onivyde®
(irinotecan liposome injection)

Sample Letter of Medical Necessity

A Letter of Medical Necessity (LMN) explains the prescriber's rationale and clinical decision-making for choosing a specific treatment option.

Health plans often require LMNs as part of a prior authorization or when appealing a coverage determination.

On the last page of this document is a sample LMN for ONIVYDE that uses an editable template. Read through to get a better idea of what a LMN looks like, and then use the template to customize based on your medical opinion and your individual patients' needs.

Please note: This template is for informational purposes only, providing an outline of the types of information that may be required or helpful when seeking medical exception from a patient's health plan. Use of this information does not constitute medical or legal advice and does not guarantee reimbursement for coverage. It is not intended to be a substitute for, or an influence on, the independent clinical decision of the prescribing healthcare professional. IPSEN makes no representations or warranties about the template or its fitness for any specific use. IPSEN is not responsible for any changes made to the template document. All billing and coding decisions are the responsibility of the relevant physician

For additional information:
Call 1-866-435-5677 Monday – Friday, 8:00 am – 8:00 pm ET
or visit us online at IPSENCARES.com

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.

Please see additional Important Safety Information on pages 1-3 and full Prescribing Information, including BOXED WARNING, for ONIVYDE.

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WARNINGS AND PRECAUTIONS

Severe Neutropenia: ONIVYDE can cause severe or life-threatening neutropenia and fatal neutropenic sepsis. 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: 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): ONIVYDE can cause severe and fatal ILD. Postmarketing cases of severe and fatal ILD have been reported with ONIVYDE. Risk factors include pre-existing lung disease, use of pneumotoxic medicinal products, colony stimulating factors or having previously received radiation therapy. 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: Ilrinotecan, including ONIVYDE, can cause severe hypersensitivity reactions, including anaphylactic reactions. Permanently discontinue ONIVYDE in patients who experience a severe hypersensitivity reaction.

Embryo-Fetal Toxicity: Based on animal data with irinotecan HCl and the mechanism of action of ONIVYDE, 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.

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%).

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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

The following adverse reactions have been identified during post approval use of ONIVYDE:

- 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: Based on animal data with irinotecan HCl and the mechanism of action of ONIVYDE, ONIVYDE can cause fetal harm when administered to a pregnant woman. There are no available data in pregnant women. Advise pregnant women of the potential risk to a fetus.
- Lactation: Advise nursing women not to breastfeed during and for 1 month after the last dose of ONIVYDE.

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.

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onivyde® (irinotecan liposome injection)

[Insert Date]

To: **[Insurance Company]**
[Address]
[City, State Zip]

Re: **[Patient Name]**
Policy/ID #: **[Policy #]**
DOB: **[DOB]**
Case ID: **[ID #]**

To Whom It May Concern:

I am writing this letter of medical necessity in support of my request for **[Patient Name]** to begin treatment with ONIVYDE® (irinotecan liposome injection), an FDA-approved therapy indicated, in combination with oxaliplatin, fluorouracil, and leucovorin (NALIRIFOX), 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. ONIVYDE as part of the NALIRIFOX regimen received FDA approval based on NAPOLI 3 (#NCT04083235), a randomized, multicenter, open-label, active-controlled trial including 770 patients with metastatic pancreatic adenocarcinoma who had not previously received chemotherapy in the metastatic setting. ONIVYDE cannot be substituted for other drugs containing irinotecan hydrochloride (HCl). ONIVYDE is not indicated as a single agent for the treatment of patients with metastatic pancreatic adenocarcinoma and is contraindicated in patients with a history of severe allergic reactions with irinotecan HCl or ONIVYDE. Risk factors include pre-existing lung disease, use of pneumotoxic medicinal products, colony stimulating factors or having previously received radiation therapy.

Consistent with the ONIVYDE® Prescribing Information, the patient has been assessed for risk factors including: preexisting lung disease and embryo-fetal toxicity, and advised of the potential risk for serious adverse reactions to ONIVYDE, including severe neutropenia, severe diarrhea, interstitial lung disease, and severe hypersensitivity reactions, **[as well as of the need for nursing women to discontinue breastfeeding during treatment and for one month after the last dose.]**

This letter outlines **[Patient Name]**'s medical history **[and previous treatments]** that support my recommendation for treatment with ONIVYDE.

Patient History, Past Treatments, and Therapies Utilized:
[Include information outlining date of diagnosis with ICD-10 code, severity of symptoms, and past treatments, including start/end dates and reason for discontinuation.]

Rationale for Treatment With ONIVYDE:
[Provide information on clinical rationale for prescribing ONIVYDE, including patient response to past treatments and anticipated prognosis; include laboratory test results for pregnancy status, if applicable.]

Supporting Study Data:
[Provide clinical rationale for treatment; clinical trial information for ONIVYDE can be found in Section 14 (Clinical Studies) of the Prescribing Information for ONIVYDE.]

In summary, in my medical judgment, based on the patient's current condition and available clinical data, treatment with ONIVYDE for **[Patient Name]** is medically appropriate and necessary. Please feel free to contact me if you require additional information. I look forward to receiving your timely response and approval of this request.

Sincerely,

[Physician Name and Signature]
[Physician Medical Specialty]
[Physician Practice Name]
NPI #: **[Physician NPI#]**
Phone: **[Phone #]**
Fax: **[Fax #]**

Onivyde (irinotecan liposome injection) Prescribing Information. Ipsen Biopharmaceuticals, Inc.; 2024.

Please click here to download and customize the Letter of Medical Necessity

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