Medical Policy:

Onivyde® (irinotecan liposome) Intravenous

POLICY NUMBER	LAST REVIEW	ORIGIN DATE
MG.MM.PH.158	March 7, 2025	

The treating physician or primary care provider must submit to EmblemHealth, or ConnectiCare, as applicable (hereinafter jointly referred to as "EmblemHealth"), the clinical evidence that the member meets the criteria for the treatment or surgical procedure. Without this documentation and information, EmblemHealth will not be able to properly review the request preauthorization or post-payment review. The clinical review criteria expressed below reflects how EmblemHealth determines whether certain services or supplies are medically necessary. This clinical policy is not intended to pre-empt the judgment of the reviewing medical director or dictate to health care providers how to practice medicine. Health care providers are expected to exercise their medical judgment in rendering appropriate care. Health care providers are expected to exercise their medical judgment in rendering appropriate care.

EmblemHealth established the clinical review criteria based upon a review of currently available clinical information (including clinical outcome studies in the peer reviewed published medical literature, regulatory status of the technology, evidence-based guidelines of public health and health research agencies, evidence-based guidelines and positions of leading national health professional organizations, views of physicians practicing in relevant clinical areas, and other relevant factors). EmblemHealth expressly reserves the right to revise these conclusions as clinical information changes and welcomes further relevant information. Each benefit program defines which services are covered. The conclusion that a particular service or supply is medically necessary does not constitute a representation or warranty that this service or supply is covered and/or paid for by EmblemHealth, as some programs exclude coverage for services or supplies that EmblemHealth considers medically necessary.

If there is a discrepancy between this guideline and a member's benefits program, the benefits program will govern. Identification of selected brand names of devices, tests and procedures in a medical coverage policy is for reference only and is not an endorsement of any one device, test or procedure over another. In addition, coverage may be mandated by applicable legal requirements of a state, the Federal Government or the Centers for Medicare & Medicaid Services (CMS) for Medicare and Medicaid members. All coding and web site links are accurate at time of publication.

EmblemHealth may also use tools developed by third parties, such as the MCG™ Care Guidelines, to assist us in administering health benefits. The MCG™ Care Guidelines are intended to be used in connection with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice. EmblemHealth Services Company, LLC, has adopted this policy in providing management, administrative and other services to EmblemHealth Plan, Inc., EmblemHealth Insurance Company, EmblemHealth Services Company, LLC, and Health Insurance Plan of Greater New York (HIP) related to health benefit plans offered by these entities. ConnectiCare, an EmblemHealth company, has also adopted this policy. All of the aforementioned entities are affiliated companies under common control of EmblemHealth Inc.

Definitions

Onivyde (irinotecan liposome) is irinotecan, a topoisomerase inhibitor, encapsulated in lipid bilayer vesicle or lipsome. The lipid bilayer vesicle allows higher concentrations in the body with lower doses compared to irinotecan HCL (non liposomal formulation).

Irinotecan and its active metabolite SN-38 bind reversibly to the topoisomerase 1-DNA complex and prevent re- ligation of the single strand breaks, leading to exposure time-dependent double-strand DNA damage and cell death.

Length of Authorization

Coverage will be provided for 6 months and may be renewed.

Dosing Limits [Medical Benefit]

Max Units (per dose and over time):

172 billable units per 14 days

Guideline

I. Initial Approval Criteria

Onivyde *may be considered medically necessary if one of the below conditions are met* ***AND*** *use is consistent with the medical necessity criteria that follows:*

1. Pancreatic Adenocarcinoma † ‡ Φ

A. Used in combination with oxaliplatin, fluorouracil and leucovorin; **AND**

i. Used as first-line therapy; **AND**

a. Patient has metastatic disease; **OR**

b. Patient has locally advanced disease; **AND**

1.) Patient has good performance status (defined as ECOG PS 0-1, with good biliary drainage and adequate nutritional intake); **OR**

ii. Used as induction therapy followed by chemoradiation in patients without systemic metastases; **AND**

a. Patient has locally advanced disease; **AND**

b. Patient has good performance status (defined as ECOG PS 0-1, with good biliary drainage and adequate nutritional intake); **OR**

B. Used in combination with fluorouracil and leucovorin; **AND**

i. Patient has locally advanced or metastatic disease; **AND**

a. Used as subsequent therapy after disease progression with one of the following:

1.) Fluoropyrimidine (5-FU or capecitabine) based therapy with no prior irinotecan; **OR**

2.) Gemcitabine-based therapy; **OR**

ii. Patient has local or metastatic disease recurrence after resection; **AND**

a. Patient completed primary therapy < 6 months ago; **AND**

1.) Patient previously received one of the following:

- Fluoropyrimidine (5-FU or capecitabine) based therapy that did not include irinotecan; **OR**
- Gemcitabine-based therapy; **OR**

b. Patient completed primary therapy ≥ 6 months ago; **AND**

1.) Used as alternate systemic therapy not previously used

† FDA Approved Indication(s); ‡ Compendia Recommended Indication(s); Φ Orphan Drug

Limitations/Exclusions

Onivyde (irinotecan liposome) is not considered medically necessary when any of the following selection criteria is met:

1. Disease progression while taking Onivyde (irinotecan liposome)
2. Disease progression while taking irinotecan HCL (non liposomal formulation)
3. Dosing exceeds single dose limit of Onivyde (irinotecan liposome)
    a. 70 mg/m^2
4. Member with absolute neutrophil count below 1500/mm^2 or neutropenic fever
5. Member with bowel obstruction

6. Member with diarrhea of Grade 2-4 severity
7. Onivyde (irinotecan liposome) **CANNOT** be substituted for irinotecan HCL (non liposomal formulation)
8. Member with hypersensitivity to Onivyde (irinotecan liposome) or irinotecan HCL (non liposomal formulation)
9. Member with interstitial lung disease
    a. Withhold Onivyde (irinotecan liposome) in member with new or progressive dyspnea, cough, and fever, pending diagnostic evaluation
10. Indications not supported by CMS recognized compendia or acceptable peer reviewed literature may be deemed as not approvable and therefore not reimbursable.

II. Renewal Criteria

1. Patient continues to meet initial approval criteria; **AND**
2. Tumor response with stabilization of disease or decrease in tumor spread or size; **AND**
3. Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include: severe diarrhea, severe neutropenia, interstitial lung disease, severe hypersensitivity reactions (including anaphylactic reactions), etc.

Dosage/Administration

Indication	Dose
Pancreatic Adenocarcinoma	First line or induction therapy in combination with oxaliplatin, fluorouracil, and leucovorin: • Administer 50 mg/m² intravenously every 14 days (regardless of UGT1A1*28 allele genotype) Subsequent therapy in combination with fluorouracil and leucovorin: • Administer 70 mg/m² intravenously every 14 days • Note: Patients homozygous for the UGT1A1*28 allele: Administer 50 mg/m² intravenously every 14 days and may titrate up to 70 mg/m2 as tolerated in subsequent cycles.

Applicable Procedure Codes

Code	Description
J9205	Injection, irinotecan liposome, 1 mg, 1 billable unit = 1 mg

Applicable NDCs

Code	Description
15054-0043-01	Onivyde 43 mg/10 ml single dose vial

ICD-10 Diagnoses

Code	Description
C25.0	Malignant neoplasm of head of pancreas
C25.1	Malignant neoplasm of body of the pancreas
C25.2	Malignant neoplasm of tail of pancreas

C25.3	Malignant neoplasm of pancreatic duct
C25.7	Malignant neoplasm of other parts of pancreas
C25.8	Malignant neoplasm of overlapping sites of pancreas
C25.9	Malignant neoplasm of pancreas, unspecified
C78.89	Secondary malignant neoplasm of other digestive organs

Revision History

Company(ies)	DATE	REVISION
EmblemHealth & ConnectiCare	03/07/2025	Annual Review: removed Z85.07, added C78.89, updated dosing chart. Initial Criteria: Removed to reword: "Metastatic Adenocarcinoma of the Pancreas Onivyde (irinotecan liposome) must be used in combination with fluorouracil and leucovorin; AND Member must have progressed on prior treatment of a gemcitabine-based therapy; AND Member must not have failed prior therapy with irinotecan HCL (non liposomal formulation)." Reworded as: Pancreatic Adenocarcinoma † ‡ Φ Used in combination with oxaliplatin, fluorouracil and leucovorin; AND Used as first-line therapy; AND Patient has metastatic disease; OR Patient has locally advanced disease; AND Patient has good performance status (defined as ECOG PS 0-1, with good biliary drainage and adequate nutritional intake); OR Used as induction therapy followed by chemoradiation in patients without systemic metastases; AND Patient has locally advanced disease; AND Patient has good performance status (defined as ECOG PS 0-1, with good biliary drainage and adequate nutritional intake); OR Used in combination with fluorouracil and leucovorin; AND Patient has locally advanced or metastatic disease; AND Used as subsequent therapy after disease progression with one of the following: Fluoropyrimidine (5-FU or capecitabine) based therapy with no prior irinotecan; OR Gemcitabine-based therapy; OR Patient has local or metastatic disease recurrence after resection; AND Patient completed primary therapy < 6 months ago; AND Patient previously received one of the following: Fluoropyrimidine (5-FU or capecitabine) based therapy that did not include irinotecan; OR- Gemcitabine-based therapy; OR Patient completed primary therapy ≥ 6 months ago; AND Used as alternate systemic therapy not previously used" Renewal Criteria: Added: "Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include: severe diarrhea, severe neutropenia, interstitial lung disease, severe hypersensitivity reactions (including anaphylactic reactions), etc."
EmblemHealth & ConnectiCare	1/31/2024	Annual Review: no criteria changes
EmblemHealth & ConnectiCare	5/30/2023	Annual review: no criteria changes
EmblemHealth & ConnectiCare	09/14/2022	Transferred policy to new template.
EmblemHealth & ConnectiCare	07/15/2019	Annual review

References

1. Onivyde prescribing information. Merrimack Pharmaceuticals, Inc. October 2016.
2. Clinical Pharmacology Elsevier Gold Standard. 2017.

3. Micromedex® Healthcare Series: Thomson Micromedex, Greenwood Village, Co. 2017.
4. UpToDate, Waltham, MA. (Accessed on January 19, 2016.)
5. National Comprehensive Cancer Network. Cancer Guidelines and Drugs and Biologics Compendium. 2017.