information presented in the Medicare Advantage Policy Guidelines is believed to be accurate and current as of the date of publication, and is provided on an "AS IS" basis. Where there is a conflict between this document and Medicare source materials, the Medicare source materials will apply.

You are responsible for submission of accurate claims. Medicare Advantage Policy Guidelines are intended to ensure that coverage decisions are made accurately based on the code or codes that correctly describe the health care services provided. UnitedHealthcare Medicare Advantage Policy Guidelines 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 or guarantee claims payment.

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*For more information on a specific member’s benefit coverage, please call the customer service number on the back of the member ID card or refer to the Administrative Guide.