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Medical benefit drug policies are a source for BCBSM and BCN medical policy information only. These documents are not to be used to determine benefits or reimbursement. Please reference the appropriate certificate or contract for benefit information. This policy may be updated and therefore subject to change.

P&T Date: 06/11/2026

Onivyde[®] (liposomal irinotecan)

HCPCS: J9205

Policy:

Requests must be supported by submission of chart notes and patient specific documentation.

- A. Coverage of the requested drug is provided when all the following are met:
 - a. Prescribed by or in consultation with an oncologist
 - b. As first-line therapy for metastatic adenocarcinoma of the pancreas
 - i. Must be used in combination with oxaliplatin, fluorouracil, and leucovorin
 - OR
 - c. Diagnosis of metastatic adenocarcinoma of the pancreas
 - i. Disease progression following gemcitabine-based therapy
 - ii. Used in combination with fluorouracil and leucovorin
 - iii. No prior use of irinotecan
 - d. ECOG performance status of 0 – 2
 - e. Trial and failure, contraindication, OR intolerance to the preferred drugs as listed in BCBSM/BCN's utilization management medical drug list
- B. Quantity Limitations, Authorization Period and Renewal Criteria
 - a. Quantity Limits: Align with FDA recommended dosing
 - b. Authorization Period: Aligns with FDA recommended or guideline supported treatment duration and provided for at least 60 days and up to 6 months at a time
 - c. Renewal Criteria: Continuation of therapy until disease progression or unacceptable toxicity

***Note: Coverage and approval duration may differ for Medicare Part B members based on any applicable criteria outlined in Local Coverage Determinations (LCD) or National Coverage Determinations (NCD) as determined by Center for Medicare and Medicaid Services (CMS). See the CMS website at <http://www.cms.hhs.gov/>. Determination of coverage of Part B drugs is based on medically accepted indications which have supported citations included or approved for inclusion determined by CMS approved compendia.

Background Information:

- Onivyde is a topoisomerase inhibitor indicated in combination with fluorouracil and leucovorin, for the treatment of patients with metastatic adenocarcinoma of the pancreas after disease progression following gemcitabine-based therapy and in combination with oxaliplatin, fluorouracil and leucovorin, for the first-line treatment of adult patients with metastatic pancreatic adenocarcinoma.
- Safety and efficacy in previously treated disease were established in the NAPOLI-1 trial, a three-arm, randomized, open label study in 417 patients with metastatic pancreatic adenocarcinoma with documented disease progression after gemcitabine or gemcitabine-based therapy. Patients were included in the study if they had a ECOG performance status less than or equal to 2 and were excluded if they had prior treatment with irinotecan. Patients were randomized to Onivyde plus fluorouracil and leucovorin, fluorouracil and leucovorin, or Onivyde alone. The primary efficacy endpoint was overall survival (OS) versus fluorouracil and leucovorin. The OS of Onivyde combination therapy vs. fluorouracil and leucovorin therapy was 1.9 months and the progression-free survival (PFS) was 1.6 months. There was no improvement in overall survival for the Onivyde arm over the fluorouracil and leucovorin arm (hazard ratio = 1.00, p-value = 0.97).
- Safety and efficacy for use as first-line therapy were established in the NAPOLI-3 trial, a randomized, multicenter, open-label, active-controlled trial of 770 patients with metastatic pancreatic adenocarcinoma who had not previously received chemotherapy in the metastatic setting. Patients were randomized to receive either NALIRIFOX or gemcitabine plus Abraxane® and excluded if they had a ECOG performance status greater than 2. The primary endpoint was OS which was 11.1 months in the NALIRIFOX arm versus 9.2 months in the gemcitabine plus Abraxane arm (HR = 0.84; 95% CI: 0.71, 0.99; p-value = 0.0403). Treatment with NALIRIFOX improved median progression-free survival (7.4 vs 5.6 months, respectively; HR = 0.70; 95% CI: 0.59, 0.85; p-value = 0.0001) and led to a favorable overall response rate as well (41.8% vs 36.2%).
- The 2026 National Comprehensive Cancer Network pancreatic adenocarcinoma treatment guidelines recommend FOLFIRINOX or gemcitabine plus Abraxane as the preferred first-line treatment regimens. For second-line treatment of refractory metastatic pancreatic adenocarcinoma NCCN guidelines recommend a clinical trial, fluoropyrimidine-based regimens if previously treated with gemcitabine-based therapy, or gemcitabine-based regimens if previously treated with fluoropyrimidine-based therapy. Onivyde plus fluorouracil and leucovorin is recommended as subsequent treatment following second-line treatment failure.

References:

1. Onivyde [prescribing information]. Basking Ridge, NJ: Ipsen Biopharmaceuticals, Inc.; December 2024.
2. National Comprehensive Cancer Network. Pancreatic adenocarcinoma (Version 1.2026). 2026 March 18. Available at: https://www.nccn.org/professionals/physician_gls/pdf/pancreatic.pdf. Accessed on April 14, 2026.
3. Gillam A, Li, VP, Bodoky G, et al. Nanoliposomal irinotecan with fluorouracil and folinic acid in metastatic pancreatic cancer after previous gemcitabine-based therapy (NAPOLI-1): a global, randomized, open-label, phase 3 trial. *Lancet*. 2016 Feb 6; 387 (10018): 545 – 57.
4. Clinicaltrials.gov. An open-label, randomized, multicenter, phase III study of irinotecan liposome injection, oxaliplatin, 5-fluorouracil/leucovorin versus nab-paclitaxel plus gemcitabine in subjects who have not previously received chemotherapy for metastatic adenocarcinoma of the pancreas (NCT04083235). Available at: <https://classic.clinicaltrials.gov/ct2/show/NCT04083235>. Accessed on February 20, 2024.

Policy History												
#	Date	Change Description										
2.5	Effective Date: 06/11/2026	Annual review of criteria was performed, no changes were made										
2.4	Effective Date: 07/21/2025 P&T Date: 06/05/2025	Updated to include the trial and failure of preferred products statement										
2.3	Effective Date: 10/03/2024	Updated to remove the statement that this policy is for Medicare Part B only										
2.2	Effective Date: 04/11/2024	Updated to include the new indication allowing for use as first-line therapy in pancreatic adenocarcinoma										
2.1	Effective Date: 02/08/2024	Annual review of criteria was performed, no changes were made										
2.0	Effective Date: 02/02/2023	Updated approval length to allow for FDA recommended dosing for at least 60 days and up to 6 months at a time. Policy will now only be active for the Medicare Part B line of business only										
1.9	Effective Date: 02/10/2022	Annual review of criteria was performed, no changes were made										
1.8	Effective Date: 02/04/2021	Update the authorization period to 6 months										
1.7	Effective Date: 12/01/2020	UM medical management system update for BCBS <table><tr><th>Line of Business</th><th>PA Required (Yes/No)</th></tr><tr><td>BCBS</td><td>Yes</td></tr><tr><td>BCN</td><td>Yes</td></tr><tr><td>MAPPO</td><td>Yes</td></tr><tr><td>BCNA</td><td>Yes</td></tr></table>	Line of Business	PA Required (Yes/No)	BCBS	Yes	BCN	Yes	MAPPO	Yes	BCNA	Yes
Line of Business	PA Required (Yes/No)											
BCBS	Yes											
BCN	Yes											
MAPPO	Yes											
BCNA	Yes											
1.6	Effective Date: 02/06/2020	Annual review of criteria was performed, no changes were made										
1.5	Effective Date: 01/01/2020	UM medical management system update for MAPPO and BCNA <table><tr><th>Line of Business</th><th>PA Required (Yes/No)</th></tr><tr><td>BCBS</td><td>No</td></tr><tr><td>BCN</td><td>Yes</td></tr><tr><td>MAPPO</td><td>Yes</td></tr><tr><td>BCNA</td><td>Yes</td></tr></table>	Line of Business	PA Required (Yes/No)	BCBS	No	BCN	Yes	MAPPO	Yes	BCNA	Yes
Line of Business	PA Required (Yes/No)											
BCBS	No											
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1.4	Effective Date: 02/14/2019	Updated criteria per oncology vendor										
1.3	Effective Date: 11/01/2018	Updated criteria per oncology vendor										
1.2	Effective Date: 08/09/2018	Annual review of criteria was performed, no changes were made										
1.1	Effective Date: 08/10/2017	Annual review of criteria was performed, no changes were made										

This policy and any information contained herein is the property of Blue Cross Blue Shield of Michigan and its subsidiaries, is strictly confidential, and its use is intended for the P&T committee, its members and BCBSM employees for the purpose of coverage determinations.

1.0	Effective Date: 05/05/2016	New Medical Policy	

** The prescribing information for a drug is subject to change. To ensure you are reading the most current information it is advised that you reference the most updated prescribing information by visiting the drug or manufacturer website or <http://dailymed.nlm.nih.gov/dailymed/index.cfm>.*