Clinical Policy: Irinotecan Liposome (Onivyde)

Reference Number: CP.PHAR.304
Effective Date: 02.01.17
Last Review Date: 11.26
Line of Business: Medicaid, HIM/ICHRA

Coding Implications
Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

Irinotecan liposome injection (Onivyde®) is a topoisomerase inhibitor.

FDA Approved Indication(s)

Onivyde is indicated:

- In combination with oxaliplatin, fluorouracil and leucovorin, for the first-line treatment of adult patients with metastatic pancreatic adenocarcinoma;
- In combination with fluorouracil and leucovorin, for the treatment of adult patients with metastatic pancreatic adenocarcinoma after disease progression following gemcitabine-based therapy.

Limitation(s) of use: Onivyde is not indicated as a single agent for the treatment of patients with metastatic adenocarcinoma of the pancreas.

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® that Onivyde is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Pancreatic Adenocarcinoma (must meet all)**:**

1. Diagnosis of locally advanced, metastatic, or recurrent pancreatic adenocarcinoma;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Prescribed in one of the following ways (a or b):
   a. In combination with oxaliplatin, fluorouracil, and leucovorin (i.e., as a component of the NALIRIFOX regimen; *see Appendix D*) as first-line therapy;
   b. In combination with fluorouracil and leucovorin for disease progression following gemcitabine-based therapy, or fluoropyrimidine-based therapy without prior irinotecan;
5. Request meets one of the following (a, b, or c):*
   a. Dose does not exceed 50 mg/m^2 every 2 weeks when used as a component of the NALIRIFOX regimen;
   b. Dose does not exceed 70 mg/m^2 every 2 weeks when prescribed in combination with flurouracil and leucovorin only;

c. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration: 12 months

B. Ampullary Adenocarcinoma (off-label) (must meet all)**:**

1. Diagnosis of ampullary adenocarcinoma;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Member meets one of the following (a or b):
   a. Prescribed in combination with fluorouracil and leucovorin for disease progression if previously treated with one of the following (i, ii, or iii):
      i. Gemcitabine-based therapy;
      ii. Fluoropyrimidine-based therapy without prior irinotecan;
      iii. Oxaliplatin-based therapy without prior irinotecan;
   b. For metastatic disease: Prescribed in combination with oxaliplatin, fluorouracil, and leucovorin (i.e., as a component of the NALIRIFOX regimen; *see Appendix D*) as first-line therapy;
5. Dose is within FDA maximum limit for any FDA-approved indication or is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).*

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration: 12 months

C. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (health insurance marketplace/ICHRA) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: HIM.PA.33 for health insurance marketplace/ICHRA and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (health insurance marketplace/ICHRA) or PDL (Medicaid), the non-formulary policy for the relevant line of business: HIM.PA.103 for health insurance marketplace/ICHRA and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: HIM.PA.154 for health insurance marketplace/ICHRA and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. All Indications in Section I (must meet all)**:**

1. Currently receiving medication via Centene benefit, or documentation supports that member is currently receiving Onivyde for a covered indication and has received this medication for at least 30 days;

2. Member is responding positively to therapy;
3. If request is for a dose increase, request meets one of the following (a, b, or c):*
   a. New dose does not exceed 50 mg/m^2 every 2 weeks as a component of the NALIRIFOX regimen;
   b. New dose does not exceed 70 mg/m^2 every 2 weeks in combination with fluorouracil and leucovorin only;
   c. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

   **Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (health insurance marketplace/ICHRA) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: HIM.PA.33 for health insurance marketplace/ICHRA and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (health insurance marketplace/ICHRA) or PDL (Medicaid), the non-formulary policy for the relevant line of business: HIM.PA.103 for health insurance marketplace/ICHRA and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: HIM.PA.154 for health insurance marketplace/ICHRA and CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.PMN.53 for Medicaid and HIM.PA.154 for health insurance marketplace/ICHRA, or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key
FDA: Food and Drug Administration
NCCN: National Comprehensive Cancer Network

Appendix B: Therapeutic Alternatives
This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Pancreatic Adenocarcinoma Examples of gemcitabine-containing regimens: gemcitabine alone or with any of the following: capecitabine, fluorouracil and leucovorin, albumin-bound paclitaxel and/or cisplatin, erlotinib, docetaxel and capecitabine	Varies	Varies
Pancreatic Adenocarcinoma Examples of fluoropyrimidine-based regimens: fluorouracil with any of the following: leucovorin, oxaliplatin	Varies	Varies
Ampullary Adenocarcinoma Examples of gemcitabine-based therapy: gemcitabine alone or with any of the following: albumin-bound paclitaxel, capecitabine, cisplatin, durvalumab	Various	Various
Ampullary Adenocarcinoma Examples of fluoropyrimidine based therapy: fluorouracil with any of the following: leucovorin, oxaliplatin	Various	Various
Ampullary Adenocarcinoma Examples of oxaliplatin-based therapy: oxaliplatin with any of the following: fluorouracil, leucovorin, capecitabine	Various	Various

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): severe hypersensitivity reaction to Onivyde or irinotecan HCl
- Boxed warning(s): severe neutropenia and severe diarrhea; do not administer in patients with bowel obstruction

Appendix D: NALIRIFOX

- NALIRIFOX regimen contains fluorouracil, leucovorin, liposomal irinotecan, and oxaliplatin

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Pancreatic adenocarcinoma	• 50 mg/m^2 IV every 2 weeks when used prior to leucovorin, fluorouracil, and oxaliplatin • 70 mg/m^2 IV every 2 weeks when used prior to leucovorin and fluorouracil only • If homozygous for UGT1A1*28 allele: 50 mg/m^2 IV every 2 weeks. Increase the dose to 70 mg/m^2 as tolerated in subsequent cycles.	70 mg/m^2 every 2 weeks

VI. Product Availability

Single-dose vial: 43 mg/10 mL

VII. References

1. Onivyde Prescribing Information. Cambridge, MA: Merrimack Pharmaceuticals, Inc.; December 2024. Available at: https://www.onivyde.com. Accessed July 10, 2026.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed August 12, 2026.
3. National Comprehensive Cancer Network. Pancreatic Adenocarcinoma Version 3.2026. Available at: https://www.nccn.org/professionals/physician_gls/pdf/pancreatic.pdf. Accessed August 12, 2026.
4. National Comprehensive Cancer Network. Ampullary Adenocarcinoma. Version 2.2026. Available at: https://www.nccn.org/professionals/physician_gls/pdf/ampullary.pdf. Accessed August 12, 2026.

Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J9205	Injection, irinotecan liposome, 1 mg

Reviews, Revisions, and Approvals	Date	P&T Approval Date
4Q 2022 annual review: per NCCN and FDA label, added that disease must be locally advanced, metastatic, or recurrent and added requirement for disease progression following gemcitabine-based therapy or FOLFIRINOX; references reviewed and updated. Template changes applied to other diagnoses/indications.	07.28.22	11.22
4Q 2023 annual review: per NCCN compendium and Pancreatic Adenocarcinoma guidelines version 2.2023, updated "FOLFIRINOX" to "fluoropyrimidine-based therapy and no prior irinotecan" and added "component of NALIRIFOX regimen"; updated Appendix B to include examples of fluoropyrimidine-based therapy; references reviewed and updated.	08.06.23	11.23
RT4: added newly FDA-approved use as first-line use when prescribed in combination with oxaliplatin, fluorouracil, and leucovorin for metastatic disease.	02.29.24	
4Q 2024 annual review: updated FDA approved indications section to align with prescriber information; updated continued therapy section from "pancreatic adenocarcinoma" to "all indications in Section I"; added ampullary adenocarcinoma off-label criteria as supported by NCCN compendium and guideline; references reviewed and updated.	07.15.24	11.24
4Q 2025 annual review: for ampullary adenocarcinoma, added option for prescribed in combination with NALIRIFOX regimen as first-line	07.10.25	11.25

Reviews, Revisions, and Approvals	Date	P&T Approval Date
therapy for metastatic disease per NCCN; for initial approval criteria, extended approval duration from 6 months to 12 months; references reviewed and updated.		
4Q 2026 annual review: no significant changes; added ICHRA line of business; references reviewed and updated.	07.10.26	11.26

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions, and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment, or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members, and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note: For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

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