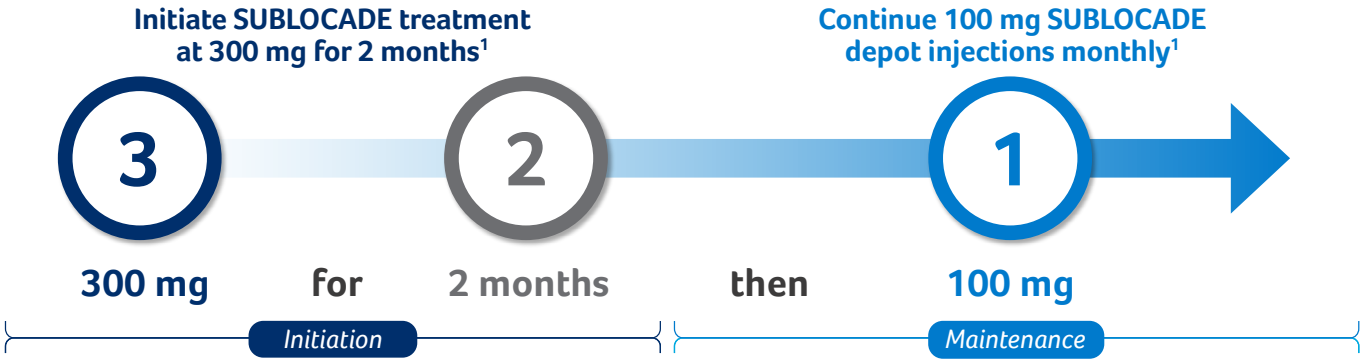
SUBLOCADE® (buprenorphine extended-release) injection, for subcutaneous use (CIII) is indicated for the treatment of moderate to severe opioid use disorder in patients who have initiated treatment with a buprenorphine-containing product, followed by dose adjustment for a minimum of 7 days.

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

Dosing and Administration

STRAIGHTFORWARD DOSING HELPS PATIENTS REACH AND SUSTAIN THERAPEUTIC LEVELS[1]



Before starting SUBLOCADE, patients must be dose-stabilized for a minimum of 7 days on buprenorphine equal to 8-24 mg/day of transmucosal buprenorphine (TM BUP).[1]

Please see full recommended dosing instructions in section 2.4 of Prescribing Information.

SUBLOCADE contains buprenorphine, a Schedule III controlled substance that can be abused in a manner similar to other opioids.[1]

IMPORTANT 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.**

ONCE-MONTHLY
Sublocade®
(buprenorphine extended-release) injection for subcutaneous use
100mg·300mg

Prescription use of this product is limited under the Drug Addiction Treatment Act.

CONTRAINDICATIONS: SUBLOCADE should not be administered to patients who are hypersensitive to buprenorphine or any component of the ATRIGEL® delivery system.

Please see additional Important Safety Information throughout and accompanying full Prescribing Information, including BOXED WARNING, and Medication Guide.

SUBLOCADE® provides consistent treatment exposure over the monthly dosing interval[1,2]

Before starting SUBLOCADE*

- Patients must be dose-stabilized for a minimum of 7 days on buprenorphine (equal to 8-24 mg/day TM BUP)[1]
- Liver function tests prior to initiation of treatment are recommended to establish a baseline[1]
- In clinical studies, patients could receive loperamide and non-opioid medications to alleviate opioid withdrawal symptoms[3]

Transitioning from TM BUP to SUBLOCADE

- Clinically stable patients on transmucosal buprenorphine (8-24 mg/day) and whose disease symptoms are controlled may be directly transitioned to SUBLOCADE[1]
- Patients established on long-term doses of TM BUP (8-18 mg) are eligible to reduce their dose to 100 mg at the second injection if opioid withdrawal and craving are controlled[1]

Keeping patients on SUBLOCADE

- For patients who tolerate the 100 mg dose, but do not demonstrate a satisfactory clinical response, the maintenance dose may be increased to 300 mg[1]
- Administer SUBLOCADE monthly with a minimum of 26 days between doses[1]
- Monthly monitoring of liver function during treatment, particularly with 300 mg maintenance dose, is also recommended[1]
- A patient who misses a dose should receive the next dose as soon as possible[1]
  - Occasional delays in dosing up to 2 weeks are not expected to have a clinically significant impact on treatment effect[1]

- Strongly consider prescribing naloxone along with SUBLOCADE because patients being treated for opioid use disorder (OUD) are at increased risk of overdose[1]

*Initiating treatment with SUBLOCADE as the first buprenorphine product has not been studied

IMPORTANT SAFETY INFORMATION (CONT'D)

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. Buprenorphine is sought by people with opioid use disorder and is subject to criminal diversion. Monitor patients for conditions indicative of diversion or progression of opioid dependence and addictive behaviors.

Risk of Life-Threatening Respiratory Depression and Concomitant Use of Benzodiazepines or Other CNS Depressants with Buprenorphine: Buprenorphine has been associated with life-threatening respiratory depression, overdose, and death, particularly when misused by self-injection or with concomitant use of benzodiazepines or other CNS depressants, including alcohol. Warn patients of the potential danger of self-administration of benzodiazepines, other CNS depressants, opioid analgesics, and alcohol while under treatment with SUBLOCADE. Counsel patients that such medications should not be used concomitantly unless supervised by a healthcare provider.

Use with caution in patients with compromised respiratory function (e.g., chronic obstructive pulmonary disease, cor pulmonale, decreased respiratory reserve, hypoxia, hypercapnia, or pre-existing respiratory depression).

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 the time SUBLOCADE is initiated or renewed 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, if naloxone is prescribed, how to treat with naloxone. Emphasize the importance of calling 911 or getting emergency help, even if naloxone is administered.

Please see additional Important Safety Information throughout and accompanying full Prescribing Information, including BOXED WARNING, and Medication Guide.

SUBLOCADE can remain at room temperature for up to 7 days[1]

SUBLOCADE is available in a single dose, prefilled syringe with safety needle

- Remove SUBLOCADE from refrigerator at least 15 minutes prior to administration to allow it to come to room temperature (59 – 86°F) in its original packaging[1]
  - Do not open the foil pouch until the patient has arrived for their injection[1]
  - Keep refrigerated at 35.6 - 46.4°F when not in use[1]
  - Discard if left at room temperature over 7 days[1]

- SUBLOCADE is for abdominal subcutaneous injection only; do not administer intravenously, intramuscularly or intradermally. Serious harm or death could result if administered intravenously[1]
- Always wear gloves when preparing or administering SUBLOCADE[1]

IMPORTANT SAFETY INFORMATION (CONT'D)

WARNINGS AND PRECAUTIONS (CONT'D)

Risk of Serious Injection Site Reactions: The most common injection site reactions are pain, erythema and pruritus with some involving abscess, ulceration, and necrosis. Some cases resulted in surgical depot removal, debridement, antibiotic administration, and SUBLOCADE discontinuation. The likelihood of serious injection site reactions may increase with inadvertent intramuscular or intradermal administration. Carefully review injection technique.

Neonatal Opioid Withdrawal Syndrome: Neonatal opioid withdrawal syndrome (NOWS) is an expected and treatable outcome of prolonged use of opioids during pregnancy. NOWS may be life-threatening if not recognized and treated in the neonate. Newborns should be observed for signs of NOWS and managed accordingly. Advise pregnant women receiving opioid addiction treatment with SUBLOCADE of the risk of neonatal opioid withdrawal syndrome.

Adrenal Insufficiency: Adrenal insufficiency has been reported with opioid use. If adrenal insufficiency is diagnosed, treat with physiologic replacement doses of corticosteroids. Wean the patient off the opioid.

Discontinuation of SUBLOCADE Treatment: Due to the long-acting nature of SUBLOCADE, if treatment is discontinued, monitor patients for several months for withdrawal and treat appropriately.

Inform patients that they may have detectable levels of buprenorphine for a prolonged period of time after treatment with SUBLOCADE. Considerations of drug-drug interactions, buprenorphine effects, and analgesia may continue to be relevant for several months after the last injection.

Risk of Hepatitis, Hepatic Events: Because cases of cytolytic hepatitis and hepatitis with jaundice have been observed in individuals receiving buprenorphine, monitor liver function tests prior to treatment and monthly during treatment.

Hypersensitivity Reactions: Hypersensitivity to buprenorphine-containing products have been reported most commonly as rashes, hives, and pruritus. Some cases of bronchospasm, angioneurotic edema, and anaphylactic shock have also been reported.

Precipitation of Opioid Withdrawal in Patients Dependent on Full Agonist Opioids: Buprenorphine may precipitate opioid withdrawal signs and symptoms in persons who are currently physically dependent on full opioid agonists such as heroin, morphine, or methadone before the effects of the full opioid agonist have subsided. Verify that patients have tolerated and are dose adjusted on transmucosal buprenorphine before subcutaneously injecting SUBLOCADE.

Risks Associated With Treatment of Emergent Acute Pain: When patients need acute pain management, or may require anesthesia, treat patients receiving SUBLOCADE currently or within the last 6 months with a non-opioid analgesic whenever possible. If opioid therapy is required, patients may be treated with a high-affinity full opioid analgesic under the supervision of a physician, with particular attention to respiratory function, as higher doses may be required for analgesic effect and therefore, a higher potential for toxicity exists with opioid administration.

Advise patients of the importance of instructing their family members, in the event of emergency, to inform the treating healthcare provider or emergency room staff that the patient is physically dependent on an opioid and that the patient is being treated with SUBLOCADE.

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ONCE-MONTHLY

Sublocade®

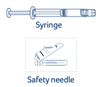
(buprenorphine extended-release) injection for subcutaneous use

Summary of how to administer SUBLOCADE®

Only health care providers* should prepare and administer SUBLOCADE[1]

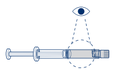
Step 1: Getting Ready

Remove the foil pouch and safety needle from the carton. Open the pouch and remove the syringe.[1]



Step 2: Check the Liquid Clarity

Check that the medication does not contain contaminants or particles. SUBLOCADE ranges from colorless to yellow to amber.[1]



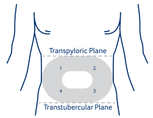
Step 3: Attach the Safety Needle

Remove the cap from the syringe and the safety needle supplied in the carton from its sterile package. Gently twist the needle clockwise until it is tight and firmly attached.[1]

Step 4: Prepare the Abdominal Injection Site

Choose an injection site on the abdomen (as shown in the figure on the right) with adequate subcutaneous tissue that is free of skin conditions (eg, nodules, lesions, excessive pigment). It is recommended that the patient is in the supine position.[1]

Clean the injection site well with an alcohol swab. To avoid irritation, rotate injection sites following a pattern similar to the illustration.[1]



Step 5: Remove Excess Air From Syringe

Hold the syringe upright for several seconds to allow air bubbles to rise.[1]

Remove needle cover and slowly depress the plunger to push out the excess air from the syringe.[1]

*Physicians, nurse practitioners, physician's assistants, or suitable qualified designees (eg, nursing staff)

IMPORTANT SAFETY INFORMATION (CONT'D)

WARNINGS AND PRECAUTIONS (CONT'D)

Use in Opioid Naïve Patients: Because death has been reported for opioid naïve individuals who received buprenorphine sublingual tablet, SUBLOCADE is not appropriate for use in opioid naïve patients.

Use in Patients With Impaired Hepatic Function: Because buprenorphine levels cannot be rapidly decreased, SUBLOCADE is not recommended for patients with pre-existing moderate to severe hepatic impairment. Patients who develop moderate to severe hepatic impairment while being treated with SUBLOCADE should be monitored for several months for signs and symptoms of toxicity or overdose caused by increased levels of buprenorphine.

Use in Patients at Risk for Arrhythmia: Buprenorphine has been observed to prolong the QTc interval in some patients participating in clinical trials. Avoid use of buprenorphine in patients with a history of Long QT Syndrome or an immediate family member with this condition or those taking Class IA antiarrhythmic medications (e.g., quinidine, procainamide, disopyramide) or Class III antiarrhythmic medications (e.g., sotalol, amiodarone, dofetilide), or other medications that prolong the QT interval.

Impairment of Ability to Drive or Operate Machinery: SUBLOCADE may impair the mental or physical abilities required for the performance of potentially dangerous tasks such as driving a car or operating machinery. Caution patients about driving or operating hazardous machinery until they are reasonably certain that SUBLOCADE does not adversely affect their ability to engage in such activities.

Orthostatic Hypotension: Buprenorphine may produce orthostatic hypotension.

Elevation of Cerebrospinal Fluid Pressure: Buprenorphine may elevate cerebrospinal fluid pressure and should be used with caution in patients with head injury, intracranial lesions, and other circumstances when cerebrospinal pressure may be increased. Buprenorphine can produce miosis and changes in the level of consciousness that may interfere with patient evaluation.

Elevation of Intracholedochal Pressure: Buprenorphine has been shown to increase intracholedochal pressure, as do other opioids, and thus should be administered with caution to patients with dysfunction of the biliary tract.

Effects in Acute Abdominal Conditions: Buprenorphine may obscure the diagnosis or clinical course of patients with acute abdominal conditions.

Please see additional Important Safety Information throughout and accompanying full Prescribing Information, including BOXED WARNING, and Medication Guide.

Step 6: Pinch the Injection Site

Pinch the skin around the injection area. Be sure to pinch enough skin to accommodate the size of the needle. Lift the adipose tissue from the underlying muscle to prevent accidental intramuscular injection.[1]

Step 7: Inject the Medication

SUBLOCADE is for subcutaneous injection only. Do not inject intravenously, intramuscularly, or intradermally. Insert needle fully into the abdominal subcutaneous tissue.[1]

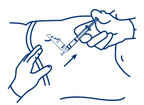
Use a slow, steady push to inject the medication. Continue pushing until all of the medication is given.[1]

Total volume: 0.5 mL for 100 mg and 1.5 mL for 300 mg.[1]

Step 8: Withdraw the Needle

Withdraw the needle at the same angle used for insertion and release the pinched skin.[1]

Do not rub the injection area after the injection. There may be a small amount of blood or fluid at the injection site; wipe with a cotton ball or gauze before applying a gauze pad or bandage using minimal pressure.[1]



IMPORTANT SAFETY INFORMATION (CONT'D)

WARNINGS AND PRECAUTIONS (CONT'D)

Unintentional Pediatric Exposure: Buprenorphine can cause severe, possibly fatal, respiratory depression in children who are accidentally exposed to it.

ADVERSE REACTIONS: Adverse reactions commonly associated with SUBLOCADE (≥5% of subjects) during clinical trials were constipation, headache, nausea, vomiting, increased hepatic enzymes, fatigue, and injection site pain and pruritus. This is not a complete list of potential adverse events. Please see the full Prescribing Information for a complete list.

DRUG INTERACTIONS

CYP3A4 Inhibitors and Inducers: Monitor patients starting or ending CYP3A4 inhibitors or inducers for potential over- or under-dosing.

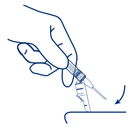
Serotonergic Drugs: If concomitant use with serotonergic drugs is warranted, monitor for serotonin syndrome, particularly during treatment initiation, and during dose adjustment of the serotonergic drug.

Consult the full Prescribing Information for SUBLOCADE for more information on potentially significant drug interactions.

Step 9: Lock the Needle Guard and Discard the Syringe

Lock the needle guard into place by pushing it against a hard surface such as a table. Dispose of all syringe components in a secure sharps disposal container.[1]

After administration, syringes should be properly disposed, per facility procedure for a Schedule III drug product, and per applicable federal, state, and local regulations.[1]



Step 10: Instruct the Patient

Advise the patient that they may have a lump for several weeks that will decrease in size over time. Instruct the patient not to rub or massage the injection site and to be aware of the placement of any belts or clothing waistbands.[1]

Reference: 1. SUBLOCADE [prescribing information]. North Chesterfield, VA: Indivior Inc.; 2021. **2.** Jones AK, Ngaimisi E, Gopalakrishnan M, Young MA, Laffont CM. Population Pharmacokinetics of a Monthly Buprenorphine Depot Injection for the Treatment of Opioid Use Disorder: A Combined Analysis of Phase II and Phase III Trials. *Clin Pharmacokinet.* 2021;60(4):527-540. doi:10.1007/s40262-020-00957-0 **3.** Haight BR, Learned SM, Laffont CM, et al. Efficacy and safety of a monthly buprenorphine depot injection for opioid use disorder: a multicentre, randomised, double-blind, placebo-controlled, phase 3 trial. *Lancet.* 2019;393(10173):778-790. doi:10.1016/ S0140-6736(18)32259-1 **4.** Rosenthal RN, Goradia VV. Advances in the delivery of buprenorphine for opioid dependence. *Drug Des Devel Ther.* 2017;11:2493-2505. Published 2017 Aug 28. doi:10.2147/DDDT.S72543

USE IN SPECIFIC POPULATIONS

Pregnancy: Opioid-dependent women on buprenorphine maintenance therapy may require additional analgesia during labor.

Lactation: Buprenorphine passes into the mother's milk. Advise breastfeeding women to monitor the infant for increased drowsiness and breathing difficulties.

Fertility: Chronic use of opioids may cause reduced fertility. It is not known whether these effects on fertility are reversible.

Geriatric Patients: Monitor geriatric patients receiving SUBLOCADE for sedation or respiratory depression.

To report pregnancy or side effects associated with taking SUBLOCADE, please call 1-877-782-6966.

ONCE-MONTHLY

Sublocade®

(buprenorphine extended-release) injection for subcutaneous use

SUBLOCADE® is designed to be there for your patients every moment between doses[1]

Lift the burden of daily dosing by continuously delivering buprenorphine with a once-monthly injection[1,4]

Watch the SUBLOCADE administration video

Scan

OR

Visit sublocadehcp.com/dosing-administration

INDICATION

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

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

ONCE-MONTHLY

Sublocade®

(buprenorphine extended-release) injection for subcutaneous use Ⓒ

100mg·300mg

INDIVIOR®

P-BAG-US-01044 Expiry November 2023 Intended for US audience.