Onivyde® (irinotecan liposome injection)
(Intravenous)

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Document Number: IC-0428

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I. Length of Authorization

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

II. Dosing Limits

Max Units (per dose and over time) [HCPCS Unit]:

- All indications: 172 billable units per 14 days

III. Initial Approval Criteria [1]

Coverage is provided in the following conditions:

- Patient is at least 18 years of age; **AND**

Universal Criteria [1]

- Patient does not have a bowel obstruction; **AND**
- Therapy will not be substituted for other drugs containing irinotecan HCl; **AND**

Pancreatic Adenocarcinoma † ‡ Φ [1-4]

- 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 **Ω**; **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 **Ω**; **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 gemcitabine-based therapy; **OR**
    - Patient has local or metastatic disease recurrence after resection **Ω**; **AND**
        - Patient completed primary therapy < 6 months ago; **AND**
            - Patient previously received gemcitabine-based therapy; **OR**
        - Patient completed primary therapy ≥ 6 months ago; **AND**
            - Used as alternate systemic therapy not previously used

Ampullary Adenocarcinoma ‡ Ω [2]

- Patient has pancreatobiliary or mixed type disease with good performance status (defined as ECOG PS 0-1, with good biliary drainage and adequate nutritional intake); **AND**
    - Used as first line therapy; **AND**
        - Used in combination with oxaliplatin, fluorouracil, and leucovorin; **AND**
        - Patient has metastatic disease; **OR**
    - Used as subsequent therapy for disease progression; **AND**
        - Used in combination with fluorouracil and leucovorin; **AND**
        - Patient has previously been treated with one of the following:
            - Gemcitabine-based therapy; **OR**
            - Fluoropyrimidine (5-FU or capecitabine) based therapy with no prior irinotecan; **OR**
            - Oxaliplatin-based therapy with no prior irinotecan

Preferred therapies and recommendations are determined by review of clinical evidence. NCCN category of recommendation is taken into account as a component of this review. Regimens deemed equally efficacious (i.e., those having the same NCCN categorization) are considered to be therapeutically equivalent.

Ω *Please note that the supporting data for this indication has been assessed and deemed to be of insufficient quality based on the review conducted for the Enhanced Oncology Value (EOV) program. However, due to the absence of viable alternative treatment options, this indication will be retained in our policy and evaluated on a case-by-case basis.*

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

IV. Renewal Criteria [1]

Coverage can be renewed based upon the following criteria:

- Patient continues to meet universal and other indication-specific relevant criteria such as concomitant therapy requirements (not including prerequisite therapy), performance status, etc. identified in section III; **AND**

- Disease response with treatment as defined by stabilization of disease or decrease in size of tumor or tumor spread; **AND**
- 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.

V. Dosage/Administration [1,3,5]

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.
Ampullary Adenocarcinoma	**First line 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.

VI. Billing Code/Availability Information

HCPCS Code:

- J9205 – Injection, irinotecan liposome, 1 mg: 1 billable unit = 1 mg

NDC:

- Onivyde 43 mg/10 mL (4.3 mg/mL) single dose vial: 15054-0043-xx

VII. References (STANDARD)

1. Onivyde [package insert]. Cambridge, MA; Ipsen Biopharmaceuticals, Inc.; February 2024. Accessed January 2025.
2. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) irinotecan liposomal. National Comprehensive Cancer Network, 2025. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks

owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed January 2025.

3. Wang-Gillam A, Li CP, Bodky G, NAPOLI-1 study group. Nanoliposomal irinotecan with fluorouracil and folinic acid in metastatic pancreatic cancer after previous gemcitabine-based therapy (NAPOLI-1): a global, randomised, open-label, phase 3 trial. Lancet. 2016 Feb 6;387(10018):545-557. doi: 10.1016/S0140-6736(15)00986-1. Epub 2015 Nov 29.
4. O'Reilly EM, Melisi D, Macarulla T, et al. Liposomal irinotecan + 5-fluorouracil/leucovorin + oxaliplatin (NALIRIFOX) versus nab-paclitaxel + gemcitabine in treatment-naive patients with metastatic pancreatic ductal adenocarcinoma (mPDAC): 12- and 18-month survival rates from the phase 3 NAPOLI 3 trial. JCO 41, 4006-4006(2023). DOI:10.1200/JCO.2023.41.16_suppl.4006
5. Wainberg ZA, Melisi D, Macarulla T, et al. NALIRIFOX versus nab-paclitaxel and gemcitabine in treatment-naive patients with metastatic pancreatic ductal adenocarcinoma (NAPOLI 3): a randomised, open-label, phase 3 trial. Lancet 2023;402:1272-1281.

VIII. References (ENHANCED)

1e. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) Pancreatic Adenocarcinoma, Version 1.2025. National Comprehensive Cancer Network, 2025. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the NCCN Guidelines, go online to NCCN.org. Accessed January 2025.

2e. Pelzer U, Schwaner I, Stieler J, et al. Best supportive care (BSC) versus oxaliplatin, folinic acid and 5-fluorouracil (OFF) plus BSC in patients for second-line advanced pancreatic cancer: a phase III-study from the German CONKO-study group. Eur J Cancer. 2011 Jul;47(11):1676-81.

3e. Oettle H, Riess H, Stieler JM, et al. Second-Line Oxaliplatin, Folinic Acid, and Fluorouracil Versus Folinic Acid and Fluorouracil Alone for Gemcitabine-Refractory Pancreatic Cancer: Outcomes From the CONKO-003 Trial. Journal of Clinical Oncology 2014 32:23, 2423-2429.

4e. Gill S, Ko YJ, Cripps C, et al. PANCREOX: A Randomized Phase III Study of Fluorouracil/Leucovorin With or Without Oxaliplatin for Second-Line Advanced Pancreatic Cancer in Patients Who Have Received Gemcitabine-Based Chemotherapy. Journal of Clinical Oncology 2016 34:32, 3914-3920.

5e. Heinemann V, Vehling-Kaiser U, Waldschmidt D, et al. Gemcitabine plus erlotinib followed by capecitabine versus capecitabine plus erlotinib followed by gemcitabine in advanced pancreatic cancer: final results of a randomised phase 3 trial of the 'Arbeitsgemeinschaft Internistische Onkologie' (AIO-PK0104). Gut. 2012;62(5):751-9.

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7e. Neuzillet C, Hentic O, Rousseau B, et al. FOLFIRI regimen in metastatic pancreatic adenocarcinoma resistant to gemcitabine and platinum-salts. World J Gastroenterol. 2012;18(33):4533-41.

8e. Assaf E, Verlinde-Carvalho M, Delbaldo C, et al. 5-fluorouracil/leucovorin combined with irinotecan and oxaliplatin (FOLFIRINOX) as second-line chemotherapy in patients with metastatic pancreatic adenocarcinoma. Oncology. 2011;80(5-6):301-6.

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11e. Portal A, Pernot S, Tougeron D, et al. Nab-paclitaxel plus gemcitabine for metastatic pancreatic adenocarcinoma after Folfirinox failure: an AGEO prospective multicentre cohort. Br J Cancer. 2015;113(7):989-95.

12e. Conroy T, Desseigne F, Ychou M, et al. FOLFIRINOX versus gemcitabine for metastatic pancreatic cancer. N Engl J Med 2011;364:1817-1825.

13e. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) Ampullary Adenocarcinoma, Version 2.2025. National Comprehensive Cancer Network, 2025. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the NCCN Guidelines, go online to NCCN.org. Accessed January 2025.

14e. Prime Therapeutics Management. Onivyde Clinical Literature Review Analysis. Last updated January 2025. Accessed January 2025.

Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
C24.1	Malignant neoplasm of ampulla of Vater
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
Z85.07	Personal history of malignant neoplasm of pancreas
Z85.09	Personal history of malignant neoplasm of other digestive organs

Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

The preceding information is intended for non-Medicare coverage determinations. Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determinations (NCDs) and/or Local Coverage Determinations (LCDs) may exist and compliance with these policies is required where applicable. Local Coverage Articles (LCAs) may also exist for claims payment purposes or to clarify benefit eligibility under Part B for drugs which may be self-administered. The following link may be used to search for NCD, LCD, or LCA documents: https://www.cms.gov/medicare-coverage-database/search.aspx. Additional indications, including any preceding information, may be applied at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCD/LCA): N/A

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdictio	**Applicable State/US Territory**	**Contractor**
E (1)	CA, HI, NV, AS, GU, CNMI	Noridian Healthcare Solutions, LLC
F (2 & 3)	AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ	Noridian Healthcare Solutions, LLC
5	KS, NE, IA, MO	Wisconsin Physicians Service Insurance Corp (WPS)
6	MN, WI, IL	National Government Services, Inc. (NGS)
H (4 & 7)	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions, Inc.
8	MI, IN	Wisconsin Physicians Service Insurance Corp (WPS)
N (9)	FL, PR, VI	First Coast Service Options, Inc.
J (10)	TN, GA, AL	Palmetto GBA
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA
L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA)	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC