onivyde®
(irinotecan liposome injection)

REIMBURSEMENT RESOURCE GUIDE

ONIVYDE® (irinotecan liposome injection)

- Indications and Important Safety Information
- Coverage, Coding, and Payment in the Physician Office
- Coverage, Coding, and Payment in the Hospital Outpatient Setting
- IPSEN CARES® Overview

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Hours: Monday – Friday, 8:00 AM – 8:00 PM ET
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Please see Indications and Important Safety Information on pages 3 and 4 and accompanying full Prescribing Information, including **BOXED WARNING**.

This guide is provided for informational purposes only. Correct coding is the responsibility of the provider submitting the claim for the item or service. Please check with the payer to verify codes and specific billing requirements. Ipsen Biopharmaceuticals, Inc. (Ipsen) does not make any representation or guarantees concerning reimbursement or coverage for any service or item, nor does Ipsen guarantee patient assistance to the limits described.

INDICATIONS AND IMPORTANT SAFETY INFORMATION

INDICATIONS

- ONIVYDE® (irinotecan liposome injection) is indicated, in combination with oxaliplatin, fluorouracil, and leucovorin, for the first-line treatment of adult patients with metastatic pancreatic adenocarcinoma.
- ONIVYDE is indicated, in combination with fluorouracil and leucovorin, for the treatment of adult patients with metastatic pancreatic adenocarcinoma after disease progression following gemcitabine-based therapy.

Limitations of Use: ONIVYDE is not indicated as a single agent for the treatment of patients with metastatic pancreatic adenocarcinoma.

IMPORTANT SAFETY INFORMATION

WARNING: SEVERE NEUTROPENIA AND SEVERE DIARRHEA

Neutropenia

- **Severe and life-threatening neutropenia, including fatal neutropenic sepsis and fatal neutropenic fever, has occurred in patients receiving ONIVYDE in combination with oxaliplatin, fluorouracil, and leucovorin and in combination with fluorouracil and leucovorin. Withhold ONIVYDE for absolute neutrophil count below 1500/mm^3 or neutropenic fever. Monitor blood cell counts periodically during treatment.**

Diarrhea

- **Severe and life-threatening diarrhea has occurred in patients receiving ONIVYDE in combination with oxaliplatin, fluorouracil, and leucovorin and in combination with fluorouracil and leucovorin. Do not administer ONIVYDE to patients with bowel obstruction. Withhold ONIVYDE for diarrhea of Grade 2-4 severity. Administer loperamide for late diarrhea of any severity. Administer atropine, if not contraindicated, for early diarrhea of any severity.**

CONTRAINDICATIONS

ONIVYDE is contraindicated in patients who have experienced a severe hypersensitivity reaction or anaphylaxis to ONIVYDE or irinotecan HCl.

WARNINGS AND PRECAUTIONS

Severe Neutropenia: See Boxed WARNING. In NAPOLI 3, Grade 3 and 4 neutropenia occurred in 26% of patients receiving ONIVYDE in combination with oxaliplatin, fluorouracil, and leucovorin (NALIRIFOX) and fatal neutropenic fever in 0.3% of patients. In NAPOLI 3, the incidence of Grade 3 or 4 neutropenia was similar among Asian patients [6 of 20 (30%)] compared to White patients [76 of 289 (26%)]. Neutropenic fever/neutropenic sepsis was reported in 5% of Asian patients (1 of 20) compared to 2.3% of White patients (7 of 306).

In NAPOLI-1, Grade 3 and 4 neutropenia occurred in 20% of patients receiving ONIVYDE in combination with fluorouracil and leucovorin (ONIVYDE/FU/LV). Neutropenic sepsis occurred in 3% and fatal neutropenic sepsis in 0.8%. In NAPOLI-1, the incidence of Grade 3 or 4 neutropenia was higher among Asian patients [18 of 33 (55%)] compared to White patients [13 of 73 (18%)]. Neutropenic fever/neutropenic sepsis was reported in 6% of Asian patients compared to 1% of White patients.

Monitor complete blood cell counts on Days 1 and 8 of every cycle and more frequently if clinically indicated. Withhold ONIVYDE if the absolute neutrophil count (ANC) is below 1500/mm^3 or if neutropenic fever occurs. Resume ONIVYDE when the ANC is 1500/mm^3 or above. Reduce ONIVYDE dose for Grade 3-4 neutropenia or neutropenic fever following recovery in subsequent cycles.

Severe Diarrhea: See Boxed WARNING. In NAPOLI 3, Grade 3 and 4 diarrhea (early-onset [within 24 hours of chemotherapy] and late-onset [more than 24 hours following chemotherapy]) occurred in 20% receiving NALIRIFOX. In NAPOLI-1, Grade 3 or 4 diarrhea occurred in 13% receiving ONIVYDE/FU/LV. The incidence of Grade 3 or 4 late-onset diarrhea was 9% in patients receiving ONIVYDE/FU/LV. The incidence of Grade 3 or 4 early-onset diarrhea was 3% in patients receiving ONIVYDE/FU/LV.

To reduce the risk of severe diarrhea, patients should stop lactose-containing products, eat a low-fat diet, and maintain hydration during treatment with ONIVYDE. Withhold ONIVYDE for Grade 2-4 diarrhea. Local institutional guidelines should be followed for the treatment of diarrhea that does not improve within 48 hours and may include the addition of diphenoxylate hydrochloride plus atropine sulfate or octreotide. Following recovery to Grade 1 diarrhea, resume ONIVYDE at a reduced dose.

Interstitial Lung Disease (ILD): Irinotecan HCl can cause severe and fatal ILD. Patients with risk factors should be closely monitored for respiratory symptoms before and during ONIVYDE therapy. Withhold ONIVYDE in patients with new or progressive dyspnea, cough, and fever, pending diagnostic evaluation. Discontinue ONIVYDE in patients with a confirmed diagnosis of ILD.

Severe Hypersensitivity Reaction: Irinotecan, including ONIVYDE, can cause severe hypersensitivity reactions, including anaphylactic reactions. Permanently discontinue ONIVYDE in patients who experience a severe hypersensitivity reaction.

Embryo-Fetal Toxicity: ONIVYDE can cause fetal harm when administered to a pregnant woman. Advise pregnant women of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during and for 7 months after the last dose of ONIVYDE treatment.

Please see accompanying full Prescribing Information, including BOXED WARNING.

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INDICATIONS AND IMPORTANT SAFETY INFORMATION
(continued)

ADVERSE REACTIONS FOR NALIRIFOX

- The most common adverse reactions (≥20%) of NALIRIFOX were diarrhea (72%), fatigue (62%), nausea (59%), vomiting (40%), decreased appetite (37%), abdominal pain (35%), mucosal inflammation (28%), constipation (25%), and weight decreased (22%).
- Permanent discontinuation of ONIVYDE due to an adverse reaction occurred in 17% of patients. Adverse reactions that resulted in permanent discontinuation of ONIVYDE in ≥1% of patients included neutropenia, thrombocytopenia, diarrhea, fatigue, infections, and cerebrovascular accident.
- Dosage reduction of ONIVYDE due to an adverse reaction occurred in 52% of patients. Adverse reactions that required dosage reduction in ≥1% of patients included anemia, decreased appetite, diarrhea, fatigue, febrile neutropenia, hypokalemia, liver function test abnormalities, nausea, mucosal inflammation, neutropenia, peripheral neuropathy, vomiting, thrombocytopenia, and weight decreased.
- Dosage interruptions of ONIVYDE due to an adverse reaction occurred in 1.9% of patients. Adverse reactions which required dosage interruption in ≥0.5% of patients included hypersensitivity and infusion-related reaction.
- The most common laboratory abnormalities (≥10% Grade 3 or 4) were decreased neutrophils (26%), decreased potassium (22%), decreased lymphocytes (11%), and decreased hemoglobin (10%).

ADVERSE REACTIONS FOR ONIVYDE/FU/LV

- The most common adverse reactions (≥20%) were diarrhea (59%), fatigue/asthenia (56%), vomiting (52%), nausea (51%), decreased appetite (44%), stomatitis (32%), and pyrexia (23%).
- Adverse reactions led to permanent discontinuation of ONIVYDE in 11% of patients receiving ONIVYDE/FU/LV; the most frequent adverse reactions resulting in discontinuation of ONIVYDE were diarrhea, vomiting, and sepsis.
- Dose reductions of ONIVYDE for adverse reactions occurred in 33% of patients receiving ONIVYDE/FU/LV; the most frequent adverse reactions requiring dose reductions were neutropenia, diarrhea, nausea, and anemia.
- ONIVYDE was withheld or delayed for adverse reactions in 62% of patients receiving ONIVYDE/FU/LV; the most frequent adverse reactions requiring interruption or delays were neutropenia, diarrhea, fatigue, vomiting, and thrombocytopenia.
- The most common severe laboratory abnormalities (≥10% Grade 3 or 4) were lymphopenia and neutropenia.

Postmarketing Experience: Immune system disorders: Hypersensitivity (including anaphylactic reaction and angioedema).

DRUG INTERACTIONS

- Avoid the use of strong CYP3A4 inducers, if possible, and substitute non-enzyme inducing therapies ≥2 weeks prior to initiation of ONIVYDE.
- Avoid the use of strong CYP3A4 or UGT1A1 inhibitors, if possible, and discontinue strong CYP3A4 inhibitors ≥1 week prior to starting therapy.

USE IN SPECIFIC POPULATIONS

- Pregnancy and Reproductive Potential: See WARNINGS & PRECAUTIONS. Advise males with female partners of reproductive potential to use condoms during and for 4 months after the last dose of ONIVYDE treatment.
- Lactation: Advise nursing women not to breastfeed during and for 1 month after the last dose of ONIVYDE treatment.

To report SUSPECTED ADVERSE REACTIONS, contact Ipsen Biopharmaceuticals, Inc. at 1-855-463-5127 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Please see accompanying full Prescribing Information, including BOXED WARNING.

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COVERAGE, CODING, AND PAYMENT IN THE PHYSICIAN OFFICE

ONIVYDE® (irinotecan liposomal injection) received FDA approval on February 13, 2024, in combination with oxaliplatin, fluorouracil, and leucovorin (NALIRIFOX), for the first-line treatment of adult patients with metastatic pancreatic adenocarcinoma. Previously, ONIVYDE was FDA-approved in combination with fluorouracil and leucovorin for the treatment of adult patients with metastatic pancreatic adenocarcinoma after disease progression following gemcitabine-based therapy. Both indications are included as Category 1 recommendations in the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for metastatic pancreatic adenocarcinoma.[a] ONIVYDE is not indicated as a single agent for the treatment of patients with metastatic pancreatic adenocarcinoma. ONIVYDE has a BOXED WARNING on the risks of severe neutropenia and severe diarrhea. ONIVYDE is contraindicated in patients who have experienced a severe hypersensitivity reaction or anaphylaxis to ONIVYDE or irinotecan HCl. Please see Important Safety Information on pages 3 and 4 of this guide.

[a]Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines® for Pancreatic Adenocarcinoma V.1.2024 © National Comprehensive Cancer Network, Inc. 2023 All rights reserved. Accessed January 22, 2024. To view the most recent and complete version of the guideline, go online to NCCN.org.

NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way.

Coverage

For Medicare patients, ONIVYDE is covered under Medicare Part B when used for an FDA-approved indication and when medically reasonable and necessary.[b] There are no prior authorization requirements for ONIVYDE under traditional fee-for-service Medicare. For patients enrolled in Medicaid, a Medicare Advantage plan, or a commercial health plan, coverage of ONIVYDE will vary by payer. Some payers may also apply utilization restrictions for ONIVYDE.

Coding

Please refer to the table below to support appropriate claims processing for ONIVYDE.[b]

Code Type	Code	Code Description
ICD-10-CM	C25.0	Malignant neoplasm of head of pancreas
	C25.1	Malignant neoplasm of body of 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
ICD-10-CM (Secondary Diagnosis Code)	C79.89	Secondary malignant neoplasm of other specified sites
	C79.9	Secondary neoplasm of unspecified site
CPT	96413	Chemotherapy administration, intravenous infusion technique, up to 1 hour, single or initial substance/drug (Code covers infusions lasting up to 90 minutes)
HCPCS	J9205	Injection, irinotecan liposome, 1 mg
NDC	15054-0043-01	ONIVYDE single-dose 10 mL vial containing 43 mg of irinotecan liposome for injection

CPT, current procedural terminology; HCPCS, Healthcare Common Procedure Coding System; ICD-10-CM, International Classification of Diseases, 10th Revision, Clinical Modification; NDC, national drug code.

[b]It is always the provider's responsibility to determine the appropriate healthcare setting and to submit true and correct claims for actual products and services rendered. Providers should contact third-party payers for specific information on their coding, coverage, and payment policies.

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IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

ONIVYDE is contraindicated in patients who have experienced a severe hypersensitivity reaction or anaphylaxis to ONIVYDE or irinotecan HCl.

Please see Important Safety Information on pages 3 and 4 and accompanying full Prescribing Information, including BOXED WARNING.

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COVERAGE, CODING, AND PAYMENT IN THE PHYSICIAN OFFICE (continued)

Payment

Payer Type	Payment Methodology
Medicare	Average Sales Price (ASP) + 6% (Beginning April 1, 2013, Medicare provider payments were cut by 2% due to sequestration. This reduces Medicare payments for drugs to ASP + 4.3% until 2030 or until there is a legislative change.)
Medicaid and Commercial Payers	Most non-Medicare payers are expected to pay separately for ONIVYDE; however, payment rates will vary by payer and provider contract.

JW Modifier

Effective January 1, 2017, Medicare required providers to use the JW modifier (drug amount discarded/not administered to any patient) for all claims with unused drugs or biologicals from single-use vials that are appropriately discarded, and to document the discarded drug or biological in the patient's medical record.

Wastage-reporting requirements for payers other than Medicare may vary—providers should check with their specific plans about policies related to use of the JW modifier.

JZ Modifier

Effective July 1, 2023, providers and suppliers are required to report the JZ modifier on all claims that bill for drugs from single-dose containers that are separately payable under Medicare Part B when there are no discarded amounts.

Medicare Medically Unlikely Edits (MUEs)

Centers for Medicare and Medicaid Services (CMS) developed MUEs to reduce the paid claims error rate for Part B claims. A MUE for a HCPCS/CPT code is the maximum units of service that a provider would report under most circumstances for a single beneficiary on a single date of service. Not all HCPCS/CPT codes have a MUE.

ONIVYDE has a MUE of 120 billing units.

CPT, current procedural terminology; HCPCS, Healthcare Common Procedure Coding System.

IMPORTANT SAFETY INFORMATION (continued)

WARNINGS AND PRECAUTIONS

Severe Neutropenia: See Boxed WARNING. In NAPOLI 3, Grade 3 and 4 neutropenia occurred in 26% of patients receiving ONIVYDE in combination with oxaliplatin, fluorouracil, and leucovorin (NALIRIFOX) and fatal neutropenic fever in 0.3% of patients. In NAPOLI 3, the incidence of Grade 3 or 4 neutropenia was similar among Asian patients [6 of 20 (30%)] compared to White patients [76 of 289 (26%)]. Neutropenic fever/neutropenic sepsis was reported in 5% of Asian patients (1 of 20) compared to 2.3% of White patients (7 of 306). In NAPOLI-1, Grade 3 and 4 neutropenia occurred in 20% of patients receiving ONIVYDE in combination with fluorouracil and leucovorin (ONIVYDE/FU/LV). Neutropenic sepsis occurred in 3% and fatal neutropenic sepsis in 0.8%. In NAPOLI-1, the incidence of Grade 3 or 4 neutropenia was higher among Asian patients [18 of 33 (55%)] compared to White patients [13 of 73 (18%)]. Neutropenic fever/neutropenic sepsis was reported in 6% of Asian patients compared to 1% of White patients.

Monitor complete blood cell counts on Days 1 and 8 of every cycle and more frequently if clinically indicated. Withhold ONIVYDE if the absolute neutrophil count (ANC) is below 1500/mm^3 or if neutropenic fever occurs. Resume ONIVYDE when the ANC is 1500/mm^3 or above. Reduce ONIVYDE dose for Grade 3-4 neutropenia or neutropenic fever following recovery in subsequent cycles.

Severe Diarrhea: See Boxed WARNING. In NAPOLI 3, Grade 3 and 4 diarrhea (early-onset [within 24 hours of chemotherapy] and late-onset [more than 24 hours following chemotherapy]) occurred in 20% receiving NALIRIFOX. In NAPOLI-1, Grade 3 or 4 diarrhea occurred in 13% receiving ONIVYDE/FU/LV. The incidence of Grade 3 or 4 late-onset diarrhea was 9% in patients receiving ONIVYDE/FU/LV. The incidence of Grade 3 or 4 early-onset diarrhea was 3% in patients receiving ONIVYDE/FU/LV.

To reduce the risk of severe diarrhea, patients should stop lactose-containing products, eat a low-fat diet, and maintain hydration during treatment with ONIVYDE. Withhold ONIVYDE for Grade 2-4 diarrhea.

Please see Important Safety Information on pages 3 and 4 and accompanying full Prescribing Information, including BOXED WARNING.

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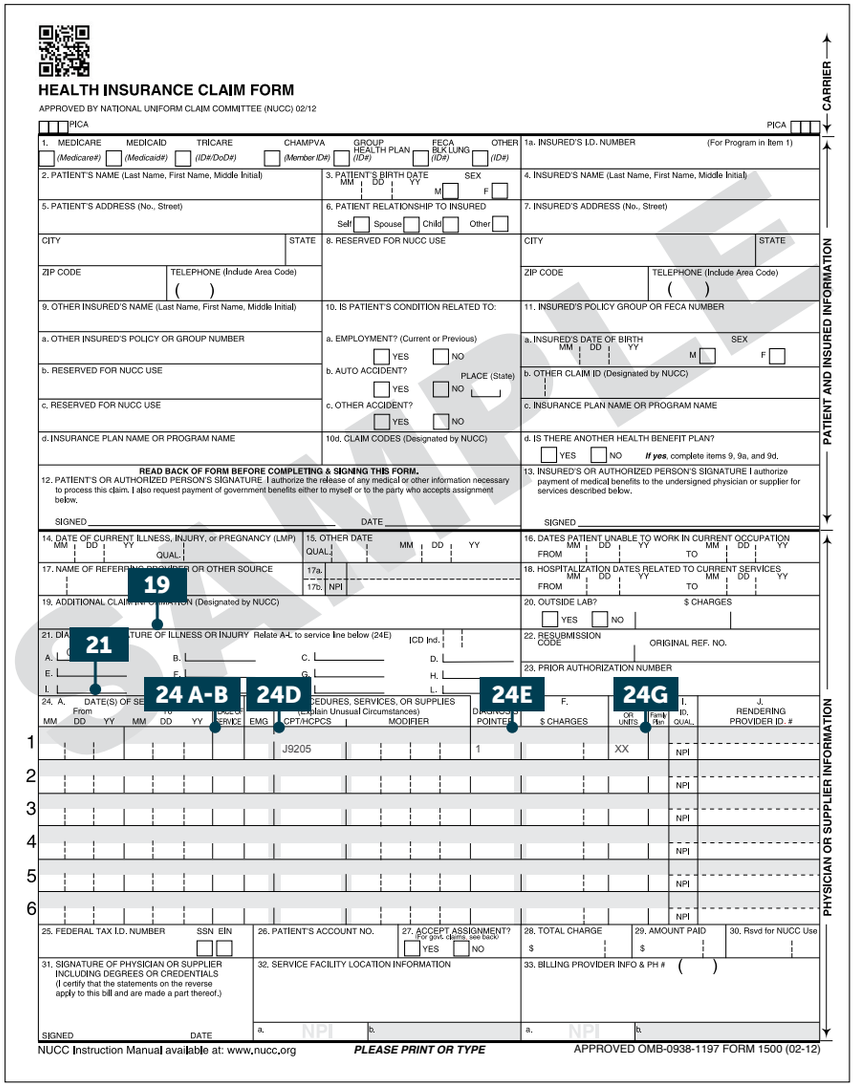
SAMPLE CMS-1500 CLAIM FORM PHYSICIAN OFFICE

ONIVYDE and the associated services provided in a physician office are billed on the CMS-1500 claim form or its electronic equivalent. A sample CMS-1500 claim form for billing ONIVYDE is provided below.

The sample claim form provided below is only an example. It is always the provider's responsibility to determine the appropriate healthcare setting and to submit true and correct claims for the products and services rendered. Providers should contact third-party payers for specific information on their coding, coverage, and payment policies.



LOCATOR 19:

Reserved for local use. This area may be used to list the drug name.

LOCATOR 21:

Enter the appropriate primary diagnosis code from the patient's medical record in Locator 21A, and any secondary diagnosis code(s) in Locator 21B-L.

LOCATOR 24 A-B:

Enter the date of service and the appropriate place of service code.

LOCATOR 24D:

Enter the appropriate HCPCS code.

J9205 - Injection, irinotecan liposome, 1 mg

LOCATOR 24E:

Specify the diagnosis, from Locator 21, that relates to the product or procedure listed in Locator 24D.

LOCATOR 24G:

Enter the number of service units for each line item. A single-dose vial (10 mL) contains 43 billable units of J9205.

Use the JW modifier to report discarded units (if applicable) as required by Medicare or other payers.

IMPORTANT SAFETY INFORMATION (continued)

WARNINGS AND PRECAUTIONS (continued)

Severe Diarrhea (continued): Local institutional guidelines should be followed for the treatment of diarrhea that does not improve within 48 hours and may include the addition of diphenoxylate hydrochloride plus atropine sulfate or octreotide. Following recovery to Grade 1 diarrhea, resume ONIVYDE at a reduced dose.

Interstitial Lung Disease (ILD): Irinotecan HCl can cause severe and fatal ILD. Patients with risk factors should be closely monitored for respiratory symptoms before and during ONIVYDE therapy. Withhold ONIVYDE in patients with new or progressive dyspnea, cough, and fever, pending diagnostic evaluation. Discontinue ONIVYDE in patients with a confirmed diagnosis of ILD.

Severe Hypersensitivity Reaction: Irinotecan, including ONIVYDE, can cause severe hypersensitivity reactions, including anaphylactic reactions. Permanently discontinue ONIVYDE in patients who experience a severe hypersensitivity reaction.

Please see Important Safety Information on pages 3 and 4 and accompanying full Prescribing Information, including BOXED WARNING.

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COVERAGE, CODING, AND PAYMENT IN THE HOSPITAL OUTPATIENT SETTING

ONIVYDE® (irinotecan liposomal injection) received FDA approval on February 13, 2024, in combination with oxaliplatin, fluorouracil, and leucovorin (NALIRIFOX), for the first-line treatment of adult patients with metastatic pancreatic adenocarcinoma. Previously, ONIVYDE was FDA-approved in combination with fluorouracil and leucovorin for the treatment of adult patients with metastatic pancreatic adenocarcinoma after disease progression following gemcitabine-based therapy. Both indications are included as Category 1 recommendations in the NCCN Guidelines® for metastatic pancreatic adenocarcinoma.[a] ONIVYDE is not indicated as a single agent for the treatment of patients with metastatic pancreatic adenocarcinoma. ONIVYDE has a BOXED WARNING on the risks of severe neutropenia and severe diarrhea. ONIVYDE is contraindicated in patients who have experienced a severe hypersensitivity reaction or anaphylaxis to ONIVYDE or irinotecan HCl. Please see Important Safety Information on pages 3 and 4 of this guide.

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Coverage

For Medicare patients, ONIVYDE is covered under Medicare Part B when used for an FDA-approved indication and when medically reasonable and necessary.[b] There are no prior authorization requirements for ONIVYDE under traditional fee-for-service Medicare. For patients enrolled in Medicaid, a Medicare Advantage plan, or a commercial health plan, coverage of ONIVYDE will vary by payer. Some payers may also apply utilization restrictions for ONIVYDE.

Coding

Please refer to the table below to support appropriate claims processing for ONIVYDE.[b]

Code Type	Code	Code Description
ICD-10-CM (Primary Diagnosis Code)	C25.0	Malignant neoplasm of head of pancreas
	C25.1	Malignant neoplasm of body of 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
ICD-10-CM (Secondary Diagnosis Code)	C79.89	Secondary malignant neoplasm of other specified sites
	C79.9	Secondary neoplasm of unspecified site
CPT	96413	Chemotherapy administration, intravenous infusion technique, up to 1 hour, single or initial substance/drug (Code covers infusions lasting up to 90 minutes)
HCPCS	J9205	Injection, irinotecan liposome, 1 mg
Revenue	025X	Pharmacy
	0636	Pharmacy, drugs requiring detailed coding
NDC	15054-0043-01	ONIVYDE single-dose 10 mL vial containing 43 mg of irinotecan liposome for injection

CPT, current procedural terminology; HCPCS, Healthcare Common Procedure Coding System; ICD-10-CM, International Classification of Diseases, 10th Revision, Clinical Modification; NDC, national drug code

[b]It is always the provider's responsibility to determine the appropriate healthcare setting and to submit true and correct claims for actual products and services rendered. Providers should contact third-party payers for specific information on their coding, coverage, and payment policies.

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IMPORTANT SAFETY INFORMATION (continued)

WARNINGS AND PRECAUTIONS (continued)

Embryo-Fetal Toxicity: ONIVYDE can cause fetal harm when administered to a pregnant woman. Advise pregnant women of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during and for 7 months after the last dose of ONIVYDE treatment.

Please see Important Safety Information on pages 3 and 4 and accompanying full Prescribing Information, including BOXED WARNING.

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COVERAGE, CODING, AND PAYMENT IN THE HOSPITAL OUTPATIENT SETTING (continued)

Payment

Payer Type	Payment Methodology
Medicare	Average Sales Price (ASP) + 6% (Beginning April 1, 2013, Medicare provider payments were cut by 2% due to sequestration. This reduces Medicare payments for drugs to ASP + 4.3% until there is a legislative change.)
Medicaid and Commercial Payers	Most non-Medicare payers are expected to pay separately for ONIVYDE; however, payment rates will vary by payer and provider contract.

JW Modifier

Effective January 1, 2017, Medicare required providers to use the JW modifier (drug amount discarded/not administered to any patient) for all claims with unused drugs or biologicals from single-use vials that are appropriately discarded, and to document the discarded drug or biological in the patient's medical record.

Wastage-reporting requirements for payers other than Medicare may vary—providers should check with their specific plans about policies related to use of the JW modifier.

JZ Modifier

Effective July 1, 2023, providers and suppliers are required to report the JZ modifier on all claims that bill for drugs from single-dose containers that are separately payable under Medicare Part B when there are no discarded amounts.

JG Modifier

As of January 1, 2024, CMS is requiring all 340B covered entities, including hospital-based and non-hospital-based entities, that submit claims for separately payable Part B drugs and biologicals to report the JG modifier on claim lines for drugs acquired through the 340B Program.

TB Modifier

As of January 1, 2024, CMS is requiring all 340B covered entities, including hospital-based and non-hospital-based entities, that submit claims for separately payable Part B drugs and biologicals to report the TB modifier on claim lines for drugs acquired through the 340B Program.

Medicare Medically Unlikely Edits (MUEs)

Centers for Medicare and Medicaid Services (CMS) developed MUEs to reduce the paid claims error rate for Part B claims. A MUE for a HCPCS/CPT code is the maximum units of service that a provider would report under most circumstances for a single beneficiary on a single date of service. Not all HCPCS/CPT codes have a MUE.

ONIVYDE has a MUE of 120 billing units.

CPT, current procedural terminology; HCPCS, Healthcare Common Procedure Coding System.

IMPORTANT SAFETY INFORMATION (continued)

ADVERSE REACTIONS FOR NALIRIFOX

- The most common adverse reactions (≥20%) of NALIRIFOX were diarrhea (72%), fatigue (62%), nausea (59%), vomiting (40%), decreased appetite (37%), abdominal pain (35%), mucosal inflammation (28%), constipation (25%), and weight decreased (22%).
- Permanent discontinuation of ONIVYDE due to an adverse reaction occurred in 17% of patients. Adverse reactions that resulted in permanent discontinuation of ONIVYDE in ≥1% of patients included neutropenia, thrombocytopenia, diarrhea, fatigue, infections, and cerebrovascular accident.
- Dosage reduction of ONIVYDE due to an adverse reaction occurred in 52% of patients. Adverse reactions that required dosage reduction in ≥1% of patients included anemia, decreased appetite, diarrhea, fatigue, febrile neutropenia, hypokalemia, liver function test abnormalities, nausea, mucosal inflammation, neutropenia, peripheral neuropathy, vomiting, thrombocytopenia, and weight decreased.

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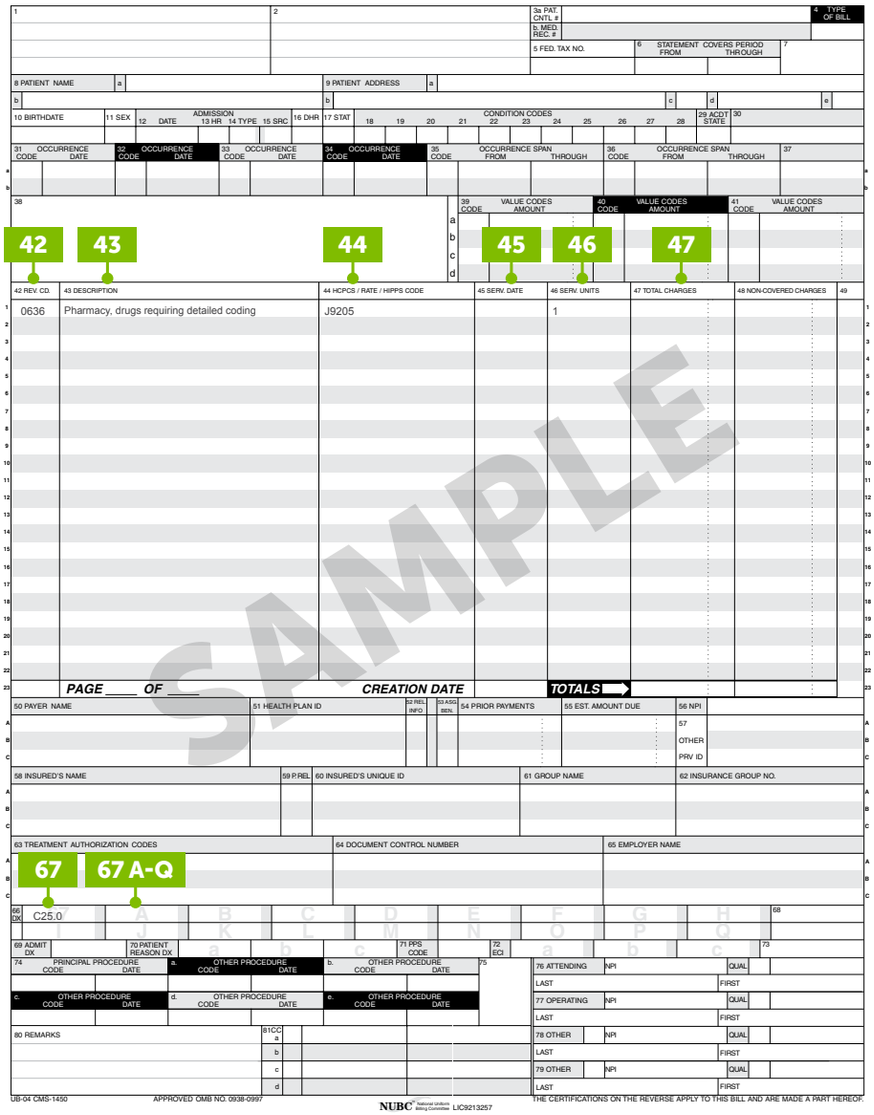
SAMPLE CMS-1450 CLAIM FORM HOSPITAL OUTPATIENT SETTING

ONIVYDE and the associated services provided in a hospital outpatient setting are billed on the CMS-1450 claim form or its electronic equivalent. A sample CMS-1450 claim form for billing ONIVYDE is provided below.

The sample claim form provided below is only an example. It is always the provider's responsibility to determine the appropriate healthcare setting and to submit true and correct claims for the products and services rendered. Providers should contact third-party payers for specific information on their coding, coverage, and payment policies.



LOCATOR 42:
List the appropriate revenue code for the service provided.

For Medicare: 0636 - Pharmacy, drugs requiring detailed coding.

For payers other than Medicare, the revenue code for ONIVYDE may vary; although some private payers and Medicaid plans accept revenue code 0636 in the hospital outpatient setting, others may require revenue code 025X (Pharmacy).

LOCATOR 43:
Enter the corresponding description for the revenue code listed in Locator 42.

LOCATOR 44:
Enter the appropriate HCPCS code.

J9205 - Injection, irinotecan liposome, 1 mg

LOCATOR 45:
Enter the service date.

LOCATOR 46:
Enter the number of service units for each line item. A single-dose vial (10 mL) contains 43 billable units of J9205.

Use the JW modifier to report discarded units (if applicable) as required by Medicare or other payers.

LOCATOR 47:
Enter the total charge for each line item.

LOCATOR 67:
Enter the primary diagnosis code.

LOCATOR 67 A-Q:
Enter any secondary diagnosis code(s) listed in the patient's medical record.

IMPORTANT SAFETY INFORMATION (continued)

ADVERSE REACTIONS FOR NALIRIFOX (continued)

- Dosage interruptions of ONIVYDE due to an adverse reaction occurred in 1.9% of patients. Adverse reactions which required dosage interruption in ≥0.5% of patients included hypersensitivity and infusion-related reaction.
- The most common laboratory abnormalities (≥10% Grade 3 or 4) were decreased neutrophils (26%), decreased potassium (22%), decreased lymphocytes (11%), and decreased hemoglobin (10%).

ADVERSE REACTIONS FOR ONIVYDE/FU/LV

- The most common adverse reactions (≥20%) were diarrhea (59%), fatigue/asthenia (56%), vomiting (52%), nausea (51%), decreased appetite (44%), stomatitis (32%), and pyrexia (23%).

Please see Important Safety Information on pages 3 and 4 and accompanying full Prescribing Information, including BOXED WARNING.

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IPSEN CARES® OVERVIEW

Helping Patients Get Access to Their Prescribed Medications With the Information They Need

IPSEN CARES serves as a central point of contact between patients/caregivers, healthcare providers, insurance companies, and specialty pharmacies.

The IPSEN CARES Program is staffed by dedicated Patient Access Managers who can assist in a variety of ways:

Phone: 1-866-435-5677
Fax: 1-888-525-2416

Hours: Monday – Friday, 8:00 AM – 8:00 PM ET

Website: IPSENCARES.com

Reimbursement Assistance

- **Benefits Verification** — Verifies patients' coverage, restrictions (if applicable), and copayment/coinsurance amounts
- **Prior Authorization (PA)/Appeals**
  - Provides information on documentation required by payers on PA specifics and recommendations for next steps based on payer policy
  - Provides information on the payer appeals process
- **Billing and Coding Information**

Financial Support

- **Copayment Assistance** — The Onivyde Copay Assistance Program offers copay assistance to eligible[a] commercially-insured patients
- **Patient Assistance Program (PAP)** — Determines patients' eligibility[b] for PAP and dispenses free product to eligible patients

Product Distribution

- **Institutions** — ONIVYDE can be acquired from wholesaler
- **Private Practices**
  - Direct (buy-and-bill) acquisition from a group of approved specialty distributors
  - Specialty pharmacy delivery (IPSEN CARES can provide helpful information on selection of the appropriate specialty pharmacy for the patient by calling 1-866-435-5677)

Patient Support

- **Communication With Providers and Patients** — Conducts calls to both healthcare provider and patient with status updates about patient's IPSEN CARES enrollment, benefits verification results, coverage status, dispense date, etc.
- **Medication Nurse Support Program**
  - Patients prescribed ONIVYDE who are enrolled in IPSEN CARES can receive individualized support provided by an IPSEN CARES Nurse to help them through their treatment journey.

[a]See page 13 for Copay Assistance Program Patient Eligibility & Terms and Conditions.

[b]Patients may be eligible for free medication through our PAP. Patients may be eligible to receive free drug if they 1) are experiencing financial hardship, 2) are uninsured or functionally uninsured, 3) are US residents, 4) received a prescription for an on-label use of an Ipsen medication as supported by information provided in the program application, and 5) meet income criteria based on Experian soft credit check. Eligibility does not guarantee approval for participation in the program. The PAP provides ONIVYDE product only, and does not cover the cost of previously purchased product or medical services.

Please see Important Safety Information on pages 3 and 4 and accompanying full Prescribing Information, including BOXED WARNING.

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onivyde® (irinotecan liposome injection)

IPSEN CARES® OVERVIEW

Onivyde Copay Assistance Program

Eligible* commercially-insured patients may pay as little as $0 per prescription

Steps for Patients to Receive Onivyde Assistance

1. Provider and patient complete the Enrollment Form and send to IPSEN CARES
2. Patient is administered Onivyde
3. Provider submits claim to patient's insurance company
4. Once claim is paid, provider submits the following documents via fax 1-888-525-2416 or via the upload function at IPSENCARES.com
   - Completed CMS-1500 or CMS-1450 form
   - Explanation of benefits (EOB)/remittance from the patient's primary private insurance showing itemized allowed charges and remaining cost share for Onivyde therapy
5. IPSEN CARES typically processes eligible claim payments to a patient's provider within 7-10 business days via EFT (wire transfer) or check

*See page 13 for Copay Assistance Program Eligibility & Terms and Conditions.

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IPSEN CARES® OVERVIEW

Copay Assistance Program

*Patient Eligibility & Terms and Conditions: Patients are not eligible for copay assistance through IPSEN CARES® if they are enrolled in any state or federally funded programs for which drug prescriptions or coverage could be paid in part or in full, including, but not limited to, Medicare Part B, Medicare Part D, Medicaid, Medigap, VA, DoD, or TRICARE (collectively, "Government Programs"), or where prohibited by law. Patients must be United States residents (including its territories) and enrolled in IPSEN CARES® to receive copay program benefits. Patients residing in Massachusetts or Rhode Island can only receive assistance with the cost of Ipsen products but not the cost of related medical services (injection). Patients receiving assistance through another assistance program or foundation, free trial, or other similar offer or program, are not eligible for the copay assistance program during the current enrollment year.

An annual calendar year maximum copay benefit applies. Patients may remain enrolled in copay assistance as long as eligibility criteria is met.

Patients or guardians are responsible for reporting receipt of copay savings benefit to any insurer, health plan, or other third party who pays for or reimburses any part of the prescription filled through the program, as may be required. Additionally, patients or guardians may not submit any benefit provided by this program for reimbursement through a Flexible Spending Account, Health Savings Account, Health Reimbursement Account, or otherwise to a government or private payor. Ipsen reserves the right to rescind, revoke, or amend these offers without notice at any time. Ipsen and/or its copay assistance vendor are not responsible for any transactions processed under this program where Medicaid, Medicare, or Medigap payment in part or full has been applied. Claim reimbursement requests must be submitted within 180 days of treatment date. Data related to patient participation may be collected, analyzed, and shared with Ipsen for market research and other purposes related to assessing the program. Data shared with Ipsen will be de-identified, meaning it will not identify the patient. Void outside of the United States and its territories or where prohibited by law, taxed, or restricted. This program is not health insurance. No other purchase is necessary. Copay assistance cannot be sold, purchased, traded, or counterfeited. Void if reproduced.

IMPORTANT SAFETY INFORMATION (continued)

ADVERSE REACTIONS FOR ONIVYDE/FU/LV (continued)

- Adverse reactions led to permanent discontinuation of ONIVYDE in 11% of patients receiving ONIVYDE/FU/LV; the most frequent adverse reactions resulting in discontinuation of ONIVYDE were diarrhea, vomiting, and sepsis.
- Dose reductions of ONIVYDE for adverse reactions occurred in 33% of patients receiving ONIVYDE/FU/LV; the most frequent adverse reactions requiring dose reductions were neutropenia, diarrhea, nausea, and anemia.
- ONIVYDE was withheld or delayed for adverse reactions in 62% of patients receiving ONIVYDE/FU/LV; the most frequent adverse reactions requiring interruption or delays were neutropenia, diarrhea, fatigue, vomiting, and thrombocytopenia.
- The most common severe laboratory abnormalities (≥10% Grade 3 or 4) were lymphopenia and neutropenia.

Postmarketing Experience: Immune system disorders: Hypersensitivity (including anaphylactic reaction and angioedema).

DRUG INTERACTIONS

- Avoid the use of strong CYP3A4 inducers, if possible, and substitute non-enzyme inducing therapies ≥2 weeks prior to initiation of ONIVYDE.
- Avoid the use of strong CYP3A4 or UGT1A1 inhibitors, if possible, and discontinue strong CYP3A4 inhibitors ≥1 week prior to starting therapy.

USE IN SPECIFIC POPULATIONS

- Pregnancy and Reproductive Potential: See WARNINGS & PRECAUTIONS. Advise males with female partners of reproductive potential to use condoms during and for 4 months after the last dose of ONIVYDE treatment.
- Lactation: Advise nursing women not to breastfeed during and for 1 month after the last dose of ONIVYDE treatment.

Please see Important Safety Information on pages 3 and 4 and accompanying full Prescribing Information, including BOXED WARNING.

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ONIVYDE COPAY ASSISTANCE PROGRAM

Frequently Asked Questions

Q: What are the Onivyde Copay Assistance Program eligibility criteria?*

A: Patients are not eligible for copay assistance through IPSEN CARES® if they are enrolled in any state or federally funded programs for which drug prescriptions or coverage could be paid in part or in full, including, but not limited to, Medicare Part B, Medicare Part D, Medicaid, Medigap, VA, DoD, or TRICARE (collectively, "Government Programs"), or where prohibited by law. Patients must be United States residents (including its territories) and enrolled in IPSEN CARES to receive copay program benefits. Patients receiving assistance through another assistance program or foundation, free trial, or other similar offer or program, are not eligible for the Onivyde Copay Assistance Program during the current enrollment year.

Q: What does the Onivyde Copay Assistance Program cover?*

A: The Copay Assistance Program covers the patient's out of pocket cost for the prescription medicine, and its applicable administration copay, where allowed by state law up to the annual calendar year maximum copay program benefit amount. Any surgical, physician, and/or laboratory expenses will be excluded from payment.

Q: How do patients know that they have been enrolled?

A: Patients will receive notification of copay enrollment and will be mailed a welcome letter. The provider will also be sent a welcome fax.

Q: Where can the Onivyde Copay Assistance Program be used?

A: The Onivyde Copay Assistance Program is available to be used in the provider's office/practice or hospital when using the patient's medical benefits. The Copay Assistance Program is also available when using the patient's pharmacy benefit and obtaining the prescription through a specialty pharmacy.

Q: Are cash-pay patients allowed to use the Onivyde Copay Assistance Program?

A: No. Patients must be enrolled in a commercial insurance plan to be eligible for the Copay Assistance Program.

Q: Are patients with government insurance eligible for the Onivyde Copay Assistance Program?

A: No. Patients are not eligible for copay assistance if they are enrolled in any state or federally funded programs for which drug prescription or coverage could be paid in part or in full, including but not limited to Medicare Part B, Medicare Part D, Medicaid, Medigap, VA, DoD, or Tricare (collectively, "Government Programs").

Q: What is the timely filing submission requirement for reimbursement requests?

A:: Claim reimbursement requests must be submitted within 180 days of treatment date.

Q: When does the program reset? What do the patient and provider have to do to remain enrolled?

A: The program resets on January 1. Patients may remain enrolled in copay assistance as long as eligibility criteria are met.

*See page 13 for Patient Eligibility & Terms and Conditions.

For questions about the Onivyde Copay Assistance Program, call us:

1-866-435-5677

Monday – Friday, 8:00 AM – 8:00 PM ET

For additional information, visit us online at **IPSENCARES.com**

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REGIONAL REIMBURSEMENT DIRECTORS ARE AVAILABLE TO EDUCATE HEALTHCARE PROFESSIONALS

- Increase healthcare professionals' knowledge about reimbursement of Ipsen products
- Provide information to help address complex reimbursement issues for healthcare professionals
- Explain IPSEN CARES® services and support offerings for patients and healthcare professionals

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Hours: Monday – Friday, 8:00 AM – 8:00 PM ET
Phone: 1-866-435-5677
Fax: 1-888-525-2416
IPSENCARES.com

To learn more about ONIVYDE® (irinotecan liposome injection), visit ONIVYDE.com.

Please see accompanying full Prescribing Information, including BOXED WARNING.

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