onivyde®
(irinotecan liposome injection)

Dear Healthcare Professional:

This packet contains a set of educational resources compiled to help navigate the prior authorization (PA) process for patients who have been prescribed ONIVYDE® (irinotecan liposome injection).

1. PA background, tips, and checklist (pages 2–5)
2. Letter of Medical Necessity tips, checklist, and template (pages 6–7)
3. Letter of Appeal tips and checklist (pages 8–9)

Please note: These resources are provided for information purposes only and include general guidance related to requesting prior authorization and appealing coverage decisions. Use of this information does not guarantee that a health plan will provide reimbursement for ONIVYDE and is not intended to be a substitute for or an influence on your independent medical judgment. IPSEN makes no representations or warranties about the information or template provided, 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 AND LIMITATIONS OF USE:

- 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.

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

IMPORTANT SAFETY INFORMATION (ISI)

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 10–11 and full Prescribing Information, including BOXED WARNING, for ONIVYDE.

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PRIOR AUTHORIZATION (PA)

A payer may require a Prior Authorization. This requirement does not necessarily mean a product is not covered. For example, ONIVYDE® (irinotecan liposome injection) is covered on most payer plans; however, based on varying plan criteria, you may find that completion of one or more of the following documents is required for PA approval.

1. **Prior Authorization (PA)**—sometimes called preauthorization or precertification—is a process by which physicians and other healthcare providers must obtain advance approval from a health plan before a specific service or treatment option is delivered to the patient in order to qualify for payment coverage.[1]

2. **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.[2]

3. **Letter of Appeal**—is a written request for a health insurance plan to review a decision that denies a benefit or payment for a specific treatment. An appeal letter will usually include supporting evidence for the treatment prescribed, an explanation of why the decision should be reconsidered, and a request to expedite the review.[3,4]

Step by Step Through the PA Process

Depending on payer requirements, it may be necessary to complete and submit one or more of the forms of documentation included in the steps below.

1. Is a PA required?
   - If yes ➔ Submit PA (see tips, checklist, template on pages 2–5)
   - Note: PA process may require inclusion of LMN at start of process
2. Insurance reviews documentation.
3. Is additional information required?
   - If yes ➔ Submit LMN (see tips, checklist, template on pages 6–7)
4. Has request been approved?
   - If yes ➔ You and your patient will be notified
5. Has request been denied?
   - If yes ➔ Submit Letter of Appeal (see tips and checklist on pages 8–9)

REFERENCES: 1. American Medical Association. Prior authorization practice resources. Updated May 18, 2023. Accessed September 26, 2024. HTTPS://WWW.AMA-ASSN.ORG/PRINT/PDF/NODE/36506 **2.** National Association of Insurance Commissioners. Understanding healthcare bills: What Is Medical Necessity? Accessed January 30, 2025. https://content.naic.org/sites/default/files/consumer-health-insurance-what-is-medical-necessity.pdf **3.** Healthcare.gov. Glossary: appeal. Accessed September 26, 2024. https://www.healthcare.gov/glossary/appeal/ **4.** National Association of Insurance Commissioners. Understanding healthcare bills: How to appeal denied claims. Accessed September 26, 2024. https://content.naic.org/sites/default/files/consumer-health-insurance-appeal-denied-claims.pdf

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TIPS FOR HANDLING PA REQUIREMENTS FROM HEALTH PLANS

Please be aware that PA requirements may vary according to plan. In addition to the recommendations below, be sure to provide all documentation required by the plan. Contact the plan directly if you have questions.

Understand Health Plan Requirements

- Be sure to fulfill any plan-specific guidelines and/or requirements for authorizing treatment

Provide Correct Identification (ID) Numbers

- Indicate the individual provider ID number versus the group practice/facility provider ID number on the prescription form
- Obtain the patient ID number from his or her insurance card
- Provide correct NDC number for the drug for which you are seeking authorization. The NDC number for Onivyde is 15054-9943-01 (ONIVYDE single-dose 10 mL vial container 43 mg of irinotecan liposome for injection)
- Provide correct ICD-10 diagnosis code(s) for the condition/diagnosis:

Code Type	Code	Code Description
ICD-10-CM (metastatic pancreatic adenocarcinoma)*	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
HCPCS	J9205	Injection, irinotecan liposome, 1 mg

HCPCS, Healthcare Common Procedure Coding System; ICD-10-CM, International Classification of Diseases, 10th Revision, Clinical Modification; NDC, National Drug Code.

*This table has been reviewed for accuracy and completeness; however, there may be less commonly used codes that are missing. For additional codes, please refer to a coding resource.

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Include Supporting Documents

- Whenever possible, submit all required supporting documents with the PA request
- Include a photocopy of the patient's health plan prescription card (front and back)

Check for the Letter of Medical Necessity

- The Letter of Medical Necessity may need to be updated and/or resubmitted (this letter is usually valid for 12 months from the original dated signature)

Be Aware of Deadlines

- Prepare in advance and collect any required documents to meet all deadlines for PA submission

Follow Up

- If you do not receive a decision within 5 to 7 days, consider following up via phone or email

Maintain Complete Records

- Keep a copy of everything you submit for the PA (also keep a log of every phone call you make to the patient's health plan, including the date and the name of the person with whom you spoke)

PA SUBMISSION CHECKLIST

PA criteria may vary by plan. Please be sure to consult the website for the patient's insurer to confirm PA criteria, if available. Below is a checklist of forms and documents you may need to submit to a health plan to obtain a PA (be sure to fill out all requested information).

- ☑ Sender and recipient contact information (e.g., fax number, email address)
- ☑ Completed prescription form
- ☑ Copy of the patient's health insurance card and/or prescription card (include front and back), including all relevant membership numbers
- ☑ Supporting documentation (as required)
- ☑ PA form specific to health plan
- ☑ Patient history and physical findings/diagnosis
- ☑ ONIVYDE published clinical studies, including the NAPOLI 3 trial (NCT04083235)
- ☑ American Society of Clinical Oncology (ASCO) Standards of Medical Care in Metastatic Pancreatic Cancer
- ☑ Chart notes from healthcare provider or clinician
- ☑ Hospital admission or emergency department notes, if applicable or relevant
- ☑ Patient authorization and notice of release of information

Important: Confirm receipt of documentation for all PA submissions and request additional information if criteria are unclear.

TIPS FOR WRITING AN EFFECTIVE LETTER OF MEDICAL NECESSITY

- Review the health plan's coverage criteria for ONIVYDE® (irinotecan liposome injection) and provide details for the criteria that your patient meets. If applicable, provide your rationale for excluding your patient from criteria they do not meet.
- Clearly state why ONIVYDE is the appropriate choice for the patient.
- Provide clinical justification to support your decision to prescribe ONIVYDE and attach relevant clinical data, such as chart notes, relevant laboratory test results, and pregnancy status (see full guidance in Section 5 WARNINGS AND PRECAUTIONS of the ONIVYDE Prescribing Information).
- Describe any other patient characteristics and/or clinical considerations relevant to therapy with ONIVYDE.
- Attach documentation that supports your recommendation; some information may be in the ONIVYDE Prescribing Information (consider Section 14 CLINICAL STUDIES for efficacy data and Section 12 CLINICAL PHARMACOLOGY for information regarding ONIVYDE's mechanism of action).
- Read the process for submitting the letter to ensure that you are meeting the requirements of the health plan and state guidelines, including how to submit the request (e.g., fax, phone, email, health plan website).
- Track the status of your request and follow up with the health plan if needed.

LETTER OF MEDICAL NECESSITY CHECKLIST

Having the following information ready before you begin an LMN may help make the process more efficient:

- ☑ Patient's full name and date of birth
- ☑ Patient's insurance policy/ID number
- ☑ Case ID number (for appeals)
- ☑ Brief medical history including diagnosis, ICD-10 code, comorbidities, and allergies
- ☑ Patient's current and prior therapeutic regimens (include start/stop dates and the reason[s] for discontinuation)
- ☑ Background on the patient's current condition and symptoms
- ☑ Clinical support for your recommendation

NOTE: Please see the **editable LMN template** for ONIVYDE on the next page. You will be able to customize the template based on your medical opinion and the individual needs of your patient. For a downloadable version please visit IPSENCARES.com

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

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[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 #]**

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

TIPS FOR FILING AN APPEAL OF COVERAGE DENIAL

The following tips can be helpful for handling common denial issues. Each denial is different. Refer to the original denial documentation for specific requests for additional information.

Identify the Reason for Denial

- Find out in writing why the authorization request has been denied. The reason should be in the denial letter from the patient's health plan or in the explanation of benefits letter. If you did not receive either of these, they can be obtained from the insurer.

Determine the Appeal Guidelines

- Contact the insurer to find out its deadline for appealing, the number of appeals permitted (some plans only allow one), and the mailing address or fax number to which the appeal should be sent. Some insurers have short appeal periods—you may need to respond promptly. Also, inquire whether the appeal should be submitted by the patient or the healthcare provider and proceed accordingly.

Contact the Review Department

- Many denial letters include a telephone number for the review department that physicians can call for further clarification. In some instances, if a reviewer with your rationale and approves treatment for the patient during the call, the appeal process is completed.

Compose a Written Appeal

- Most insurers require a written appeal from either the member or the healthcare provider. The insurer should tell you what is needed. A written appeal package includes an appeal letter and supporting documents.

Provide Additional Supporting Documentation

- Consider including all relevant medical documentation—including clinical notes to support your case for coverage. Any newly available information related to the patient's condition should be supplied as well.

Follow Up as Needed

- Consider contacting the patient's insurer if they have not responded within 30 to 60 days of receipt of the appeal package.

Maintain Complete Records

- Retain a duplicate copy of all documentation submitted with the patient's appeal and record all subsequent communications made to the patient's insurer. Include the date and the name of the person contacted.

Consider whether an expedited appeal pathway is available and appropriate in this case

- Be sure to fax this request for appeal to the patient's insurer.

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DOCUMENTS FOR FILING A RESPONSE TO TREATMENT DENIAL: AN APPEAL CHECKLIST

If an insurer denies coverage of a prescribed treatment for your patient, the following is a sample checklist of materials you may need for an appeal package. Note that each appeal may need different information depending on the insurer and/or patient.

- ☑ Carefully review each denial and the insurer's requirements to determine what to include in a patient's appeal package.
- ☑ Letter of Medical Necessity
- ☑ Patient authorization and notice of release of information
- ☑ Copy of the patient's health plan or prescription card (front and back)
- ☑ Denial information, including the patient's denial letter and/or explanation of benefits
- ☑ Letter of appeal
- ☑ Supporting documentation
  - ☐ ONIVYDE (irinotecan liposome injection) prescribing information
  - ☐ ONIVYDE published clinical studies, including the NAPOLI 3 trial (NCT04083235)
  - ☐ American Society of Clinical Oncology (ASCO) Standards of Medical Care in Metastatic Pancreatic Cancer
  - ☐ Patient clinical/diagnostic records within last 6 months unless otherwise noted

If you have questions, contact Ipsen Cares or your Ipsen Regional Reimbursement Director

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: 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.

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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: 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%).

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 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.

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