A GUIDE TO ASSESSING CHEMOTHERAPY-INDUCED ADVERSE EVENTS FOR NURSES

onivyde®
(irinotecan liposome injection)

INDICATION

ONIVYDE® (irinotecan liposome injection) is indicated, in combination with fluorouracil (5-FU) and leucovorin (LV), for the treatment of patients with metastatic adenocarcinoma of the pancreas after disease progression following gemcitabine-based therapy.

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

IMPORTANT SAFETY INFORMATION

WARNING: SEVERE NEUTROPENIA and SEVERE DIARRHEA

- Fatal neutropenic sepsis occurred in 0.8% of patients receiving ONIVYDE. Severe or life-threatening neutropenic fever or sepsis occurred in 3% and severe or life-threatening neutropenia occurred in 20% of patients receiving ONIVYDE in combination with 5-FU and LV. Withhold ONIVYDE for absolute neutrophil count below 1500/mm^3 or neutropenic fever. Monitor blood cell counts periodically during treatment
- Severe diarrhea occurred in 13% of patients receiving ONIVYDE in combination with 5-FU/LV. 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

CONTRAINDICATION

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 18-20 and accompanying full Prescribing Information, including Boxed WARNING, for ONIVYDE®.

ABOUT THIS GUIDE[1]

As an oncology nurse, you have a significant role in helping patients with metastatic pancreatic cancer at every phase of their treatment journey. Adverse reactions impact patients' lives, as well as their ability to continue treatment. ASCO guidelines recommend supportive symptom management early in the disease. That can help patients with metastatic pancreatic cancer manage through a difficult time.

This guide was created to support you as you help your patients navigate adverse events that may be severe, so they may have a chance to continue therapy as recommended.

MANAGING DIARRHEA

PATIENTS ON THE ONIVYDE® + 5-FU/LV REGIMEN MAY EXPERIENCE DIARRHEA, INCLUDING SEVERE DIARRHEA.

CONSIDER ASSESSING DIARRHEA ACCORDING TO NATIONAL CANCER INSTITUTE (NCI) CRITERIA[2,3]

GRADE 1	Increase of less than 4 stools per day over baseline
GRADE 2	Increase of 4-6 stools per day over baseline Further indications: • Nocturnal stools • Moderate cramping (not interfering with daily activities)
GRADE 3	Increase of 7 or more stools per day over baseline Further indications: • Severe cramping and incontinence (interfering with daily activities and self care) Response: • Hospitalization
GRADE 4	Diarrhea with life-threatening consequences Further indications: • Diarrhea that is bloody Response: • Urgent intervention

Please see Important Safety Information on pages 18-20 and accompanying full Prescribing Information, including Boxed WARNING, for ONIVYDE®.

MANAGING DIARRHEA (CONT'D)

Assessing chemotherapy-induced diarrhea (CID) **accurately** may help treatment outcomes and prevent complications, which can be important for metastatic pancreatic cancer patients, for whom *every moment matters.*[4]

IN ADDITION TO NCI ASSESSMENT, CONSIDER THESE STEPS[4,5]:

EVALUATE ABDOMEN

- Abdominal exam—check for tenderness, guarding, rigidity; signs of bloating; presence of bowel sounds
- Perianal or peristomal exam—check skin integrity; look for hemorrhoids or rectal fissures

EVALUATE HYDRATION STATUS

- Skin turgor, mucosal/conjunctival moisture, vein filling/emptying
- Changes in orthostatic blood pressure
- Lab tests for electrolytes, blood urea nitrogen, and creatinine
- Electrolyte imbalance can be a serious complication of diarrhea (see page 14 for details)

RULE OUT INFECTION

- Stool culture lab tests to assess for infection (eg, *clostridium difficile*)
- Complete blood count

EDUCATE PATIENTS AND CAREGIVERS

- Review dietary guidelines
- Review any over-the-counter medicines, vitamins, herbal therapies

ONIVYDE® Nurse's Guide to Assessing Chemotherapy-Induced Diarrhea has additional information about managing diarrhea in patients taking ONIVYDE®.

SELECTED IMPORTANT SAFETY INFORMATION FOR ONIVYDE®

WARNINGS AND PRECAUTIONS

- **Severe Neutropenia: See Boxed WARNING.** In patients receiving ONIVYDE/5-FU/LV, the incidence of Grade 3/4 neutropenia was higher among Asian (18/33 [55%]) vs White patients (13/73 [18%]). Neutropenic fever/neutropenic sepsis was reported in 6% of Asian vs 1% of White patients

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REMIND PATIENTS AND CAREGIVERS[6-9]

- Contact your healthcare provider immediately in case of: persistent vomiting or diarrhea; black or bloody stools; or symptoms of dehydration
- Risk of severe diarrhea: track symptoms when patient begins treatment and refer to the Patient Brochure on ONIVYDE.com
- Emphasize the importance of avoiding dehydration and electrolyte imbalance
- Avoid foods or beverages that could trigger bowel movements, such as:
  - Fresh fruits, juices, lactose-containing products, carbonated drinks, spicy foods, high fat foods, caffeine, and alcohol
- Frequent small meals instead of 2-3 large ones can be easier on your system

Please see Important Safety Information on pages 18-20 and accompanying full Prescribing Information, including Boxed WARNING, for ONIVYDE®.

DOSE MODIFICATIONS FOR DIARRHEA

IN THE EVENT OF DIARRHEA, ONIVYDE® + 5-FU/LV OFFERS A PROTOCOL FOR DOSE REDUCTION, DELAY, AND DISCONTINUATION[6]

ADVERSE REACTION	DIRECTIONS	ONIVYDE® ADJUSTMENT IN PATIENTS RECEIVING 70 MG/M²	PATIENTS HOMOZYGOUS FOR UGT1A1*28 (WHO ARE CURRENTLY RECEIVING 50 MG/M²)
GRADE 2 DIARRHEA	Withhold ONIVYDE®. Administer loperamide for late diarrhea of any severity. Administer atropine, if not contraindicated, for early diarrhea of any severity.*		
GRADE 3 OR 4 DIARRHEA	Withhold ONIVYDE®. Initiate loperamide for late-onset diarrhea of any severity. Administer intravenous or subcutaneous atropine 0.25 to 1 mg (unless clinically contraindicated) for early onset diarrhea of any severity. Upon recovery to ≤Grade 1, resume ONIVYDE® at a modified dose.	FIRST OCCURRENCE: 50 mg/m²	FIRST OCCURRENCE: 43 mg/m²
		SECOND OCCURRENCE: 43 mg/m²	SECOND OCCURRENCE: 35 mg/m²
		THIRD OCCURRENCE: Discontinue ONIVYDE®	THIRD OCCURRENCE: Discontinue ONIVYDE®

*See dose modifications for other adverse events on page 17 of this brochure.

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MANAGING NAUSEA AND VOMITING

CONSIDER ASSESSING NAUSEA ACCORDING TO NCI CRITERIA[2]

GRADE 1	Loss of appetite without alteration in eating habits
GRADE 2	Oral intake decreased without significant weight loss, dehydration or malnutrition
GRADE 3	Inadequate oral caloric or fluid intake; tube feeding, total parenteral nutrition (TPN), or hospitalization indicated

CONSIDER ASSESSING VOMITING ACCORDING TO NCI CRITERIA[2]

GRADE 1	Intervention not indicated
GRADE 2	Outpatient IV hydration; medical intervention indicated
GRADE 3	Tube feeding, TPN, or hospitalization indicated
GRADE 4	Life-threatening consequences

Please see Important Safety Information on pages 18-20 and accompanying full Prescribing Information, including Boxed WARNING, for ONIVYDE®.

MANAGING NAUSEA AND VOMITING (CONT'D)

IN ADDITION TO NCI ASSESSMENT, CONSIDER THESE STEPS[4]:

EVALUATE HYDRATION STATUS

- Skin turgor, mucosal/conjunctival moisture, vein filling/emptying
- Changes in orthostatic blood pressure
- Lab tests for electrolytes, blood urea nitrogen, and creatinine

EDUCATE PATIENTS AND CAREGIVERS

- Review dietary guidelines
- Review any over-the-counter medicines, vitamins, herbal therapies

RECOMMEND ANTI-EMETICS

REMIND PATIENTS AND CAREGIVERS[6,10]

There is a risk of nausea and vomiting, some of which may be serious with ONIVYDE® and they should:

- Contact your HCP immediately in case of: persistent vomiting or diarrhea; black or bloody stools; or symptoms of dehydration
- Eat a small meal or snack before chemotherapy on treatment days
- Try to sit upright for at least 1 hour after eating
- Take anti-nausea medicine at the first signs of nausea to help prevent vomiting
- See the Patient Brochure on ONIVYDE.com for more information

FOR VOMITING:

- If in bed, patient should lie on side
- After vomiting, start taking cool liquids or ice chips gradually

See dose modification information on page 17 of this brochure.

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MANAGING STOMATITIS

CONSIDER ASSESSING STOMATITIS/MUCOSITIS ACCORDING TO NCI CRITERIA[2]

GRADE 1	Endoscopic findings only; mild discomfort with normal intake
GRADE 2	Moderate pain, analgesics indicated; altered oral intake; limiting instrumental activities of daily living
GRADE 3	Severe pain; severely altered eating/swallowing; medical intervention indicated
GRADE 4	Life-threatening consequences; urgent intervention indicated

IN ADDITION TO NCI ASSESSMENT, CONSIDER THESE STEPS[9,11-13]:

- Symptoms usually develop 5 to 14 days after chemotherapy and include pain, burning, and redness in the mouth
- Determine if appropriate medications may be helpful to promote healing or as a preventive measure for high-risk patients
- Remember control of pain is critical and systemic pain medication may be called for if topicals are ineffective

REMIND PATIENTS AND CAREGIVERS[9,13]

- Swishing with ice chips during infusions may limit the development of painful oral sores
- Avoid acidic foods, alcohol, and smoking
- Good oral hygiene, including frequent mouth rinses can be helpful
- Report pain and worsening symptoms to a healthcare professional

See dose modification information on page 17 of this brochure.

Please see Important Safety Information on pages 18-20 and accompanying full Prescribing Information, including Boxed WARNING, for ONIVYDE®.

MANAGING DECREASED APPETITE

CONSIDER ASSESSING APPETITE LOSS ACCORDING TO NCI CRITERIA[2]

GRADE 1	Loss of appetite without alteration in eating habits
GRADE 2	Oral intake altered without significant weight loss or malnutrition; oral nutritional supplements indicated
GRADE 3	Associated with significant weight loss or malnutrition (e.g., inadequate oral caloric and/or fluid intake); tube feeding or TPN indicated
GRADE 4	Life-threatening consequences; urgent intervention indicated

IN ADDITION TO NCI ASSESSMENT, CONSIDER THESE STEPS[14,15]:

ASK PATIENTS

- What have you been eating, and how much?
- Are you taking any medications? These may cause drowsiness or insomnia
- How often do you experience symptoms of fatigue?
- Are you sleeping well at night, and for how long?

- If fatigue seems severe, consider checking complete blood count (CBC) for inflammatory markers, or radiography for disease progression[14,15]
- If patient shows signs of depression, consider a referral for psychiatric evaluation[14,15]

REMIND PATIENTS AND CAREGIVERS[9,14,16]

- Eating smaller meals during the day and getting adequate sleep can help
- To increase your appetite, consider moderate exercise like a short walk before meals[9]
- Avoid foods and beverages with strong smells, like garlic, onions, fish, and coffee
- Fatigue is common in patients being treated for pancreatic cancer with ONIVYDE®

See dose modification information on page 17 of this brochure.

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MANAGING FEBRILE NEUTROPENIA

PATIENTS ON THE ONIVYDE® + 5-FU/LV REGIMEN MAY EXPERIENCE NEUTROPENIA, INCLUDING SEVERE NEUTROPENIA.

CONSIDER ASSESSING FEBRILE NEUTROPENIA ACCORDING TO NCI CRITERIA[2]

GRADE 1	Not applicable
GRADE 2	Not applicable
GRADE 3	Absolute neutrophil count (ANC) <1000/mm^3 with a single temperature of >38.3 degrees C (101 degrees F) or a sustained temperature of ≥38 degrees C (100.4 degrees F) for more than one hour
GRADE 4	Life-threatening consequences; urgent intervention indicated

IN ADDITION TO NCI ASSESSMENT, CONSIDER THESE STEPS[5]:

- Watch for loss of fluids and electrolytes with severe diarrhea that can lead to greater risk of infectious complications in patients with chemotherapy-induced neutropenia
- Perform blood tests within 48 hours of scheduled treatment to assess neutropenia and changes in electrolytes

ASK

- Do you have a fever? When did it start?
- Are you experiencing chills, shortness of breath, or dizziness?

REMIND PATIENTS AND CAREGIVERS[6]

- Make sure you have a good thermometer, and use it regularly to keep track of your temperature
- Immediately contact your HCP if you're experiencing signs of infection, such as fever, chills, dizziness, or shortness of breath
- Serious or life-threatening side effects of ONIVYDE® include fever and infection associated with a low white neutrophil count

See dose modification information on page 17 of this brochure.

Please see Important Safety Information on pages 18-20 and accompanying full Prescribing Information, including Boxed WARNING, for ONIVYDE®.

MANAGING ANEMIA

CONSIDER ASSESSING ANEMIA ACCORDING TO NCI CRITERIA[2]

GRADE 1	Hemoglobin (Hgb) <LLN - 10.0 g/dL; <LLN - 6.2 mmol/L; <LLN - 100 g/L
GRADE 2	Hgb <10.0 - 8.0 g/dL; <6.2 - 4.9 mmol/L; <100 - 80 g/L
GRADE 3	Hgb <8.0 g/dL; <4.9 mmol/L; <80 g/L; transfusion indicated
GRADE 4	Life-threatening consequences; urgent intervention indicated

IN ADDITION TO NCI ASSESSMENT, CONSIDER THESE STEPS[5,17]:

- Perform blood tests within 48 hours of scheduled treatment to assess anemia and changes in electrolytes
- Depending on type of anemia, consider treatment with appropriate nutritional supplements

REMIND PATIENTS AND CAREGIVERS

- Keep a log of your symptoms and when they occur. Share with your HCP[18]
- Balance rest and activities. Only do activities that you can tolerate[9]

See dose modification information on page 17 of this brochure.

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ELECTROLYTE IMBALANCE

NORMAL VALUES FOR KEY ELECTROLYTES[19]:

- **POTASSIUM** (3.5-5.5 mEq/L)
- **SODIUM** (135-147 mEq/L)
- **MAGNESIUM** (1.5-3.0 mEq/L)

Loss of fluids and electrolytes with severe diarrhea can lead to consequences including a greater risk of infectious, renal, and cardiovascular complications in patients with chemotherapy-induced neutropenia.[5]

IN ADDITION TO ELECTROLYTE LEVEL ASSESSMENT[5]:

- Perform blood tests within 48 hours of scheduled treatment to assess neutropenia and changes in electrolytes
- Consider fluid and electrolyte replacement in patients with chemotherapy-induced diarrhea

REMIND PATIENTS AND CAREGIVERS[7,9]

- Diarrhea can cause an electrolyte imbalance
- Stay well-hydrated by drinking 8-12 glasses of clear liquids daily; it could help avoid dehydration and electrolyte imbalance

See dose modification information on page 17 of this brochure.

Please see Important Safety Information on pages 18-20 and accompanying full Prescribing Information, including Boxed WARNING, for ONIVYDE®.

MANAGING FEVER/PYREXIA

CONSIDER ASSESSING FEVER ACCORDING TO NCI CRITERIA[2]

GRADE 1	38.0-39.0 degrees C (100.4-102.2 degrees F)
GRADE 2	>39.0-40.0 degrees C (102.3-104.0 degrees F)
GRADE 3	>40.0 degrees C (>104.0 degrees F) for ≤ 24 hrs
GRADE 4	>40.0 degrees C (>104.0 degrees F) for >24 hrs

IN ADDITION TO NCI ASSESSMENT, CONSIDER THESE STEPS:

ASK

- When did your fever start?
- Are you experiencing chills, shortness of breath, or dizziness?

REMIND PATIENTS AND CAREGIVERS[19]

- Keep a good thermometer at home
- Maintain a detailed fever log (times and temperatures)
- Call your HCP immediately if signs of infection appear or your temperature rises above 100.4 degrees F

See dose modification information on page 17 of this brochure.

It is important to inform patients taking ONIVYDE® + 5-FU/LV of the risk of severe diarrhea. Advise patients to contact their healthcare provider if they experience persistent vomiting or diarrhea; black or bloody stools; or symptoms of dehydration such as lightheadedness, dizziness, or faintness.

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MANAGING FATIGUE/ASTHENIA

CONSIDER ASSESSING FATIGUE/ASTHENIA ACCORDING TO NCI CRITERIA[2]

GRADE 1	Fatigue not relieved by rest
GRADE 2	Fatigue not relieved by rest: limit daily activities
GRADE 3	Fatigue not relieved by rest, limiting self-care daily activities

IN ADDITION TO NCI ASSESSMENT, CONSIDER THESE STEPS[4,15,20]:

ASK PATIENTS

- How often they experience symptoms of fatigue?
- Are you sleeping well at night, and for how long?
- What have you been eating, and how much?
- Which other medications are you taking?

- If fatigue seems severe, consider checking CBC for inflammatory markers, or radiography for disease progression
- If patient shows signs of depression, consider a referral for psychiatric evaluation

REMIND PATIENTS AND CAREGIVERS[16,17,20]

- Fatigue is common in patients being treated for pancreatic cancer with ONIVYDE®
- Report changes in energy levels, signs of depression, or extreme tiredness to your HCP
- Eating smaller meals during the day and getting adequate sleep can help

See dose modification information on page 17 of this brochure.

Please see Important Safety Information on pages 18-20 and accompanying full Prescribing Information, including Boxed WARNING, for ONIVYDE®.

DOSE MODIFICATIONS FOR GRADE 3 OR 4 ADVERSE REACTIONS[6]

ADVERSE REACTION	DIRECTIONS	ONIVYDE® ADJUSTMENT IN PATIENTS RECEIVING 70 MG/M²	PATIENTS HOMOZYGOUS FOR UGT1A1*28 (WHO ARE CURRENTLY RECEIVING 50 MG/M²)
GRADE 3 OR 4	Withhold ONIVYDE® upon recovery to < Grade 1, resume ONIVYDE® + 5-FU/LV at a modified dose	FIRST OCCURRENCE	50 mg/m² / 43 mg/m²
		SECOND OCCURRENCE	43 mg/m² / 35 mg/m²
		THIRD OCCURRENCE	Discontinue ONIVYDE®

See Section 5.2 of the full Prescribing Information for ONIVYDE®. For guidance on dose modifications specific to diarrhea, see page 7 of this brochure.

ADDITIONAL CONSIDERATIONS

Some patients may understate or conceal the severity of their AEs[21,22]

Patients may understate the extent of their adverse events. Ask specific, probing questions to find out how they're reacting to their treatment.

How caretakers can shed a more accurate light on patient condition

Consult with your patient's caretakers: they can often have a more accurate assessment of the patient's reaction to treatment.

Involve your Supportive Care Team[1]

Some symptoms may indicate a need for involvement of a supportive care team, examples include:

- pancreatic enzyme replacement, treatment for opioid-induced constipation, anticoagulants, and antidepressants

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INDICATION

ONIVYDE® (irinotecan liposome injection) is indicated, in combination with fluorouracil (5-FU) and leucovorin (LV), for the treatment of patients with metastatic adenocarcinoma of the pancreas after disease progression following gemcitabine-based therapy.

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

IMPORTANT SAFETY INFORMATION

WARNING: SEVERE NEUTROPENIA and SEVERE DIARRHEA

- **Fatal neutropenic sepsis occurred in 0.8% of patients receiving ONIVYDE. Severe or life-threatening neutropenic fever or sepsis occurred in 3% and severe or life-threatening neutropenia occurred in 20% of patients receiving ONIVYDE in combination with 5-FU and LV. Withhold ONIVYDE for absolute neutrophil count below 1500/mm^3 or neutropenic fever. Monitor blood cell counts periodically during treatment**
- **Severe diarrhea occurred in 13% of patients receiving ONIVYDE in combination with 5-FU/LV. 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**

CONTRAINDICATION

- 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 patients receiving ONIVYDE/5-FU/LV, the incidence of Grade 3/4 neutropenia was higher among Asian (18/33 [55%]) vs White patients (13/73 [18%]). Neutropenic fever/neutropenic sepsis was reported in 6% of Asian vs 1% of White patients
- **Severe Diarrhea: See Boxed WARNING.** Severe and life-threatening late-onset (onset >24 hours after chemotherapy [9%]) and early-onset diarrhea (onset ≤24 hours after chemotherapy [3%], sometimes with other symptoms of cholinergic reaction) were observed
- **Interstitial Lung Disease (ILD):** Irinotecan HCl can cause severe and fatal ILD. 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

IMPORTANT SAFETY INFORMATION (continued)

WARNINGS AND PRECAUTIONS (continued)

- **Severe Hypersensitivity Reactions:** 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 females of reproductive potential to use effective contraception during and for 7 months after the last dose of ONIVYDE treatment

ADVERSE REACTIONS

- The most common adverse reactions (≥20%) were diarrhea (59%), fatigue/asthenia (56%), vomiting (52%), nausea (51%), decreased appetite (44%), stomatitis (32%), and pyrexia (23%)
- The most common Grade 3/4 adverse reactions (≥10%) were diarrhea (13%), fatigue/asthenia (21%), and vomiting (11%)
- Adverse reactions led to permanent discontinuation of ONIVYDE in 11% of patients receiving ONIVYDE/5-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/5-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/5-FU/LV; the most frequent adverse reactions requiring interruption or delays were neutropenia, diarrhea, fatigue, vomiting, and thrombocytopenia
- The most common laboratory abnormalities (≥20%) were anemia (97%), lymphopenia (81%), neutropenia (52%), increased ALT (51%), hypoalbuminemia (43%), thrombocytopenia (41%), hypomagnesemia (35%), hypokalemia (32%), hypocalcemia (32%), hypophosphatemia (29%), and hyponatremia (27%)
- The following adverse reactions have been identified during post approval use of ONIVYDE. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.
  Immune system disorders: Hypersensitivity (including Anaphylactic reaction and Angioedema)

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IMPORTANT SAFETY INFORMATION (continued)

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.

REFERENCES: 1. Ferrell BR, Temel JS, Temin S, et al. *J Clin Oncol*. 2016;35(1):96-112. **2.** US Department of Health and Human Services. Common Terminology Criteria for Adverse Events v5.0; 2017. **3.** Cherny N. *J Pain Symptom Manage*. 2008;36(4):413-423. **4.** Viele CS. *Semin Oncol Nurs*. 2003;19(4 suppl 3):2-5. **5.** Benson AB, Ajani JA, Catalano RB, et al. *J Clin Oncol*. 2004;22:2918-2926. **6.** ONIVYDE® [package insert]. Basking Ridge, NJ. Ipsen Biopharmaceuticals, Inc.; 2023. **7.** Shaw C, Taylor L. *Clin J Oncol Nurs*. 2018;16(4):413. **8.** Stein A, Voigt W, Jordan K. *Ther Adv Med Oncol*. 2010;2(1):51-63. **9.** US Department of Health and Human Services. National Cancer Institute. *Chemotherapy and You*; 2018. **10.** American Cancer Society. Managing nausea and vomiting at home. https://www.cancer.org/treatment/treatments-and-side-effects/physical-side-effects/nausea-and-vomiting/nausea-and-vomiting.html. Accessed March 17, 2020. **11.** Koselke E, Kraft S. *J Hematol Oncol Pharm*. 2012;2(4):1-24. **12.** Chaveli-López B, Bagán-Sebastián JV. *J Clin Exp Dent*. 2016;8(2):e201-209. **13.** O'Brien CP. *Can Fam Physician*. 2009;55:891-892. **14.** Bower JE. *Nat Rev Clin Oncol*. 2014;11(10):597-609. **15.** Olson SH, Xu Y, Herzog K, et al. *Pancreas*. 2016;45(7):986-991. **16.** US Department of Health and Human Services. National Institutes of Health. National Cancer Institute. Nutrition in cancer care. https://www.cancer.gov/about-cancer/treatment/side-effects/appetite-loss/nutrition-pdq. Accessed March 17, 2020. **17.** US Department of Health and Human Services. National Institutes of Health. National Cancer Institute. Fatigue. https://www.cancer.gov/about-cancer/treatment/side-effects/fatigue/fatigue-hp-pdq. Accessed March 17, 2020. **18.** Kinsley K, Pritchett W. *Clin J Oncol Nurs*. 2018;22(2):221-224. **19.** FDA Investigations Operations Manual. 2015. Appendix C. **20.** Mayo Clinic. Cancer fatigue. https://www.mayoclinic.org/diseases-conditions/cancer/in-depth/cancerfatigue/art-20047709. Accessed March 17, 2020. **21.** Homsi J, Walsh D, Rivera N, et al. *Support Care Cancer*. 2006;14(5):444-453. **22.** Olver I, Carey M, Boyes A, et al. *Support Care Cancer*. 2018;26(10):3579-3586.

FOR MORE INFORMATION, PLEASE VISIT ONIVYDE.COM

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