CLINICAL GUIDELINES FOR XARTEMIS™ XR

Description: Xartemis™ XR (oxycodone hydrochloride and acetaminophen) Extended-Release Tablets combine two analgesics, oxycodone hydrochloride 7.5 mg and acetaminophen 325 mg for oral administration. The activity of oxycodone hydrochloride is primaryly due to the parent drug oxycodone. Xartemis™ XR is an extended-release tablet for oral administration containing both immediate- and extended-release components. Xartemis™ XR is formulated to immediately release a portion of its oxycodone and acetaminophen doses.

Xartemis™ XR is designed to swell in gastric fluid and gradually release the remainder of oxycodone and acetaminophen to the upper gastrointestinal (GI) tract. Xartemis™ XR is an extended-release bilayer formulation of oxycodone and acetaminophen which IS NOT interchangeable with other oxycodone/acetaminophen products because of differing pharmacokinetic profiles that affect the frequency of administration.

Indication: For the treatment of acute pain severe enough to require opioid treatment and for which alternative treatment options (e.g., non-opioid analgesics) are inadequate.

Dosing: *Adults*: 2 tablets PO every 12 hours administered with or without food. A second dose of 2 tablets may be given as early as 8 hours after the initial dose if needed for analgesia at that time. Subsequent doses are to be administered every 12 hours. Individualize the dosage regimen, considering prior analgesic exposure and risk for abuse. Monitor patients closely for excessive sedation and respiratory depression, particularly in the first 24—72 hours of treatment. To discontinue, use a gradual downward titration of 50% every 2—4 days to prevent withdrawal in the physically dependent patient.

Xartemis™ XR has the following black-box warnings in the official Prescribing Information.

WARNING: ADDICTION, ABUSE, AND MISUSE; LIFE-THREATENING RESPIRATORY DEPRESSION; ACCIDENTAL EXPOSURE; NEONATAL OPIOID WITHDRAWAL SYNDROME; and HEPATOTOXICITY

Addiction, Abuse, and Misuse
XARTEMIS XR exposes patients and other users to the risks of opioid addiction, abuse, and misuse, which can lead to overdose and death. Assess each patient's risk prior to prescribing XARTEMIS XR, and monitor all patients regularly for the development of these behaviors or conditions.

Life-threatening Respiratory Depression
Serious, life-threatening, or fatal respiratory depression may occur with use of XARTEMIS XR. Monitor for respiratory depression, especially during initiation of XARTEMIS XR or following a dose increase. Instruct patients to swallow XARTEMIS XR tablets whole; crushing, chewing, or dissolving XARTEMIS XR can cause rapid release and absorption of a potentially fatal dose of oxycodone.

Accidental Exposure
Accidental ingestion of XARTEMIS XR, especially in children, can result in a fatal overdose of oxycodone.

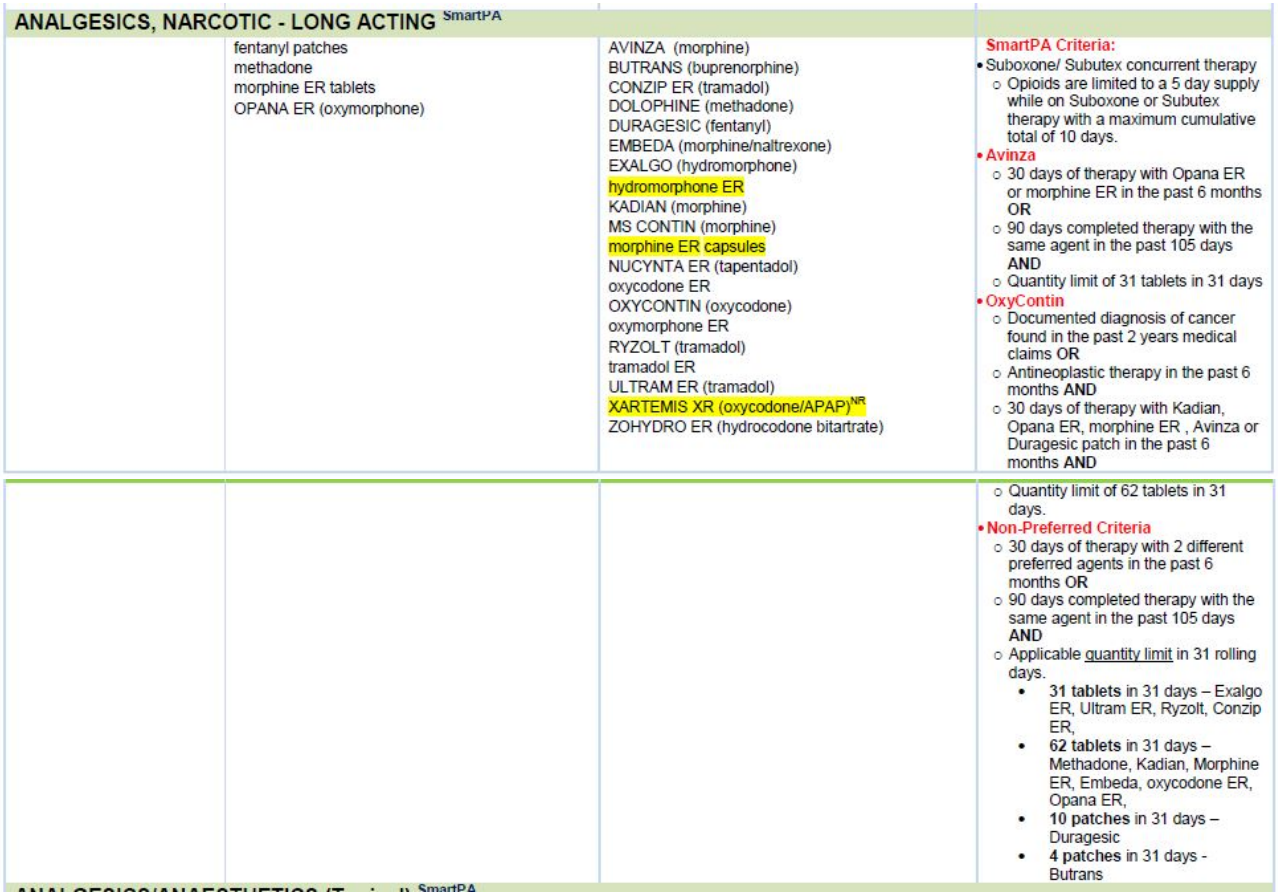
Neonatal Opioid Withdrawal Syndrome
Prolonged use of XARTEMIS XR during pregnancy can result in neonatal opioid withdrawal syndrome, which may be life-threatening if not recognized and requires management according to protocols developed by neonatology experts. If opioid use is required for a prolonged period in a pregnant woman, advise the patient of the risk of neonatal opioid withdrawal syndrome and ensure that appropriate treatment will be available.

Hepatotoxicity
XARTEMIS XR contains acetaminophen. Acetaminophen has been associated with cases of acute liver failure, at times resulting in liver transplant and death. Most of the cases of liver injury are associated with the use of acetaminophen at doses that exceed the maximum daily limit, and often involve more than one acetaminophen-containing product.

Short- and Long-acting Narcotic Analgesics are reviewed classes and the DOM P&T Committee placed Xartemis™ XR on the non-preferred list when it was introduced to the market. As shown below, the current Preferred Drug List (PDL) lists specific product related and general class related step-edits and quantity limits for the non-preferred agents in these classes.

DOM Preferred Drug List – 08-01-2014

ANALGESICS, NARCOTIC - SHORT ACTING SmartPA			
	acetaminophen/codeine codeine dihydrocodeine/ APAP/caffeine hydrocodone/APAP hydromorphone IBUDONE (hydrocodone/ibuprofen) meperidine morphine oxycodone oxycodone/APAP oxycodone/aspirin oxycodone/ibuprofen pentazocine/APAP tramadol tramadol/APAP	ABSTRAL (fentanyl) ACTIQ (fentanyl) butalbital/APAP/caffeine/codeine butalbital/ASA/caffeine/codeine butorphanol tartrate (nasal) DEMEROL (meperidine) DILAUDID (hydromorphone) fentanyl FENTORA (fentanyl) FIORICET W/ CODEINE (butalbital/APAP/caffeine/codeine) FIORINAL W/ CODEINE (butalbital/ASA/caffeine/codeine) hydrocodone/ibuprofen levorphanol LORCET (hydrocodone/APAP) LORTAB (hydrocodone/APAP) MAGNACET (oxycodone/APAP) NORCO (hydrocodone/APAP) NUCYNTA (tapentadol) ONSOLIS (fentanyl) OPANA (oxymorphone) OXECTA (oxycodone) pentazocine/naloxone PERCOCET (oxycodone/APAP) PERCODAN (oxycodone/ASA) REPREXAINE (hydrocodone/ibuprofen) ROXICET (oxycodone/acetaminophen) RYBIX (tramadol) SUBSYS (fentanyl) SYNALGOS-DC (dihydrocodeine/ aspirin/caffeine)	**SmartPA Criteria:** • Suboxone/ Subutex concurrent therapy ○ Opioids are limited to a 5 day supply while on Suboxone or Subutex therapy with a maximum cumulative total of 10 days. Other Criteria at the Point of Sale: Applicable quantity limit in 31 rolling days. • **62 tablets** in 31 days – codeine, oxycodone/ibuprofen, meperidine, hydromorphone, fentanyl, bultalbital/codeine combinations, morphine, tapentadol, dihydrocodeine combinations, tramadol, pentazocine, • **124 tablets** in 31 days – butalbital/APAP 750 • **145 tablets** in 31 days – butalbital/APAP 650 • **186 tablets** in 31 days – butalbital/APAP 325, butalbital/ASA 325 • **5mL (2 x 2.5 bottles)** in 31 days – butorphanol nasal Applicable **CUMULATIVE** quantity limit in 31 rolling days • **62 tablets** in 31 days – hydrocodone combinations, oxycodone combinations
		TYLENOL W/CODEINE (APAP/codeine) TYLOX (oxycodone/APAP) ULTRACET (tramadol/APAP) ULTRAM (tramadol) VICODIN (hydrocodone/APAP) VICOPROFEN (hydrocodone/ibuprofen) XODOL (hydrocodone/acetaminophen) ZAMICET (hydrocodone/APAP) ZOLVIT (hydrocodone/APAP) ZYDONE (hydrocodone/acetaminophen)	• **180 ml** – oxycodone liquids • **480 mL** – hydrocodone liquids



ANALGESICS, NARCOTIC - LONG ACTING SmartPA			
	fentanyl patches methadone morphine ER tablets OPANA ER (oxymorphone)	AVINZA (morphine) BUTRANS (buprenorphine) CONZIP ER (tramadol) DOLOPHINE (methadone) DURAGESIC (fentanyl) EMBEDA (morphine/naltrexone) EXALGO (hydromorphone) hydromorphone ER KADIAN (morphine) MS CONTIN (morphine) morphine ER capsules NUCYNTA ER (tapentadol) oxycodone ER OXYCONTIN (oxycodone) oxymorphone ER RYZOLT (tramadol) tramadol ER ULTRAM ER (tramadol) XARTEMIS XR (oxycodone/APAP)NR ZOHYDRO ER (hydrocodone bitartrate)	SmartPA Criteria: • Suboxone/ Subutex concurrent therapy ○ Opioids are limited to a 5 day supply while on Suboxone or Subutex therapy with a maximum cumulative total of 10 days. • Avinza ○ 30 days of therapy with Opana ER or morphine ER in the past 6 months **OR** ○ 90 days completed therapy with the same agent in the past 105 days **AND** ○ Quantity limit of 31 tablets in 31 days • OxyContin ○ Documented diagnosis of cancer found in the past 2 years medical claims **OR** ○ Antineoplastic therapy in the past 6 months **AND** ○ 30 days of therapy with Kadian, Opana ER, morphine ER , Avinza or Duragesic patch in the past 6 months **AND**
			○ Quantity limit of 62 tablets in 31 days. • Non-Preferred Criteria ○ 30 days of therapy with 2 different preferred agents in the past 6 months **OR** ○ 90 days completed therapy with the same agent in the past 105 days **AND** ○ Applicable quantity limit in 31 rolling days. • **31 tablets** in 31 days – Exalgo ER, Ultram ER, Ryzolt, Conzip ER, • **62 tablets** in 31 days – Methadone, Kadian, Morphine ER, Embeda, oxycodone ER, Opana ER, • **10 patches** in 31 days – Duragesic • **4 patches** in 31 days - Butrans
ANALGESICS/ANAESTHETICS (Topical) SmartPA			

Recommendation:

MS-DUR recommends that DOM place additional product specific PA criteria for use of Xartemis™ XR and that the DUR Board provide input on possible additional criteria.

Possible Criteria If Recommendation Approved by Board:

The following potential criteria and areas for discussion have been identified by MS-DUR and DOM.

Age edit	Minimum age of 18 years
Quantity limit	124 tablets in 31 rolling days – *this would be normal quantity limit in this category.* - *Indicated for acute, severe pain – should we specify maximum of 4 tablets/day and duration of therapy limit?*
Diagnosis	*Indicated for acute, severe pain – should we limit to specific diagnoses?*
Step-therapy	30 days of therapy with 2 different preferred agents in the past 6 months – *this would be normal step-therapy for non-preferred in this category.* - *Indicated for acute, severe pain. Need input on what would be appropriate failure with preferred agents*
Duration of therapy	Limited to 70 days of therapy per calendar year - *Indicated for acute, severe pain. Should there be a limit on days of therapy?*

Recommendation:

The DUR Board recommends that DOM adopt the product specific PA criteria for use of Xartemis™ XR identified during the discussion.