FDA Approves SUBLOCADE™ (Buprenorphine Extended-Release), the First and Only Once-Monthly Injectable Buprenorphine Formulation to Treat Moderate to Severe Opioid Use Disorder

SUBLOCADE Expected to be Available to U.S. Patients in Q1 2018

This announcement contains inside information.

Slough, UK, 1 December 2017 – Indivior PLC (LON: INDV) today announced that the U.S. Food and Drug Administration (FDA) has approved SUBLOCADE™ *(buprenorphine extended- release) injection for subcutaneous use (CIII)*, the first and only once-monthly injectable buprenorphine formulation for the treatment of moderate to severe opioid use disorder (OUD) in patients who have initiated treatment with a transmucosal buprenorphine-containing product followed by dose adjustment for a minimum of seven days. SUBLOCADE is intended to be administered only by healthcare providers and should be used as part of a complete treatment program that includes counseling and psychosocial support[1]. SUBLOCADE is expected to be available to patients in the U.S. in Q1 2018.

"SUBLOCADE is a scientific innovation that represents a new treatment option to help patients attain more illicit opioid-free weeks during their treatment program," said Shaun Thaxter, Chief Executive Officer of Indivior. "In the Opioid Blockade Study, SUBLOCADE achieved complete blockade of drug-liking effects for a full month in most patients. SUBLOCADE is the first and only therapy that, at steady state, delivers buprenorphine at a sustained rate of at least 2 ng/mL over a one month period. The urgency for this new treatment has never been greater, as the U.S. opioid crisis has been declared a national public health emergency. SUBLOCADE's approval is an important step forward for patients, families and communities battling the opioid epidemic."

SUBLOCADE contains buprenorphine, a partial agonist at the mu-opioid receptor[1]. Mu-opioid receptors in the brain are known to mediate the subjective effects of opioids, including drug-liking, which is the pleasure associated with opioid use[2]. SUBLOCADE delivers sustained plasma levels of buprenorphine that translate into high mu-opioid receptor occupancy in the brain, which blocks the drug-liking effects of opioids[1].

In the SUBLOCADE clinical trial program, average buprenorphine plasma concentrations of 2-3 ng/mL were associated with mu-opioid receptor occupancy ≥70% and the reduction of illicit opioid use. SUBLOCADE 300 mg delivers average buprenorphine plasma levels of approximately 2 ng/mL after the first injection. The average concentration of SUBLOCADE at steady-state was 3.21 ng/mL and 6.54 ng/mL for the 100 mg and 300 mg doses, respectively[1].

Indivior conducted an Opioid Blockade Study (RB-US-13-0002) which investigated the ability of SUBLOCADE 300 mg to block the subjective effects of illicit opioids, including drug-liking. In the 12-week trial evaluating the blocking effect, SUBLOCADE 300 mg fully blocked the drug-liking effects of hydromorphone[1]. Hydromorphone is a potent opioid pain medication[3] that is commonly used in human studies to evaluate opioid drug-liking[2].

SUBLOCADE was evaluated in a 24-week, Phase 3 pivotal study (RB-US-13-0001) in which patients were randomized to one of the following three regimens: six once-monthly SUBLOCADE 300 mg doses; two once-monthly SUBLOCADE 300 mg doses followed by four once-monthly 100 mg doses; or six once-monthly injections of placebo. Both dosage regimens of SUBLOCADE were shown to be superior to placebo in achieving more illicit opioid-free weeks ($p<0.0001$)[1,4]. In the clinical trials, the overall safety profile for SUBLOCADE, given by a healthcare provider, was consistent with the known safety profile of transmucosal buprenorphine, except for injection site reactions. The most common adverse reactions (≥5% patients), included constipation, nausea, vomiting, abnormal liver enzymes, headache, sedation and somnolence. Injection site reactions were reported in 16.5% of the patients. None of the injection site reactions were serious, and only one led to study treatment discontinuation[1].

“Every patient’s journey to recovery is different and they face many challenges. To help support these differences, doctors and patients need options for medication-assisted treatment,” said Dr. Brent Boyett, SUBLOCADE clinical investigator and director at Boyett Health Services, Inc. “In a Phase 3 clinical study, SUBLOCADE helped patients refrain from illicit opioids for more weeks compared to placebo. Used in combination with counseling and psychosocial support, SUBLOCADE is a transformational new drug that offers a treatment option for people with moderate to severe opioid use disorder.”

The opioid addiction epidemic in the U.S. is a national public health emergency, with nearly 12 million people impacted nationwide and an average of four people dying from opioid overdose every hour of every day[5,6,7]. OUD, commonly referred to as opioid addiction[8], is a chronic disease that changes the brain[9]. The patient journey to treatment and recovery is complex, with many barriers such as social stigma, access to treatment and prescribers, and difficulty adhering to treatment plans. Out of the more than 2.5 million patients diagnosed with OUD in the U.S., less than half are treated with medication-assisted treatment (MAT)[10].

The economic impact of the opioid epidemic to the healthcare system is significant. The amount paid for treatment of substance use disorders is only a small portion of the costs these disorders impose on society. Data published in 2016 presented the total costs of prescription opioid use disorder and overdose in the U.S. at $78 billion in 2013. Of that, only 3.6 percent, or about $2.8 billion, was for treatment[11]. A separate, recent analysis by the White House Council of Economic Advisers estimated the total annual cost of prescription opioid overdose, abuse and dependence in the U.S. at $504 billion in the year 2015[12]. Patients, physicians, policymakers and other stakeholders have expressed the need for additional treatment options in the fight against the chronic relapsing disease of opioid addiction. Indivior has an ongoing, prospective, observational study (RECOVER™) to understand the clinical, environmental and socioeconomic characteristics of OUD patients[13].

“The American Society of Addiction Medicine supports the development and manufacturing of medications that aid in the treatment of addiction,” said Dr. Kelly Clark, President, American Society

of Addiction Medicine. “The introduction of novel pharmacotherapies supports this goal. Addiction patients, like all patients, should have available to them a robust and varied array of treatment options, as no one treatment modality is appropriate or therapeutic for everyone.”

“We applaud the scientists and leaders who have been working tirelessly on the development of new, longer-acting medicines for the treatment of opioid use disorder. These exciting new developments will help our patients and families live healthy lives and accelerate the progress in the treatment of addiction,” commented Jessica Hulsey Nickel, President and CEO of the Addiction Policy Forum.

Under the Drug Addiction Treatment Act (DATA) codified at 21 U.S.C. 823(g), prescription use of SUBLOCADE in the treatment of opioid dependence is limited to healthcare providers who meet certain qualifying requirements, and who have notified the Secretary of Health and Human Services (HHS) of their intent to prescribe this product for the treatment of opioid dependence and have been assigned a unique identification number that must be included on every prescription[1].

SUBLOCADE will be distributed through a restricted distribution system, which is intended to prevent the direct distribution to a patient. This is because of risk of serious harm or death that could result from intravenous self-administration.

Indivior worked closely with the FDA to include appropriate warnings and precautions, including a BOXED WARNING in the label and implementation of a Risk Evaluation and Mitigation Strategy (REMS) program. Healthcare settings and pharmacies that order and dispense SUBLOCADE must be certified in the SUBLOCADE REMS Program. In addition, Indivior continues to enhance its compliance program to keep pace with the anticipated increase in the number of patients in treatment.

For further information, see **SUBLOCADE: Product Details, Clinical Information and Price Fact Sheet**.

About SUBLOCADE ™

INDICATION AND USAGE
SUBLOCADE is indicated for the treatment of moderate to severe opioid use disorder in patients who have initiated treatment with a transmucosal buprenorphine-containing product followed by a dose adjustment period for a minimum of seven days.

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

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.**

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

CONTRAINDICATIONS
SUBLOCADE should not be administered to patients who have been shown to be hypersensitive to buprenorphine or any component of the ATRIGEL® 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.

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 of 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.

The full prescribing information, including BOXED WARNING, for SUBLOCADE can be found here: http://indivior.com/wp-content/uploads/2017/11/SUBLOCADE-Prescribing-Information.pdf.

About Opioid Use Disorder

OUD, commonly referred to as opioid addiction[8], is a chronic, relapsing disease that changes the brain[9]. According to the DSM–5, opioid use disorder is characterized by signs and symptoms that reflect compulsive, prolonged self-administration of opioid substances that are used for no legitimate medical purpose or, if another medical condition is present that requires opioid treatment, they are used in doses greatly in excess of the amount needed for that medical condition[13].

Based on 2016 data from the most recent National Survey on Drug Use and Health report, nearly 12 million Americans (age 12+ years) engaged in misuse of opioids in the last year[6]. Between 1999 and

2014 the rate of deadly opioid overdoses quadrupled[14], and in the United States alone, an average of four people die of opioid overdose every hour of every day[7]. In 2015 opioids accounted for 70 percent of the negative health impact associated with drug use disorders worldwide[15]. Approximately 2.5 million American adults (age 18+ years old) met criteria for opioid use disorder in the past year[10]. The same report suggested that 935,000 adults have used heroin in the past year and 471,000 used in the past month. There were approximately 625,000 adults who had a heroin use disorder in the past year[6]. In a recent report by the White House Council of Economic Advisers, estimated economic costs of the opioid crisis in the U.S. were $504 billion in 2015[12].

About Indivior

Indivior is a global specialty pharmaceutical company with a 20-year legacy of leadership in patient advocacy and health policy while providing education on evidence-based treatment models that have revolutionized modern addiction treatment. The name is the fusion of the words individual and endeavour, and the tagline "Focus on you" makes the Company's commitment clear. Indivior is dedicated to transforming addiction from a global human crisis to a recognized and treated chronic disease. Building on its global portfolio of opioid dependence treatments, Indivior has a strong pipeline of product candidates designed to both expand on its heritage in this category and address other chronic conditions and co-occurring disorders of addiction, including alcohol use disorder and schizophrenia. Headquartered in the United States in Richmond, VA, Indivior employs more than 900 individuals globally and its portfolio of products is available in over 40 countries worldwide. Visit www.indivior.com to learn more.

Forward-Looking Statements

This press release contains certain statements that are forward-looking and which should be considered, amongst other statutory provisions, in light of the safe harbour provisions of the United States Private Securities Litigation Reform Act of 1995. By their nature, forward-looking statements involve risk and uncertainty as they relate to events or circumstances that will or may occur in the future. Actual results may differ materially from those expressed or implied in such statements because they relate to future events. Forward-looking statements include, among other things, statements regarding our financial guidance for 2017 and our medium- and long-term growth outlook, our operational goals, our product development pipeline and statements regarding ongoing litigation.

Various factors may cause differences between Indivior's expectations and actual results, including: factors affecting sales of Indivior Group's products; the outcome of research and development activities; decisions by regulatory authorities regarding the Indivior Group's drug applications; the speed with which regulatory authorizations, pricing approvals and product launches may be achieved; the outcome of post-approval clinical trials; competitive developments; difficulties or delays in manufacturing; the impact of existing and future legislation and regulatory provisions on product exclusivity; trends toward managed care and healthcare cost containment; legislation or regulatory action affecting pharmaceutical product pricing, reimbursement or access; claims and concerns that may arise regarding the safety or efficacy of the Indivior Group's products and product candidates; risks related to legal proceedings; the Indivior Group's ability to protect its patents and other intellectual property; the outcome of patent infringement litigation relating to Indivior Group's products, including the ongoing ANDA lawsuits; changes in governmental laws and regulations; issues related to the outsourcing of certain operational and staff functions to third parties; uncertainties related to general economic, political, business, industry, regulatory and market conditions; and the impact of acquisitions, divestitures, restructurings, internal reorganizations, product recalls and withdrawals and other unusual items.

This press release does not constitute an offer to sell, or the solicitation of an offer to subscribe for or otherwise acquire or dispose of shares in the Company to any person in any jurisdiction to whom it is unlawful to make such offer or solicitation.

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Sublocade™
(buprenorphine extended-release) injection for subcutaneous use Ⓒ
100mg·300mg

FOR MODERATE TO SEVERE OPIOID USE DISORDER

SUBLOCADE: Product Details, Clinical Information and Price

This announcement contains inside information.

See Important Safety Information on page 6, including BOXED WARNING.

SUBLOCADE™ is the first once-monthly injectable buprenorphine formulation for the treatment of moderate to severe opioid use disorder (OUD) in patients who have initiated treatment with a transmucosal buprenorphine-containing product followed by dose adjustment for a minimum of seven days. SUBLOCADE should be used as part of a complete treatment program that includes counseling and psychosocial support. SUBLOCADE should only be prepared and administered by a healthcare provider[1].

SUBLOCADE represents an evidence-based, paradigm shift from how we approach treatment of moderate to severe opioid use disorder today.

SUBLOCADE was reviewed and approved by the U.S. Food and Drug Administration (FDA) with Fast Track and Priority Review designation.

SUBLOCADE is a buprenorphine medication-assisted treatment, or BMAT, and offers a new treatment choice at a time when doctors and patients need multiple medication-assisted treatment options.

How SUBLOCADE Works

SUBLOCADE is a scientific innovation that represents a new treatment option to help patients attain more illicit opioid-free weeks during their treatment program.

SUBLOCADE is an injectable, extended-release formulation that uses the ATRIGEL® technology to deliver buprenorphine at a controlled rate over a one month period. As a once-monthly injectable, SUBLOCADE removes the need for patients to remember to take their medication every day, while providing them with the opportunity to focus on psychosocial support, which is an important part of their treatment program[1].

Opioid dependence and other opioid-related physiological effects depend on the activation of mu-opioid receptors in a person's brain. Mu-opioid receptors in the brain are known to

mediate the subjective effects of opioids, including drug-liking, which is the pleasure associated with opioid use[2].

SUBLOCADE is the first and only therapy that, at steady state, delivers buprenorphine plasma concentrations at a sustained rate of at least 2 ng/mL, over a one month period.

- In the SUBLOCADE clinical trial program, average buprenorphine plasma concentrations of 2-3 ng/mL were associated with mu-opioid receptor occupancy ≥70% and the reduction of illicit opioid use[1].
- The average concentration of SUBLOCADE at steady-state was 3.21 ng/mL and 6.54 ng/mL for the 100 mg and 300 mg doses, respectively[1].
- This is important because the observed plateau for maximal response was reached at buprenorphine plasma concentrations of approximately 2-3 ng/mL for illicit opioid use and 4 ng/mL for opioid withdrawal symptoms[1].

Pharmacokinetic parameters[1]	**SL buprenorphine daily stabilization[1]**		**SUBLOCADE[1]**		
Mean	**12 mg (steady-state)**	**24 mg (steady-state)**	**300 mg (1st injection)**	**100 mg (steady-state)**	**300 mg (steady-state)**
$C_{avg,ss}$ (ng/mL)	1.71	2.91	2.19	3.21	6.54
$C_{max,ss}$ (ng/mL)	5.35	8.27	5.37	4.88	10.12
$C_{min,ss}$ (ng/mL)	0.81	1.54	1.25	2.48	5.01

In the 12-week Opioid Blockade Study (RB-US-13-0002), SUBLOCADE 300 mg completely blocked the drug-liking effects of low (6 mg) and high (18 mg) doses of hydromorphone, a potent opioid pain medication that is commonly used in human studies to evaluate opioid drug-liking. Wide variation was seen for individual patients. For comparison, stabilization doses of sublingual buprenorphine (8-24 mg daily) failed to provide full blockade of high dose (18 mg) hydromorphone[1].

SUBLOCADE was evaluated in a 24-week, Phase 3 pivotal study (RB-US-13-0001) in which patients were randomized to one of the following three regimens: six once-monthly SUBLOCADE 300 mg doses; two once-monthly SUBLOCADE 300 mg doses followed by four once-monthly 100 mg doses; or 6 once-monthly injections of placebo. All regimens received weekly individualized drug counseling (IDC). Both dosage regimens of SUBLOCADE were shown to be superior to placebo in achieving more illicit opioid-free weeks ($p<0.0001$)[1,6].

Percentage Opioid-Free Weeks[1]	Number (%) of Subjects		
	SUBLOCADE 300mg/100mg + IDC (N = 194)[1]	SUBLOCADE 300mg/300mg + IDC (N = 196)[1]	Placebo + IDC (N = 99)[1]
≥ 0%	194 (100.0)	196 (100.0)	99 (100.0)
≥ 10%	139 (71.6)	126 (64.3)	11 (11.1)
≥ 20%	115 (59.3)	111 (56.6)	7 (7.1)
≥ 30%	101 (52.1)	101 (51.5)	6 (6.1)
≥ 40%	90 (46.4)	90 (45.9)	6 (6.1)
≥ 50%	86 (44.3)	82 (41.8)	4 (4.0)
≥ 60%	78 (40.2)	70 (35.7)	4 (4.0)
≥ 70%	66 (34.0)	67 (34.2)	2 (2.0)
≥ 80%	55 (28.4)	57 (29.1)	2 (2.0)
≥ 90%	41 (21.1)	48 (24.5)	2 (2.0)
= 100%	25 (13)	23 (12)	1 (1.0)

Population PK/PD modeling indicated that patients using opioids by the injectable route at baseline may require higher buprenorphine exposure compared to patients not using opioids by the injectable route at baseline[1].

The overall safety profile of SUBLOCADE, given by a healthcare provider in clinical trials, was consistent with the known safety profile of transmucosal buprenorphine, except for injection site reactions. In the clinical trials, 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[1].

The Impact of the Opioid Addiction Epidemic

There is an urgent public health need for new treatment options for patients with OUD. An average of four people die of an opioid overdose every hour of every day[3].

Data published in 2016 presented the total costs of prescription opioid use disorder and overdose in the U.S. at $78 billion in 2013. Of that, only 3.6 percent, or about $2.8 billion, was for treatment[4]. A separate, recent analysis by the White House Council of Economic Advisers estimated the total annual cost of prescription opioid overdose, abuse and dependence in the U.S. at $504 billion in the year 2015[5].

SUBLOCADE Price

The wholesale acquisition cost (WAC) of SUBLOCADE in the U.S. will be $1,580 per monthly dose. The price for both the 100 mg and 300 mg doses of SUBLOCADE will be the same.

We want to help ensure our products are affordable to appropriate patients. We will be offering a SUBLOCADE co-pay assistance program, and also a SUBOXONE® (buprenorphine and naloxone) Sublingual Film co-pay assistance program, that may reduce initial out-of-pocket costs for eligible patients to as little as $5 each month.

When determining the price of SUBLOCADE, a number of factors were considered, including the value this new innovation delivers to patients with OUD, the significant new scientific evidence generated in the robust clinical development program, and the potential benefits to the healthcare system.

Indivior has an ongoing, prospective, observational study (RECOVER™) to understand the health economic value of the clinical, environmental and socioeconomic characteristics of OUD patients.

Indivior is committed to investing in new science and new technologies to treat the chronic relapsing diseases and co-occurring disorders of addiction. Future revenues from SUBLOCADE will enable Indivior to continue to invest in studies, building on current technologies and developing new treatment innovations.

We have designed, invested in and will implement a restricted distribution system that is intended to ensure SUBLOCADE is only dispensed directly to a healthcare provider for administration so that our product does not end up in a patient's hand.

SUBLOCADE is priced similar to other long-acting injectable medicines in the OUD and central nervous system disease area where adherence to treatment is a key objective.

SUBLOCADE Dosing and Administration

SUBLOCADE is available in dosage strengths of 100 mg/0.5 mL and 300 mg/1.5 mL buprenorphine. Each dose is provided in a prefilled syringe with a 19 gauge 5/8-inch needle. The recommended dose of SUBLOCADE following induction and dose adjustment with transmuscosal buprenorphine is 300 mg monthly for the first two months followed by a maintenance dose of 100 mg monthly. The maintenance dose may be increased to 300 mg monthly for patients who tolerate the 100 mg dose, but do not demonstrate a satisfactory clinical response, as evidenced by self-reported illicit opioid use or urine drug screens positive for illicit opioid use[1].

SUBLOCADE should only be prepared and administered by a healthcare provider. It should be administered monthly only by subcutaneous injection in the abdominal region. Each injection should be administered only using the syringe and safety needle included with the product[1].

Due to the chronic nature of OUD, the need for continuing medication-assisted treatment (MAT) should be re-evaluated periodically. There is no maximum recommended duration of maintenance treatment, and for some patients, treatment may continue indefinitely. If considering stopping treatment, healthcare providers should consider the clinical status of the patient.

Safety and Restricted Distribution

The overall safety profile of SUBLOCADE, given by a healthcare provider in clinical trials, was consistent with the known safety profile of transmucosal buprenorphine, except for injection site reactions. Common adverse reactions associated with buprenorphine included constipation, nausea, vomiting, abnormal liver enzymes, headache, sedation and somnolence. In the Phase 3 study, 16.5% of participants had at least one injection site reaction; none of these reactions were reported as serious and only one led to treatment discontinuation[1].

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[1].

SUBLOCADE will be distributed through a restricted distribution system, which is intended to prevent the direct distribution of the medication to a patient. Because of the risk of serious harm or death that could result from intravenous self-administration, SUBLOCADE will only be available through restricted distribution under the SUBLOCADE Risk Evaluation and Mitigation Strategy (REMS) Program. Pursuant to the SUBLOCADE REMS, all healthcare settings and pharmacies that order and dispense SUBLOCADE must be certified, and establish processes and procedures to verify the medication is dispensed directly to a healthcare provider for administration by a healthcare provider. Moreover, certified healthcare settings and pharmacies must not distribute, transfer, loan, or sell SUBLOCADE[1].

About SUBLOCADE™

INDICATION AND USAGE
SUBLOCADE contains buprenorphine, a partial opioid agonist, and is indicated for the treatment of moderate to severe opioid use disorder in patients who have initiated treatment with a transmucosal buprenorphine-containing product followed by a dose adjustment period for a minimum of seven days.

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

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.**

IMPORTANT SAFETY INFORMATION

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

CONTRAINDICATIONS

SUBLOCADE should not be administered to patients who have been shown to be hypersensitive to buprenorphine or any component of the ATRIGEL® 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.

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 of 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.

The full prescribing information, including BOXED WARNING, for SUBLOCADE can be found here: http://indivior.com/wp-content/uploads/2017/11/SUBLOCADE-Prescribing-Information.pdf.

About SUBOXONE® (BUPRENORPHINE AND NALOXONE) SUBLINGUAL FILM (CIII)

Indication

SUBOXONE® (buprenorphine and naloxone) Sublingual Film (CIII) is a prescription medicine indicated for treatment of opioid dependence and should be used as part of a complete treatment plan to include counseling and psychosocial support.

Treatment should be initiated under the direction of healthcare providers qualified under the Drug Addiction Treatment Act.

Important Safety Information

Do not take SUBOXONE Film if you are allergic to buprenorphine or naloxone as serious negative effects, including anaphylactic shock, have been reported.

SUBOXONE Film can be abused in a manner similar to other opioids, legal or illicit.

SUBOXONE Film contains buprenorphine, an opioid that can cause physical dependence with chronic use. Physical dependence is not the same as addiction. Your healthcare provider can tell you more about the difference between physical dependence and drug addiction. Do not stop taking SUBOXONE Film suddenly without talking to your healthcare provider. You could become sick with uncomfortable withdrawal symptoms because your body has become used to this medicine.

SUBOXONE Film can cause serious life-threatening breathing problems, overdose and death, particularly when taken by the intravenous (IV) route in combination with benzodiazepines or other medications that act on the nervous system (ie, sedatives, tranquilizers, or alcohol). It is extremely dangerous to take nonprescribed benzodiazepines or other medications that act on the nervous system while taking SUBOXONE Film.

You should not drink alcohol while taking SUBOXONE Film, as this can lead to loss of consciousness or even death.

Death has been reported in those who are not opioid dependent.

Your healthcare provider may monitor liver function before and during treatment.

SUBOXONE Film is not recommended in patients with severe hepatic impairment and may not be appropriate for patients with moderate hepatic impairment. However, SUBOXONE Film may be used with caution for maintenance treatment in patients with moderate hepatic impairment who have initiated treatment on a buprenorphine product without naloxone.

Keep SUBOXONE Film out of the sight and reach of children. Accidental or deliberate ingestion of SUBOXONE Film by a child can cause severe breathing problems and death.

Do not take SUBOXONE Film before the effects of other opioids (eg, heroin, hydrocodone, methadone, morphine, oxycodone) have subsided as you may experience withdrawal symptoms.

Injecting the SUBOXONE Film product may cause serious withdrawal symptoms such as pain, cramps, vomiting, diarrhea, anxiety, sleep problems, and cravings.

Before taking SUBOXONE Film, tell your healthcare provider if you are pregnant or plan to become pregnant. If you are pregnant, tell your healthcare provider as withdrawal signs and symptoms should be monitored closely and the dose adjusted as necessary. If you are pregnant or become pregnant while taking SUBOXONE Film, alert your healthcare provider immediately and you should report it using the contact information provided below. *

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

Neonatal opioid withdrawal syndrome (NOWS) is an expected and treatable outcome of prolonged use of opioids during pregnancy, whether that use is medically-authorized or illicit. Unlike opioid withdrawal syndrome in adults, NOWS may be life-threatening if not recognized and treated in the neonate. Healthcare professionals should observe newborns for signs of NOWS and manage accordingly.

Before taking SUBOXONE Film, talk to your healthcare provider if you are breastfeeding or plan to breastfeed your baby. The active ingredients of SUBOXONE Film can pass into your breast milk. You and your healthcare provider should consider the development and health benefits of breastfeeding along with your clinical need for SUBOXONE Film and should also consider any potential adverse effects on the breastfed child from the drug or from the underlying maternal condition.

Do not drive, operate heavy machinery, or perform any other dangerous activities until you know how SUBOXONE Film affects you. Buprenorphine in SUBOXONE Film can cause drowsiness and slow reaction times during dose-adjustment periods.

Common side effects of SUBOXONE Film include nausea, vomiting, drug withdrawal syndrome, headache, sweating, numb mouth, constipation, painful tongue, redness of the mouth, intoxication (feeling lightheaded or drunk), disturbance in attention, irregular heartbeat, decrease in sleep, blurred vision, back pain, fainting, dizziness, and sleepiness.

This is not a complete list of potential adverse events associated with SUBOXONE Film. Please see full Prescribing Information for a complete list.

*To report pregnancy or side effects associated with taking SUBOXONE Film, please call 1-877-782-6966. You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch or call 1-800-FDA-1088.

For more information about SUBOXONE Film, SUBOXONE® (buprenorphine and naloxone) Sublingual Tablets (CIII), or SUBUTEX® (buprenorphine) Sublingual Tablets (CIII), please see the respective full Prescribing Information and Medication Guide at www.suboxoneREMS.com.

References

1. SUBLOCADE™ label on file.
2. Nasser AF et al. (2016). Sustained-Release Buprenorphine (RBP-6000) Blocks the Effects of Opioid Challenge with Hydromorphone in Subjects with Opioid Use Disorder. J Clin Psychopharmacol. 36(1):18-26.
3. Centers for Disease Control and Prevention. Understanding the Epidemic. Retrieved from https://www.cdc.gov/drugoverdose/epidemic/index.html. Accessed October 28, 2017.
4. Florence CS et al. The Economic Burden of Prescription Opioid Overdose, Abuse, and Dependence in the United States, 2013. Medical Care. 54(10):901-906, Oct 2016. DOI: 10.1097/MLR.0000000000000625. PMID: 27623005.
5. White House Council of Economic Advisers. (2017). The Underestimated Cost of the Opioid Crisis. Retrieved from https://www.whitehouse.gov/sites/whitehouse.gov/files/images/The%20Underestimated%20Cost%20of%20the%20Opioid%20Crisis.pdf. Accessed November 20, 2017.
6. Indivior Data on File.

INDIVIOR
Focus on you.

Sublocade™
(buprenorphine extended-release)
injection for subcutaneous use
100mg·300mg