Clinical Policy Title:	abuse-deterrent opioid formulations
Policy Number:	RxA.437
Drug(s) Applied:	Oxaydo®
Original Policy Date:	03/06/2020
Last Review Date:	09/14/2021
Line of Business Policy Applies to:	All lines of business

Background

Immediate-release oxycodone (Oxaydo®) is an abuse-deterrent formulation (ADF) of opioid agonist requiring prior authorization.

Oxaydo® is indicated for the management of acute and chronic pain severe enough to require an opioid analgesic and for which alternative treatments are inadequate.

Limitation(s) of use:
Because of the risks of addiction, abuse, and misuse with opioids, even at recommended doses, and because of the greater risks of overdose and death with extended-release opioid formulations, reserve Oxaydo® for use in patients for whom alternative treatment options (e.g., non-opioid analgesics or non-opioid combination products):

- have not been tolerated, or are not expected to be tolerated, or
- have not provided adequate analgesia or are not expected to provide adequate analgesia.

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
Oxaydo®(immediate-release oxycodone, ADF)	Pain management	5-15 mg orally every 4-6 hours as needed for pain; titrate based on pain severity and patient Response. Conservative initial dose and dose titration are required.	Not applicable

Dosage Forms

- Oxycodone immediate-release tablets (Oxaydo®): Immediate-release tablets: 5 mg, 7.5 mg

Clinical Policy

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria. The provision of provider samples does not guarantee coverage under the terms of the pharmacy benefit administered by RxAdvance. All criteria for initial approval must be met in order to obtain

coverage.

I. Initial Approval Criteria

A. Pain management (must meet all)**:**

1. Diagnosis of chronic pain;
2. Age ≥ 18 years;
3. Medical justification supports inability to use a generic non-abuse-deterrent formulation of the same active ingredient as the requested opioid;
4. A treatment plan is required, including all of the following:
   a. Diagnosis or conditions that are contributing to the pain;
   b. Pain intensity (scales or ratings);
   c. Functional status (physical and psychosocial);
   d. Patient's goal of therapy (level of pain acceptable and/or functional status);
   e. Current analgesic (opioid and adjuvant) regimen;
   f. Current non-pharmacological treatment;
   g. Opioid-related side effects;
   h. Indications of medical misuse;
   i. Action plan if analgesic failure occurs.

Approval Duration
Commercial: 3 months
Medicaid: 3 months

II. Continued Therapy Approval

A. Pain management (must meet all)**:**

1. Member is currently receiving medication that has been authorized by RxAdvance or member has previously met initial approval criteria listed in this policy;
2. Member is responding positively to therapy.

Approval Duration
Commercial: 3 months
Medicaid: 3 months

III. Appendices

APPENDIX A: Abbreviation/Acronym Key
ADF: Abuse-Deterrent Formulation
FDA: Food and Drug Administration
PI: Prescribing Information
CDC: Centers for Disease Control and Prevention

APPENDIX B: Therapeutic Alternatives
Below are suggested therapeutic alternatives based on clinical guidance. Please check drug formulary for preferred agents and utilization management requirements.

Drug Name	Dosing Regimen	Maximum Dose
oxycodone immediate-release capsules, tablets, or oral solution	Opioid naïve patients: 5-15 mg orally every 4-6 hours as needed for pain; titrate based on pain severity and patient response.	Varies

Drug Name	Dosing Regimen	Maximum Dose
	For chronic pain: Oral tablets may be administered around- the-clock rather than as needed.	

Therapeutic alternatives are listed as generic (Brand name®) when the drug is available by both generic and brand, Brand name® when the drug is available by brand only and generic name when the drug is available by generic only.

APPENDIX C: Contraindications/Boxed Warnings

- Contraindication(s):
  - Significant respiratory depression;
  - Acute or severe bronchial asthma in an unmonitored setting or in absence of resuscitative equipment;
  - Known or suspected gastrointestinal obstruction, including paralytic ileus;
  - Hypersensitivity to the opioid active ingredient, salts, or any component of the product.

- Boxed Warning(s):
  - **Potential for addiction, abuse, and misuse:**
    Oxaydo®xpose users to risks of addiction, abuse, and misuse, which can lead to overdose and death. Assess patient's risk before prescribing and monitor regularly for these behaviors and conditions.
  - **Risk evaluation and mitigation strategy (REMS):**
    To ensure that the benefits of opioid analgesics outweigh the risks of addiction, abuse, and misuse, the Food and Drug Administration (FDA) has required a Risk Evaluation and Mitigation Strategy (REMS) for these products.
  - **Life-threatening respiratory depression:**
    Serious, life-threatening, or fatal respiratory depression may occur. Monitor closely, especially upon initiation or following a dose increase.
  - **Accidental ingestion:**
    Accidental ingestion of Oxaydo®, especially by children, can result in a fatal overdose of oxycodone.
  - **Neonatal opioid withdrawal syndrome:**
    Prolonged use of Oxaydo® during pregnancy can result in neonatal opioid withdrawal syndrome, which may be life-threatening if not recognized and treated. If prolonged opioid use is required in a pregnant woman, advise the patient of the risk of neonatal opioid withdrawal syndrome and ensure that appropriate treatment will be available.
  - **Cytochrome P450 3A4 interactions:**
    Concomitant use with CYP3A4 inhibitors (or discontinuation of CYP3A4 inducers) can result in a fatal overdose of oxycodone.
  - **Risks from concomitant use with benzodiazepines or other CNS depressants:**
    Concomitant use of opioids with benzodiazepines or other central nervous system (CNS) depressants, including alcohol, may result in profound sedation, respiratory depression, coma, and death. Reserve concomitant prescribing for use in patients for whom alternative treatment options are inadequate; limit dosages and durations to the minimum required; and follow patients for signs and symptoms of respiratory depression and sedation.

APPENDIX D: General Information

- Although Oxaydo® labelling indicates reduced abuse potential via specific intranasal route, the Prescribing

Information (PI) document still contains Black Box Warnings and Limitations of Use regarding abuse potential. Per Oxaydo® PI, "The clinical significance of the difference in drug liking and difference in response to taking the drug again reported in this study has not yet been established. There is no evidence that Oxaydo® has a reduced abuse liability compared to immediate-release oxycodone." Per the 2016 CDC treatment guidelines for opioid prescribing, "As indicated in FDA guidance for industry on evaluation and labelling of abuse-deterrent opioids, although abuse-deterrent technologies are expected to make manipulation of opioids more difficult or less rewarding, they do not prevent opioid abuse through oral intake, the most common route of opioid abuse, and can still be abused by non-oral routes. The "abuse-deterrent" label does not indicate that there is no risk for abuse. No studies were found in the clinical evidence review assessing the effectiveness of abuse-deterrent technologies as a risk mitigation strategy for deterring or preventing abuse. In addition, abuse-deterrent technologies do not prevent unintentional overdose through oral intake. Experts agreed that recommendations could not be offered at this time related to use of abuse-deterrent formulations."

References

1. Oxaydo® Prescribing Information. Wayne, PA: Zyla Life Sciences US Inc; March 2021. Available at https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/202080s012lbl.pdf . Accessed on June 29, 2021.

2. Dowell D, Haegerich TM, Chou R. CDC guideline for prescribing opioids for chronic pain - United States, 2016. JAMA. 2016 Apr 19; 315(15):1624-45. Available at https://pubmed.ncbi.nlm.nih.gov/26977696/. Accessed on June 29, 2021.

Review/Revision History	Review/Revised Date	P&T Approval Date
Policy established.	01/2020	03/06/2020
Policy was reviewed: 1. Clinical Policy Title was updated. 2. Drug(s) Applied was updated. 3. Line of Business Policy Applies to was update to all lines of business. 4. Continued Therapy criteria II.A.1 was rephrased to "Currently receiving medication that has been authorized by RxAdvance..." 5. Initial Approval criteria: Commercial and Medicaid approval duration were updated to 3 months. 6. Continued Approval criteria: Commercial and Medicaid approval duration were updated to 3 months. 7. APPENDIX C: was updated to include the details information	08/03/2020	09/14/2020

for Contraindications and Boxed Warnings. 8. References were updated. 9. Updated Background: “Oxaydo® and Roxybond™ are indicated for the management of pain sever enough to require an opioid analgesic and for which alternative treatments are inadequate.”		
Policy was reviewed: 1. Clinical Policy Drugs Applied was updated to remove brand-name drug Roxybond as it is currently unavailable. (Remainder of policy was also updated to remove Roxybond accordingly). 2. Dosing Regimen was updated to include “Conservative initial dose and dose titration are required…”. 3. Dosing Regimen was updated to remove brand-name Roxybond. 4. Dosage Forms was updated to remove brand-name Roxybond. 5. Statement about provider sample ‘‘The provision of provider samples does not guarantee coverage…” was added to Clinical Policy. 6. Continued Therapy Approval Criteria II.A.1 was rephrased to "Member is currently receiving medication that has been authorized by RxAdvance...". 7. Appendix A was updated to include abbreviations PI and CDC. 8. Therapeutic alternative verbiage was updated to "Below are suggested therapeutic alternatives based on clinical guidance..".	06/29/2021	09/14/2021

9. Statement about drug listing format in Appendix B is updated to "Therapeutic alternatives are listed as generic (Brand name®) when the drug is available by both generic and brand, Brand name® when the drug is available by brand only and generic name when the drug is available by generic only". 10. Appendix C was updated to remove Roxibond. 11. Appendix D was updated to remove Roxybond. 12. References were reviewed and updated.		