Orexo is Committed to Supporting Patients with Opioid Use Disorder (OUD)

Opioid use disorder is a chronic and treatable disease and that continues to be a constant long-term threat to people in our country. In September 2023, 12-month data showed that an estimated 114,000 Americans died from overdose.[1] Orexo is encouraged that recently the number is beginning to trend downward. In September 2024, 12-month data showed that number decreased to 87,000 deaths.[1] That is a 24% percent decrease.[1] All of us at Orexo see this downward trend as validation and hope that the work we have been doing since 2013 is helping to make a difference for the OUD epidemic in America. We have so much more work ahead of us, and we are committed to fighting OUD on this passionate journey.

Since Orexo US entered the market in 2013, our people have continued to demonstrate a steadfast commitment to helping patients, families and communities struggling with OUD to take steps toward recovery. From day one, our unwavering focus has been to help serve the needs of patients so that, along with the support of their healthcare team, they may enter a path to sustained recovery. **Orexo believes that patients struggling with OUD deserve our science, our support, and, most importantly, our understanding to aid in their journey to recovery.**

To that end, Orexo US has taken many initiatives to help support patients with OUD.

Our Offerings

- **ZUBSOLV®** (buprenorphine and naloxone) sublingual tablets (CIII) combine active ingredient with an innovative proprietary quick dissolve delivery technology and an abuse deterrent
  - Over 450,000 patients have been treated with ZUBSOLV from 2013 to 2024[2]
  - Safety and efficacy demonstrated in largest US clinical drug study conducted in OUD[2]
  - Six dosage strengths to provide flexibility to individualize treatment (one tablet allows titration to the most effective doses needed by each patient)
  - F1 child resistant packaging to mitigate accidental ingestion by children
  - Serialization of packaging since launch to allow for track and trace if desired by stakeholders
  - Patient preference demonstrated in head-to-head clinical study with market leader[2]
  - Please see the Important Safety Information below*
- **MODIA®** is a web-based software program designed to help patients develop behavioral coping skills to manage their condition
  - Incorporates evidence-based counseling techniques
  - Provides educational information, reminders and motivational guidance
  - Conducted clinical study with over 430 subjects to assess effectiveness[2]
  - Conducted over 2,800 patient evaluations in real world environments[2]
- **MATCore™** is a customizable online platform designed to overcome OUD treatment barriers and increase patient engagement
  - Delivery of medication
  - Patient education, links to local resources and patient surveys
  - HCP analytics
  - Contingency Management tracking

Our Research & Development

- Over $142 million invested in Research and Development[2]
- OX124 is a high dose powder-based intranasal naloxone rescue medication in development[2]
  - Designed to be stable at a wide range of outdoor temperatures[2]
- OX390 is a rescue medication in development for highly potent drug overdoses involving newly emerging drugs of concern[2]
- OX125 is a powder-based intranasal nalmefene rescue medication in development[2]
  - Expected to have a prolonged half-life and longer duration of action than naloxone based rescuers[2]

Our Access Programs

- Voucher Program- provides two 15 free tablet prescriptions of any strength
  - Only OUD company (branded or generic) to offer program of this type
  - Provides medication for vulnerable patients while they wait for potential Prior Authorization from insurer, are between jobs, or have lost insurance coverage
  - Designed and administered by market leader McKesson
  - Insurance agnostic, it does not matter if patients' insurance covers ZUBSOLV
  - Over 230,000 patients have used vouchers
- Copay Program for commercially insured and cash-paying patients
  - Designed and administered by market leader McKesson
  - Helps patients with out-of-pocket costs associated with co-pays required by insurers
  - Helps cash-paying patients with no insurance lower the cost of their prescription
  - Patients receive up to $225 toward co-pay or cost of prescription and have no limit on number of monthly uses
- Patient Assistance Program for indigent patients with no prescription insurance
  - All healthcare providers are eligible to enroll 1 qualified patient
  - Business rules in place to ensure appropriate eligible patients and appropriate prescribing described in prescribing information
  - Administered by third party nonprofit entity, Needy Meds, Inc.
  - Patients stay in program for as long as medically and financially necessary
- Opioid Treatment Program (OTPs) discounts
  - Discounts for eligible OTPs
- Placebos (do not contain medication; offer similar taste to ZUBSOLV which are used for demonstration and under-the-tongue trial use)

Our Commitment to Advocacy

- We provide education and information to key state and national decision makers supporting responsible legislation to reduce stigma of OUD and increase appropriate access to treatment
- We publicly advocated for raising the cap/removing waiver requirement for healthcare providers
- We support open-access state policy for all products in Opioid Dependence category (eliminating prior authorizations for category in various states)
- We have negotiated 99% unrestricted commercial health insurance access in the US[2]
- We ran the award-winning OUD destigmatization campaign, "Out the Monster"

Orexo is relentlessly committed to helping patients with OUD and their treatment team receive the support they need for lifelong recovery.

***Indication**
ZUBSOLV® (buprenorphine and naloxone) sublingual tablet (CIII) is indicated for the treatment of opioid dependence. ZUBSOLV should be used as part of a complete treatment plan that includes counseling and psychosocial support.

Important Safety Information

Contraindications

- ZUBSOLV is contraindicated in patients with a history of hypersensitivity to buprenorphine or naloxone, as serious adverse reactions, including anaphylactic shock, have been reported.

Warnings and Precautions

- Addiction, Abuse, and Misuse: Buprenorphine can be abused in a similar manner to other opioids. Monitor patients for conditions indicative of diversion or progression of opioid dependence and addictive behaviors. Multiple refills should not be prescribed early in treatment or without appropriate patient follow-up visits.

- Risk of Life-Threatening Respiratory and Central Nervous System (CNS) Depression: Life-threatening respiratory depression and death have occurred in association with buprenorphine use. Warn patients of the potential danger of self-administration of benzodiazepines or other CNS depressants while under treatment with ZUBSOLV.
- Patient Access to Naloxone for the Emergency Treatment of Opioid Overdose: Strongly consider prescribing naloxone for the emergency treatment of opioid overdose, both when initiating and renewing treatment with ZUBSOLV, and consider prescribing naloxone if the patient has household members (including children) or other close contacts at risk for accidental ingestion or opioid overdose.
    - Advise patients and caregivers that naloxone may also be administered for a known or suspected overdose with ZUBSOLV itself.
    - Educate patients and caregivers on how to recognize respiratory depression, and if naloxone is prescribed, how to treat with naloxone. Emphasize the importance of calling 911 or getting emergency help, even if naloxone is administered.
- Managing Risks from Concomitant Use of Benzodiazepines or Other CNS Depressants: Concomitant use of buprenorphine and benzodiazepines or other CNS depressants increases the risk of adverse reactions including overdose and death. As a routine part of orientation to buprenorphine treatment, educate patients about the risks of concomitant use of benzodiazepines, sedatives, opioid analgesics, and alcohol. Develop strategies to manage use of prescribed or illicit benzodiazepines or other CNS depressants at initiation of buprenorphine treatment, or if it emerges as a concern during treatment.
    - Before co-prescribing benzodiazepines, ensure that patients are properly diagnosed and consider alternative treatments to address anxiety or insomnia.
    - Take measures to confirm that patients are taking their medication as prescribed and are not diverting or supplementing with illicit drugs, including toxicology screening to test for prescribed and illicit benzodiazepines.
- Unintentional Pediatric Exposure: Store ZUBSOLV safely out of the sight and reach of children. Buprenorphine can cause severe, possibly fatal respiratory depression in children.
- Neonatal Opioid Withdrawal Syndrome (NOWS): Neonatal opioid withdrawal syndrome (NOWS) is an expected and treatable outcome of prolonged use of opioids during pregnancy.
- Adrenal Insufficiency: If diagnosed, treat with physiologic replacement of corticosteroids, and wean patients off of the opioid.
- Risk of Opioid Withdrawal with Abrupt Discontinuation: If treatment is temporarily interrupted or discontinued, monitor patients for withdrawal and treat appropriately.
- Risk of Hepatitis; Hepatic Events: Monitor liver function tests prior to initiation and during treatment and evaluate suspected hepatic events.
- Precipitation of Opioid Withdrawal Signs and Symptoms: An opioid withdrawal syndrome is likely to occur with parenteral misuse of ZUBSOLV by individuals physically dependent on full opioid agonists or by sublingual administration before the agonist effects of other opioids have subsided.
- Risk of Overdose in Opioid-Naïve Patients: ZUBSOLV is not appropriate as an analgesic. There have been reported deaths of opioid-naïve individuals who received a 2-mg sublingual dose of buprenorphine.
- Dental Adverse Events: Cases of dental caries, some severe (i.e., tooth fracture, tooth loss), have been reported following the use of transmucosal buprenorphine-containing products. Educate patients to seek dental care and strategies to maintain or improve oral health while being treated with ZUBSOLV.
- QTc Prolongation: Thorough QT studies with buprenorphine products have demonstrated QT prolongation ≤15 msec. The risk of combining buprenorphine with other QT prolonging agents is not known. Consider these observations in clinical decisions when prescribing ZUBSOLV to patients with QT-related risk factors.

Use in Specific Populations

- Lactation: Buprenorphine passes into mother's milk.
- Geriatric Patients: Monitor for sedation and respiratory depression.
- Moderate and Severe Hepatic Impairment: Buprenorphine/naloxone products are not recommended in patients with severe hepatic impairment and may not be appropriate for patients with moderate hepatic impairment.

Adverse Reactions & Drug Interactions

- Adverse events commonly observed with the sublingual administration of ZUBSOLV are headache, nausea, vomiting, hyperhidrosis, constipation, signs and symptoms of withdrawal, insomnia, pain, and peripheral edema.
- Benzodiazepines: Use caution in prescribing ZUBSOLV for patients receiving benzodiazepines or other CNS depressants and warn patients against concomitant self-administration/misuse.
- CYP3A4 Inhibitors and Inducers: Monitor patients starting or ending CYP3A4 inhibitors or inducers for potential over or under dosing.
- Antiretrovirals: Patients who are on chronic buprenorphine treatment should have their dose monitored if NNRTIs are added to their treatment regimen. Monitor patients taking buprenorphine and atazanavir with and without ritonavir, and reduce dose of buprenorphine if warranted.
- Serotonergic Drugs: Concomitant use may result in serotonin syndrome. Discontinue ZUBSOLV if serotonin syndrome is suspected.

This is not a complete list of potential adverse events associated with buprenorphine/naloxone tablets. For additional safety information, please see Full Prescribing Information.

References:

1. https://www.cdc.gov/media/releases/2025/2025-cdc-reports-decline-in-us-drug-overdose-deaths

2. Orexo US, Inc. Data on File

Questions?
Contact Orexo US, Inc. at
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