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Section:	Prescription Drugs	**Effective Date:**	July 1, 2024
Subsection:	Antineoplastic Agents	**Original Policy Date:**	December 4, 2015
Subject:	Onivyde	**Page:**	1 of 5

Last Review Date: June 13, 2024

Onivyde

Description

Onivyde (irinotecan liposome injection)

Background
Onivyde is a topoisomerase 1 inhibitor used to treat patients with metastatic pancreatic adenocarcinoma. Onivyde inhibits topoisomerase 1, an enzyme involved in DNA untangling during DNA replication, leading to decreased DNA replication and cancer cell death. The drug is administered via intravenous infusion over 90 minutes every two weeks until disease progression or unacceptable toxicity (1).

Regulatory Status
FDA-approved indication: Onivyde is a topoisomerase inhibitor indicated: (1)

- In combination with oxaliplatin, fluorouracil, and leucovorin, for the first-line treatment of adult patients with metastatic pancreatic adenocarcinoma.
- In combination with fluorouracil and leucovorin, for the treatment of patients with metastatic pancreatic adenocarcinoma 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 pancreatic adenocarcinoma (1).

The Onivyde label includes a boxed warning citing the risk of severe neutropenia (low neutrophil count) and severe diarrhea. Onivyde can cause severe neutropenia and neutropenic sepsis.

Monitor complete blood cell counts on Days 1 and 8 of every cycle and more frequently if clinically indicated. Withhold Onivyde for absolute neutrophil count (ANC) below 1500/mm^3 or neutropenic fever. Resume Onivyde when ANC is 1500/mm^3 or greater. Reduce Onivyde dose for Grade 3-4 neutropenia or neutropenic fever following recovery in subsequent cycles. Onivyde can also cause severe diarrhea. Do not administer Onivyde to patients with bowel obstruction. Withhold Onivyde for diarrhea of Grade 2-4 severity (1).

Onivyde can cause severe interstitial lung disease (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 (1).

Onivyde can cause fetal harm. Female patients should be advised to use effective contraception during treatment with Onivyde and for 7 months following the last dose (1).

Safety and effectiveness in pediatric patients have not been established (1).

Related policies

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Onivyde may be considered **medically necessary** if the conditions indicated below are met.

Onivyde may be considered **investigational** for all other indications.

Prior-Approval Requirements

Age 18 years of age or older

Diagnosis

Patient must have the following:

Metastatic pancreatic adenocarcinoma

AND ALL of the following:

1. Patient has **ONE** of the following:
    a. First-line treatment **AND** used in combination with oxaliplatin, fluorouracil, and leucovorin
    b. Disease progression following gemcitabine-based therapy **AND** used in combination with fluorouracil and leucovorin
2. Complete blood counts will be evaluated at Day 1 and Day 8 of each cycle
3. Prescriber agrees to withhold Onivyde if patient experiences diarrhea Grade 2-4 severity
4. Absolute neutrophil count (ANC) ≥ 1500/mm^3 and prescriber agrees to monitor neutrophil count before each dose
5. Females of reproductive potential **only**: patient will be advised to use effective contraception during treatment with Onivyde and for 7 months after the last dose

AND NONE of the following:

1. Bowel obstruction
2. Diagnosis of clinically significant (symptomatic or debilitating) interstitial lung disease (ILD)

Prior – Approval *Renewal* Requirements

Age 18 years of age or older

Diagnosis

Patient must have the following:

Metastatic pancreatic adenocarcinoma

AND ALL of the following:

1. **NO** disease progression or unacceptable toxicity
2. Used in combination with fluorouracil and leucovorin
3. Complete blood counts will be evaluated at Day 1 and Day 8 of each cycle
4. Prescriber agrees to withhold Onivyde if patient experiences diarrhea Grade 2-4 severity
5. Prescriber agrees to monitor neutrophil count before each dose
6. Females of reproductive potential **only**: patient will be advised to use effective contraception during treatment with Onivyde and for 7 months after the last dose

AND NONE of the following:

1. Bowel obstruction
2. Diagnosis of clinically significant (symptomatic or debilitating) interstitial lung disease (ILD)

Policy Guidelines

Pre - PA Allowance

None

Prior - Approval Limits

Duration 12 months

Prior – Approval *Renewal* Limits

Same as above

Rationale

Summary

Onivyde is a topoisomerase 1 inhibitor used to treat metastatic pancreatic adenocarcinoma. Onivyde carries a boxed warning for severe neutropenia and severe diarrhea. Onivyde is not to be administered to patients with bowel obstruction. Onivyde can cause severe interstitial lung disease. Onivyde can cause fetal harm and female patients should be advised to use effective contraception during treatment and for 7 months after the last dose. The safety and effectiveness of Onivyde in pediatric patients less than 18 years of age have not been established (1).

Prior approval is required to ensure the safe, clinically appropriate, and cost-effective use of Onivyde while maintaining optimal therapeutic outcomes.

References

1. Onivyde [package insert]. Cambridge, MA: Ipsen Biopharmaceuticals, Inc.; February 2024.
2. NCCN Drugs & Biologics Compendium® Irinotecan 2024. National Comprehensive Cancer Network, Inc. Accessed on May 14, 2024.

Policy History

Date	Action
December 2015	Addition to PA
March 2016	Annual review Policy number changed from 5.04.67 to 5.21.67
June 2016	Annual editorial review
September 2016	Annual review
June 2017	Annual editorial review Addition of age requirement to renewal section
June 2018	Annual review and reference update
June 2019	Annual review
June 2020	Annual review
September 2021	Annual review and reference update
September 2022	Annual review and reference update
September 2023	Annual review and reference update
March 2024	Per PI update, added indication of first-line treatment of metastatic pancreatic adenocarcinoma. Added contraception warning. Changed ANC requirement to greater than or equal to. Modified renewal requirements to match initiation
June 2024	Annual review and reference update

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on June 13, 2024 and is effective on July 1, 2024.