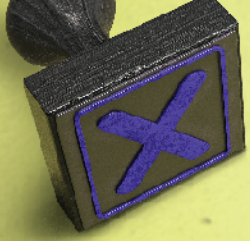


XTAMPZA® ER: THE DIFFERENCE IS XCLUSIVE

When you prescribe an ER oxycodone,

Make Xtampza® ER your ER oxycodone of choice

INDICATIONS AND USAGE

Xtampza® ER (oxycodone) is indicated for the management of pain severe enough to require daily, around-the-clock, long-term opioid treatment and for which alternative treatment options are inadequate.

Limitations 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 Xtampza ER for use in patients for whom alternative treatment options (eg, non-opioid analgesics or immediate-release opioids) are ineffective, not tolerated, or would be otherwise inadequate to provide sufficient management of pain
- Xtampza ER is not indicated as an as-needed (prn) analgesic

Xtampza® ER (oxycodone) EXTENDED-RELEASE CAPSULES CII

IMPORTANT SAFETY INFORMATION

WARNING: ADDICTION, ABUSE, AND MISUSE; RISK EVALUATION AND MITIGATION STRATEGY (REMS); LIFE-THREATENING RESPIRATORY DEPRESSION; ACCIDENTAL INGESTION; NEONATAL OPIOID WITHDRAWAL SYNDROME; CYTOCHROME P450 3A4 INTERACTION; and RISKS FROM CONCOMITANT USE WITH BENZODIAZEPINES OR OTHER CNS DEPRESSANTS

Addiction, Abuse, and Misuse

Xtampza ER 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 Xtampza ER and monitor all patients regularly for the development of these behaviors or conditions.

Opioid Analgesic 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 REMS for these products. Under the requirements of the REMS, drug companies with approved opioid analgesic products must make REMS-compliant education programs available to healthcare providers. Healthcare providers are strongly encouraged to

- complete a REMS-compliant education program,
- counsel patients and/or their caregivers, with every prescription, on safe use, serious risks, storage, and disposal of these products,
- emphasize to patients and their caregivers the importance of reading the Medication Guide every time it is provided by their pharmacist, and
- consider other tools to improve patient, household, and community safety.

Life-Threatening Respiratory Depression

Serious, life-threatening, or fatal respiratory depression may occur with use of Xtampza ER. Monitor for respiratory depression, especially during initiation of Xtampza ER or following a dose increase.

Accidental Ingestion

Accidental ingestion of even one dose of Xtampza ER, especially by children, can result in a fatal overdose of oxycodone.

Neonatal Opioid Withdrawal Syndrome

Prolonged use of Xtampza ER during pregnancy can result in neonatal opioid withdrawal syndrome, which may be life-threatening if not recognized and treated, 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.

Cytochrome P450 3A4 Interaction

The concomitant use of Xtampza ER with all cytochrome P450 3A4 inhibitors may result in an increase in oxycodone plasma concentrations, which could increase or prolong adverse drug effects and may cause potentially fatal respiratory depression. In addition, discontinuation of a concomitantly used cytochrome P450 3A4 inducer may result in an increase in oxycodone plasma concentration. Monitor patients receiving Xtampza ER and any CYP3A4 inhibitor or inducer.

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 of Xtampza ER and benzodiazepines or other CNS depressants for use in patients for whom alternative treatment options are inadequate.
- Limit dosages and durations to the minimum required.
- Follow patients for signs and symptoms of respiratory depression and sedation.

Please see additional Important Safety Information throughout this brochure and accompanying full Prescribing Information, including Boxed Warning and Medication Guide, on XtampzaER.com/PI.

Xtampza® ER provides differentiated abuse deterrence

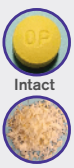
OxyContin® (oxycodone HCl)	Xtampza® ER (oxycodone) EXTENDED-RELEASE CAPSULES (II)

Efficacy

Both provide the powerful pain relief of ER oxycodone

Xtampza ER had a significant difference in pain reduction vs placebo in a clinical study.

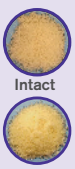
Abuse-Deterrent Technology



- Tablet can be manipulated with common household items[1]
  - 34% of abusers admitted defeating the extended-release mechanism of OxyContin to snort or inject[2]
  - Delivers a rapid release of oxycodone when manipulated, bioequivalent to oxycodone IR[3]
  - Contains boxed warning against crushing, chewing, or dissolving[5]

VS

- Capsules engineered to resist manipulation and maintain extended-release properties[3]
  - The only ER oxycodone to maintain its extended-release PK properties even when manipulated[4-6]
  - Does not deliver a rapid release of oxycodone when manipulated[3]
  - Does **not** contain boxed warning against crushing, chewing, or dissolving[4]



Actual photos from study; crushing performed with common household item.[1] There are no head-to-head studies comparing the safety or efficacy between products.

Xtampza ER 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 Xtampza ER and monitor all patients regularly for the development of these behaviors or conditions.

IMPORTANT SAFETY INFORMATION (continued)

CONTRAINDICATIONS:

- Xtampza ER is contraindicated in patients with significant respiratory depression, acute or severe bronchial asthma in an unmonitored setting or in the absence of resuscitative equipment, known or suspected gastrointestinal obstruction, including paralytic ileus, and hypersensitivity (eg, anaphylaxis) to oxycodone

Please see additional Important Safety Information throughout this brochure and accompanying full Prescribing Information, including Boxed Warning and Medication Guide, on XtampzaER.com/PI.

Xtampza® ER: The flexibility of multiple dosage strengths and administration options

OxyContin® (oxycodone HCl)		Xtampza® ER (oxycodone) EXTENDED-RELEASE CAPSULES II
Dosing		
10 mg	Equivalent to	9 mg
15 mg		13.5 mg
20 mg		18 mg
30 mg		27 mg
40 mg		36 mg
60 mg		27 mg + 27 mg
80 mg		36 mg + 36 mg

Capsules and tablets are not actual size.
A lower dosage (mg) of Xtampza ER contains the same amount of oxycodone as oxycodone HCl ER, with the molecular weight of the added HCl salt accounting for the approximate 10% difference.

Administration

1 Option

Must swallow tablet whole

More Options Available

Oral capsule

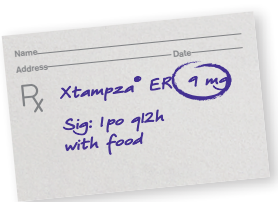
Sprinkled on food

Sprinkled into a cup

Xtampza ER capsules can be opened to suit patient needs and preferences

To ensure consistent plasma levels, Xtampza ER must be dosed every 12 hours and MUST be taken with food.

- **Taking Xtampza ER on an empty stomach can decrease drug absorption**
- **Monitor patients closely for respiratory depression, especially within the first 24 to 72 hours of initiating therapy and following dosage increases with Xtampza ER**
- **The extended-release properties of Xtampza ER are maintained no matter which administration method you choose.**



IMPORTANT SAFETY INFORMATION (continued)

WARNINGS AND PRECAUTIONS:

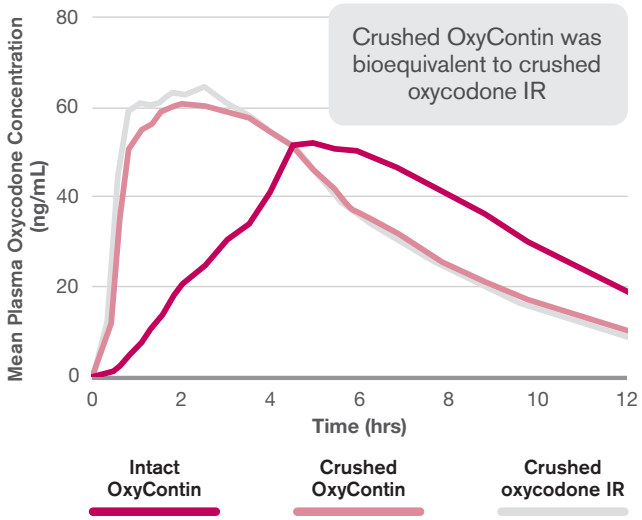
Addiction, Abuse, and Misuse

Xtampza ER contains oxycodone, a Schedule II controlled substance. As an opioid, Xtampza ER exposes users to the risks of addiction, abuse, and misuse. As extended-release products such as Xtampza ER deliver the opioid over an extended period of time, there is a greater risk for overdose and death due to the larger amount of oxycodone present.

Please see additional Important Safety Information throughout this brochure and accompanying full Prescribing Information, including Boxed Warning and Medication Guide, on XtampzaER.com/PI.

Only Xtampza® ER maintained its extended-release PK profile when crushed—OxyContin® did not

OxyContin intact and crushed[3]



These findings do not indicate that Xtampza ER can entirely prevent abuse. Abuse of Xtampza ER by injection, and by the oral and nasal routes is still possible.

IMPORTANT SAFETY INFORMATION (continued)

WARNINGS AND PRECAUTIONS:

Opioid Analgesic Risk Evaluation and Mitigation Strategy (REMS) (continued)

Opioid Analgesic 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. Under the requirements of the REMS, drug companies with approved opioid analgesic products must make REMS-compliant education programs available to healthcare providers. Healthcare providers are strongly encouraged to do all of the following:

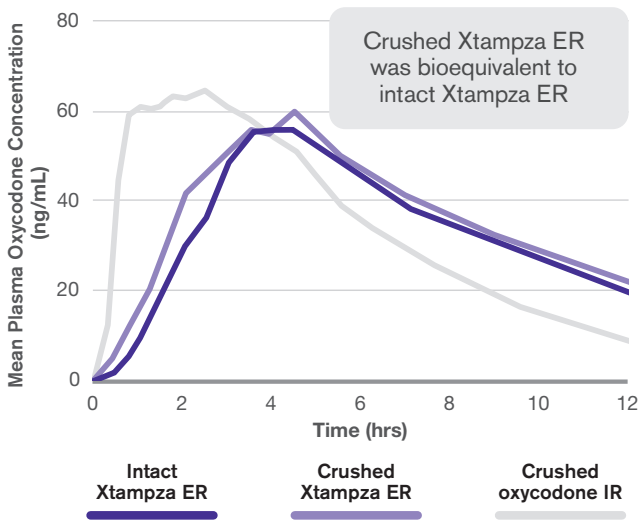
- Complete a REMS-compliant education program offered by an accredited provider of continuing education (CE) or another education program that includes all the elements of the FDA Education Blueprint for Health Care Providers Involved in the Management or Support of Patients with Pain
- Discuss with patients and/or their caregivers, with every prescription, the safe use, serious risks, and proper storage and disposal of these products. The Patient Counseling Guide (PCG) can be obtained at this link: www.fda.gov/OpioidAnalgesicREMSPCG
- Emphasize to patients and their caregivers the importance of reading the Medication Guide every time it is provided by their pharmacist
- Consider other tools to improve patient, household, and community safety such as patient-prescriber agreements that reinforce patient-prescriber responsibilities

Please see additional Important Safety Information throughout this brochure and accompanying full Prescribing Information, including Boxed Warning and Medication Guide, on XtampzaER.com/PI.

Xtampza® ER (oxycodone) EXTENDED-RELEASE CAPSULES II

Make Xtampza® ER your ER oxycodone of choice

Xtampza ER intact and crushed[3]



In a randomized, open-label, active-controlled, 5-treatment crossover study, Gudin et al compared the PK of crushed oxycodone IR to Xtampza ER (crushed and intact) and reformulated OxyContin (crushed and intact) taken orally in 42 healthy subjects.[3]

The impact of the oral PK studies on abuse, misuse, and diversion of Xtampza ER has yet to be determined. Additional data, including epidemiological data, when available, may provide further information on the impact of Xtampza ER on the abuse liability of the drug.

IMPORTANT SAFETY INFORMATION (continued)

WARNINGS AND PRECAUTIONS:

For further information on the REMS and a list of accredited REMS CME/CE, call 1-800-503-0784, or visit www.opioidanalgesicrems.com. The FDA Blueprint can be found at www.fda.gov/OpioidAnalgesicREMSBlueprint.

Life-Threatening Respiratory Depression

- Serious, life-threatening, or fatal respiratory depression has been reported with the use of opioids, even when used as recommended. Respiratory depression, if not immediately recognized and treated, may lead to respiratory arrest and death. Management of respiratory depression may include close observation, supportive measures, and use of opioid antagonists, depending on the patient's clinical status. Carbon dioxide (CO_2) retention from opioid-induced respiratory depression can exacerbate the sedating effects of opioids

Please see additional Important Safety Information throughout this brochure and accompanying full Prescribing Information, including Boxed Warning and Medication Guide, on XtampzaER.com/PI.

Xtampza® ER (oxycodone) EXTENDED-RELEASE CAPSULES CII

IMPORTANT SAFETY INFORMATION (continued)

WARNINGS AND PRECAUTIONS

Life-Threatening Respiratory Depression (continued)

- Opioids can cause sleep-related breathing disorders, including central sleep apnea (CSA) and sleep-related hypoxemia. Opioid use increases the risk of CSA in a dose-dependent fashion. In patients who present with CSA, consider decreasing the opioid dosage using best practices for opioid taper

Neonatal Opioid Withdrawal Syndrome

- Prolonged use of Xtampza ER during pregnancy can result in withdrawal in the neonate. Neonatal opioid withdrawal syndrome, unlike opioid withdrawal syndrome in adults, may be life-threatening if not recognized and treated, and requires management according to protocols developed by neonatology experts. Observe newborns for signs of neonatal opioid withdrawal syndrome and manage accordingly. Advise pregnant women using opioids for a prolonged period of the risk of neonatal opioid withdrawal syndrome, and ensure that appropriate treatment will be available

Risks of Concomitant Use or Discontinuation of Cytochrome P450 3A4 Inhibitors and Inducers

- Concomitant use of Xtampza ER with a CYP3A4 inhibitor, such as macrolide antibiotics (eg, erythromycin), azole-antifungal agents (eg, ketoconazole), and protease inhibitors (eg, ritonavir), may increase plasma concentrations of oxycodone and prolong opioid adverse reactions, which may cause potentially fatal respiratory depression, particularly when an inhibitor is added after a stable dose of Xtampza ER is achieved. Similarly, discontinuation of a CYP3A4 inducer, such as rifampin, carbamazepine, and phenytoin, in Xtampza ER-treated patients may increase oxycodone plasma concentrations and prolong opioid adverse reactions. When using Xtampza ER with CYP3A4 inhibitors or discontinuing CYP3A4 inducers in Xtampza ER-treated patients, monitor patients closely at frequent intervals and consider dosage reduction of Xtampza ER until stable drug effects are achieved
- Concomitant use of Xtampza ER with CYP3A4 inducers or discontinuation of a CYP3A4 inhibitor could decrease oxycodone plasma concentrations, decrease opioid efficacy or, possibly, lead to a withdrawal syndrome in a patient who had developed physical dependence to oxycodone. When using Xtampza ER with CYP3A4 inducers or discontinuing CYP3A4 inhibitors, monitor patients closely at frequent intervals and consider increasing the opioid dosage if needed to maintain adequate analgesia or if symptoms of opioid withdrawal occur

Risks From Concomitant Use With Benzodiazepines or Other CNS Depressants

- Profound sedation, respiratory depression, coma, and death may result from the concomitant use of Xtampza ER with benzodiazepines or other CNS depressants (eg, non-benzodiazepine sedatives/hypnotics, anxiolytics, tranquilizers, muscle relaxants, general anesthetics, antipsychotics, other opioids, alcohol). Because of these risks, reserve concomitant prescribing of these drugs for use in patients for whom alternative treatment options are inadequate
- Observational studies have demonstrated that concomitant use of opioid analgesics and benzodiazepines increases the risk of drug-related mortality compared to use of opioid analgesics alone. Because of similar pharmacological properties, it is reasonable to expect similar risk with the concomitant use of other CNS depressant drugs with opioid analgesics

Risk of Life-Threatening Respiratory Depression in Patients With Chronic Pulmonary Disease or in Elderly, Cachectic, or Debilitated Patients

The use of Xtampza ER in patients with acute or severe bronchial asthma in an unmonitored setting or in the absence of resuscitative equipment is contraindicated.

Patients with Chronic Pulmonary Disease:

Xtampza ER-treated patients with significant chronic obstructive pulmonary disease or cor pulmonale, and those with a substantially decreased respiratory reserve, hypoxia, hypercapnia, or pre-existing respiratory depression are at increased risk of decreased respiratory drive, including apnea, even at recommended dosages of Xtampza ER.

Elderly, Cachectic, or Debilitated Patients:

Life-threatening respiratory depression is more likely to occur in elderly, cachectic, or debilitated patients as they may have altered pharmacokinetics or altered clearance compared to younger, healthier patients.

Monitor such patients closely, particularly when initiating and titrating Xtampza ER and when Xtampza ER is given concomitantly with other drugs that depress respiration. Alternatively, consider the use of non-opioid analgesics in these patients. Use an alternative analgesic for patients who require a dose of Xtampza ER less than 9 mg.

Adrenal Insufficiency

- Cases of adrenal insufficiency have been reported with opioid use, more often following greater than one month of use. Presentation of adrenal insufficiency may include non-specific symptoms and signs, including nausea, vomiting, anorexia, fatigue, weakness,

Please see additional Important Safety Information throughout this brochure and accompanying full Prescribing Information, including Boxed Warning and Medication Guide, on XtampzaER.com/PI.

Xtampza® ER (oxycodone) EXTENDED-RELEASE CAPSULES II

IMPORTANT SAFETY INFORMATION (continued)

WARNINGS AND PRECAUTIONS:

Adrenal Insufficiency (continued)

dizziness, and low blood pressure. If adrenal insufficiency is suspected, confirm the diagnosis with diagnostic testing as soon as possible. If adrenal insufficiency is diagnosed, treat with physiologic replacement doses of corticosteroids. Wean the patient off of the opioid to allow adrenal function to recover, and continue corticosteroid treatment until adrenal function recovers. Other opioids may be tried as some cases reported use of a different opioid without recurrence of adrenal insufficiency. The information available does not identify any particular opioids as being more likely to be associated with adrenal insufficiency

Severe Hypotension

- Xtampza ER may cause severe hypotension, including orthostatic hypotension and syncope in ambulatory patients. There is an increased risk in patients whose ability to maintain blood pressure has already been compromised by a reduced blood volume or concurrent administration of certain CNS depressant drugs (eg, phenothiazines or general anesthetics). Monitor these patients for signs of hypotension after initiating or titrating the dosage of Xtampza ER. In patients with circulatory shock, Xtampza ER may cause vasodilation that can further reduce cardiac output and blood pressure. Avoid the use of Xtampza ER in patients with circulatory shock

Risks of Use in Patients With Increased Intracranial Pressure, Brain Tumors, Head Injury, or Impaired Consciousness

- In patients who may be susceptible to the intracranial effects of CO_2 retention (eg, those with evidence of increased intracranial pressure or brain tumors), Xtampza ER may reduce respiratory drive, and the resultant CO_2 retention can further increase intracranial pressure. Monitor such patients for signs of sedation and respiratory depression, particularly when initiating therapy with Xtampza ER
- Opioids may also obscure the clinical course in a patient with a head injury. Avoid the use of Xtampza ER in patients with impaired consciousness or coma

Risks of Use in Patients With Gastrointestinal Conditions

- Xtampza ER is contraindicated in patients with gastrointestinal obstruction, including paralytic ileus
- The oxycodone in Xtampza ER may cause spasm of the sphincter of Oddi. Opioids may cause increases in the serum amylase. Monitor patients with biliary tract disease, including acute pancreatitis, for worsening symptoms

Risk of Use in Patients With Seizure Disorders

- The oxycodone in Xtampza ER may increase the frequency of seizures in patients with seizure disorders and may increase the risk of seizures in other clinical settings associated with seizures. Monitor patients with a history of seizure disorders for worsened seizure control during Xtampza ER therapy

Withdrawal

- Do not abruptly discontinue Xtampza ER in a patient physically dependent on opioids. When discontinuing Xtampza ER in a physically dependent patient, gradually taper the dosage. Rapid tapering of oxycodone in a patient physically dependent on opioids may lead to a withdrawal syndrome and return of pain
- Additionally, avoid the use of mixed agonist/antagonist (eg, pentazocine, nalbuphine, and butorphanol) or partial agonist (eg, buprenorphine) analgesics in patients who have received or are receiving a course of therapy with a full opioid agonist analgesic, including Xtampza ER. In these patients, mixed agonist/antagonist and partial agonist analgesics may reduce the analgesic effect and/or may precipitate withdrawal symptoms

Risks of Driving and Operating Machinery

- Xtampza ER may impair the mental or physical abilities needed to perform potentially hazardous activities, such as driving a car or operating machinery. Warn patients not to drive or operate dangerous machinery unless they are tolerant to the effects of Xtampza ER and know how they will react to the medication

Laboratory Monitoring

- Not every urine drug test for "opioids" or "opiates" detects oxycodone reliably, especially those designed for in-office use. Further, many laboratories will report urine drug concentrations below a specified "cut-off" value as "negative." Therefore, if urine testing for oxycodone is considered in the clinical management of an individual patient, ensure that the sensitivity and specificity of the assay is appropriate, and consider the limitations of the testing used when interpreting results

ADMINISTRATION WITH FOOD:

- Instruct patients to always take Xtampza ER capsules with food and with approximately the same amount of food in order to ensure consistent plasma levels are achieved. For patients who have difficulty swallowing, Xtampza ER can also be taken as a sprinkle on soft foods or sprinkled into a cup and administered directly into the mouth, or through a nasogastric or gastric feeding tube

Please see additional Important Safety Information throughout this brochure and accompanying full Prescribing Information, including Boxed Warning and Medication Guide, on XtampzaER.com/PI.

Xtampza® ER (oxycodone) EXTENDED-RELEASE CAPSULES

Xtampza® ER has surpassed OxyContin to be preferred on more health plans nationwide[7]

Compared to OxyContin, **Xtampza ER has:**

- ☑ More covered lives[7]
- ☑ Lower average co-pays[8]
- ☑ Higher approval rates[8]

Pharmacy Locator Service
Call toll free (M-F, 8 AM-9 PM ET) **888-884-2655**

Visit Xtampza ER to download a copay card and for additional resources.

Eligible patients may pay as little as $35* for each prescription.

*Offer valid for commercially insured patients only. Maximum savings limit applies; patient out-of-pocket expense may vary.

IMPORTANT SAFETY INFORMATION (continued)

ADVERSE REACTIONS:

- The most common adverse reactions (>5%) reported by patients in the Phase 3 clinical trial comparing Xtampza ER with placebo were nausea, headache, constipation, somnolence, pruritus, vomiting, and dizziness

Please see additional Important Safety Information throughout this brochure and accompanying full Prescribing Information, including Boxed Warning and Medication Guide, on XtampzaER.com/PI.

References:
1. Kopecky EA, Fleming AB, Noonan PK, et al. Impact of physical manipulation on *in vitro* and *in vivo* release profiles of oxycodone DETERx®: an extended-release, abuse-deterrent formulation. *J Opioid Manag.* 2014;10(4):233-246. **2.** Cicero TJ, Ellis MS. Abuse-deterrent formulations and the prescription opioid abuse epidemic in the United States: lessons learned from OxyContin. *JAMA Psychiatry.* 2015;72(5):424-430. doi:10.1001/jamapsychiatry.2014.3043. **3.** Gudin J, Levy-Cooperman N, Kopecky EA, et al. Comparing the effect of tampering on the oral pharmacokinetic profiles of two extended-release oxycodone formulations with abuse-deterrent properties. *Pain Med.* 2015;16(11):2142-2151. doi:10.1111/pme.12834. **4.** Xtampza ER [package insert]. Stoughton, MA: Collegium Pharmaceutical, Inc.; 2019. **5.** OxyContin [package insert]. Stamford, CT: Purdue Pharma LP; 2019. **6.**Oxycodone HCl controlled-release [package insert]. Jacksonville, FL: Ranbaxy Pharmaceuticals LP; 2010. **7**.Managed Markets Insight & Technology, LLC (MMIT) data as of January 2020. **8.** IQVIA FIA for [December 2019].

Collegium PHARMACEUTICAL

Xtampza ER (oxycodone) EXTENDED-RELEASE CAPSULES