Rapid Initiation with Once-monthly SUBLOCADE® Superior to Standard Initiation for Treating Opioid Use Disorder, Including in Fentanyl-Positive Patients, According to Data Presented at CSAM 2024

November 19, 2024

- Data show rapid initiation with once-monthly SUBLOCADE significantly improves retention in opioid use disorder (OUD) patients, especially among fentanyl-positive participants. Study also administered second SUBLOCADE injection a week later vs. standard 28 days, enabling patients to achieve and maintain target medication levels more quickly.
- Presented at the 2024 Canadian Society of Addiction Medicine (CSAM) conference, this study highlights the potential of rapid initiation to transform the treatment of opioid use disorder.
- Data supporting the subcutaneous administration of SUBLOCADE to alternative injection sites including the thigh, upper arm, and buttocks vs current subcutaneous abdominal injection site, were also presented at CSAM.
- SUBLOCADE has received Priority Review designation from the U.S. Food and Drug Administration (FDA) to expand the label to include rapid initiation one hour after a single transmucosal buprenorphine dose as well as inclusion of alternative injection sites.

RICHMOND, Va., Nov. 19, 2024 -- Indivior PLC (Nasdaq/LSE: INDV) last week shared results from a randomized, open-label sub-study in opioid-dependent participants seeking treatment, (NCT04995029) that demonstrates rapid initiation (RI) with SUBLOCADE® (buprenorphine extended-release injection) for the treatment of OUD significantly improves treatment retention compared to standard initiation (SI). RI with SUBLOCADE in a single day may reduce barriers to treatment and improve patient retention especially those who frequently inject opioids or use fentanyl without increasing the risk of precipitated opioid withdrawal (POW) symptoms. The data were presented at the 2024 Canadian Society of Addiction Medicine (CSAM) conference in Hamilton, Ontario, Canada.

“These findings underscore the potential for rapid initiation to transform opioid use disorder treatment,” said Dr. Christian Heidbreder, Ph.D., Chief Scientific Officer at Indivior. “Rapid initiation may improve patient retention and meet the immediate needs brought on by synthetic opioids in real-world settings, offering a practicable path to stabilization and long-lasting, meaningful recovery.”

Conducted across multiple sites, this non-inferiority study included 729 participants (mean age 42, average opioid use of 15 years), stratified by fentanyl presence in urine screens, with an observed 78% fentanyl-positive rate. Patients randomized to RI received a single dose of 4 mg transmucosal buprenorphine (TM-BUP), followed by a SUBLOCADE injection within 1 hour. The primary endpoint was treatment retention at injection 2, administered 1 week after injection 1 comparing it to the current standard regimen of 28 days. Those in the SI group received daily TM-BUP doses over ≥7 days before injection, and if non-inferiority was met, superiority was assessed.

Among the participants, RI was superior to SI in retention rates at injection 2, with a 12% improvement overall and 15% in the fentanyl-positive group. The shorter dose interval between BUP-XR injection 1 and 2 was designed to achieve and maintain buprenorphine plasma concentrations more quickly at target levels of 2 ng/mL. The overall Treatment Emergent Adverse Events (TEAE) profile up to Injection 2 was comparable for RI and SI. There were no unexpected safety findings.

Data supporting the subcutaneous administration of SUBLOCADE to alternative injection sites including the thigh, upper arm, and buttocks were also presented at CSAM (NCT04995029).

SUBLOCADE has received Priority Review designation granted by the U.S. Food and Drug Administration (FDA) for a labeling supplement, which would expand the label to include rapid initiation one hour after a single transmucosal buprenorphine dose and also expands from the current subcutaneous abdominal injection site for induction and maintenance to alternative injection sites including the thigh, upper arm, and buttocks. With a Prescription Drug User Fee Act (PDUFA) action date set for February 7, 2025, this Prior Approval Supplement (PAS) submission, if approved, could allow healthcare providers a flexible approach to initiate treatment rapidly, supporting better retention outcomes for OUD patients, particularly those testing positive for fentanyl. A Priority Review designation means that the FDA's goal is to take action on an application within 6 months (compared to 10 months under standard review). If approved, this label change could translate into significant improvements in OUD treatment with SUBLOCADE.

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of Addiction Medicine.

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About SUBLOCADE®

SUBLOCADE ® (buprenorphine extended-release) injection, for subcutaneous use, CIII

INDICATION AND HIGHLIGHTED SAFETY INFORMATION

INDICATION

SUBLOCADE is indicated for the treatment of moderate to severe opioid use disorder in patients who have initiated treatment with a buprenorphine-containing product, followed by dose adjustment for a minimum of 7 days.

SUBLOCADE should be used as part of a complete treatment plan that includes counseling and psychosocial support.

HIGHLIGHTED SAFETY INFORMATION

WARNING: RISK OF SERIOUS HARM OR DEATH WITH INTRAVENOUS ADMINISTRATION; SUBLOCADE RISK EVALUATION AND MITIGATION STRATEGY

- **Serious harm or death could result if administered intravenously. SUBLOCADE forms a solid mass upon contact with body fluids and may cause occlusion, local tissue damage, and thrombo-embolic events, including life threatening pulmonary emboli, if administered intravenously.**
- **Because of the risk of serious harm or death that could result from intravenous self-administration, SUBLOCADE is only available through a restricted program called the SUBLOCADE REMS Program. Healthcare settings and pharmacies that order and dispense SUBLOCADE must be certified in this program and comply with the REMS requirements.**

CONTRAINDICATIONS

SUBLOCADE should not be administered to patients who have been shown to be hypersensitive to buprenorphine or any component of Indivior's proprietary buprenorphine gel depot delivery system.

WARNINGS AND PRECAUTIONS

Addiction, Abuse, and Misuse: SUBLOCADE contains buprenorphine, a Schedule III controlled substance that can be abused in a manner similar to other opioids. Monitor patients for conditions indicative of diversion or progression of opioid dependence and addictive behaviors.

Respiratory Depression: Life threatening respiratory depression and death have occurred in association with buprenorphine. Warn patients of the potential danger of self-administration of benzodiazepines or other CNS depressants while under treatment with SUBLOCADE.

Opioids can cause sleep-related breathing disorders e.g., central sleep apnea (CSA), sleep-related hypoxemia. Opioid use increases the risk of CSA in a dose-dependent fashion. Consider decreasing the opioid using best practices for opioid taper if CSA occurs.

Strongly consider prescribing naloxone at SUBLOCADE initiation or renewal because patients being treated for opioid use disorder have the potential for relapse, putting them at risk for opioid overdose. Educate patients and caregivers on how to recognize respiratory depression and how to treat with naloxone if prescribed.

Risk of Serious Injection Site Reactions: The most common injection site reactions are pain, erythema and pruritus with some involving abscess, ulceration, and necrosis. The likelihood of serious injection site reactions may increase with inadvertent intramuscular or intradermal administration.

Neonatal Opioid Withdrawal Syndrome: Neonatal opioid withdrawal syndrome 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 patient off the opioid.

Risk of Opioid Withdrawal With Abrupt Discontinuation: If treatment with SUBLOCADE is discontinued, monitor patients for several months for withdrawal and treat appropriately.

Risk of Hepatitis, Hepatic Events: Monitor liver function tests prior to and during treatment.

Risk of Withdrawal in Patients Dependent on Full Agonist Opioids: Verify that patient is clinically stable on transmucosal buprenorphine before injecting SUBLOCADE.

Treatment of Emergent Acute Pain: Treat pain with a non-opioid analgesic whenever possible. If opioid therapy is required, monitor patients closely because higher doses may be required for analgesic effect.

ADVERSE REACTIONS

Adverse reactions commonly associated with SUBLOCADE (in ≥5% of subjects) were constipation, headache, nausea, injection site pruritus, vomiting, increased hepatic enzymes, fatigue, and injection site pain.

For more information about SUBLOCADE, the full Prescribing information including BOXED WARNING, and Medication Guide, visit www.sublocade.com.

About Opioid Use Disorder (OUD)

Opioid Use Disorder (OUD) is a chronic disease in which people develop a pattern of using opioids that can lead to negative consequences.1 OUD may affect the parts of the brain that are necessary for life-sustaining functions.1,2

Important Cautionary Note Regarding Forward-Looking Statements

This press release contains certain statements that are forward-looking. Forward-looking statements include, among other things, express and implied statements regarding: Indivior PLC's expectations regarding the timing of approval for the PAS for rapid induction and injection sites, and the potential impact on OUD treatments and Sublocade from such; and other statements containing the words "believe," "anticipate," "plan," "expect," "expectations," "intend," "estimate," "forecast," "strategy," "target," "guidance," "outlook," "potential," "project," "priority," "may," "will," "should," "would," "could," "can," the negatives thereof, and variations thereon and similar expressions. By their nature, forward-looking statements involve risks and uncertainties as they relate to events or circumstances that may or may not occur in the future. Actual results may differ materially from those expressed or implied in these forward-looking statements due to a number of factors, including: failure or delay in obtaining approval of the PAS and the acceptance by HCPs and their patients of the perceived benefits of such PAS changes. For information about some of the risks and important factors that could affect our future results and financial condition, see "Risk Factors" in Indivior's Annual Report on Form 20-F for the fiscal year 2023 and its other filings with the U.S. Securities and Exchange Commission. We have based the forward-looking statements in this press release on our current expectations and beliefs concerning future events. Forward-looking statements contained in this press release apply only at the date of this press release and, except as required by law, we undertake no obligation to update or revise any forward-looking statement, whether due to new information, future developments, or otherwise.

About Indivior

Indivior is a global pharmaceutical company working to help change patients' lives by developing medicines to treat substance use disorders (SUD). Our vision is that all patients around the world will have access to evidence-based treatment for the chronic conditions and co-occurring disorders of SUD. Indivior is dedicated to transforming SUD from a global human crisis to a recognized and treated chronic disease. Building on its global portfolio of OUD treatments, Indivior has a pipeline of product candidates designed to expand on its heritage in this category. Headquartered in the United States in Richmond, VA, Indivior employs over 1,000 individuals globally and its portfolio of products is available in over 30 countries worldwide.
Visit www.indivior.com to learn more. Connect with Indivior on LinkedIn by visiting www.linkedin.com/company/indivior.

Media Contacts:

US Media:

Cassie France-Kelly
VP, Communications
Indivior PLC
Tel: +1(804) 724-0327

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2. NIDA. 2022, March 22. Drugs and the Brain. Accessed October 30,2023, from https://nida.nih.gov/publications/drugs-brains-behavior-science-addiction/drugs-brain