Summary

WHAT IS OPIOID USE DISORDER?

Opioid Use Disorder (OUD) is marked by a problematic pattern of opioid use that leads to clinically significant impairment or distress. In 2016, an estimated 2.1 million people suffered from OUD in the United States, and an average of 116 people in America died each day from opioid-related drug overdoses. Due to the possibility of patients relapsing back in the illicit use of opioids, OUD requires long-term treatment that focuses on recovery rather than a cure.

TREATMENT OPTIONS

OUD treatments include methadone, buprenorphine, and naltrexone. ICER's assessment focused on four extended-release variations, including a buprenorphine implant (Probuphine®, Titan), an extended-release naltrexone injection (Vivitrol®, Alkermes), and two extended-release buprenorphine injections: CAM2038 (Braeburn), an investigational agent currently under FDA review, and Sublocade™ (Indivior).

KEY REPORT FINDINGS

ICER's report found that the extended-release treatments for OUD resulted in only small clinical benefits compared to sublingual buprenorphine/naloxone, but at far higher costs. The report was the subject of a public meeting of the New England Comparative Effectiveness Public Advisory Council (New England CEPAC).

KEY POLICY RECOMMENDATIONS

- All stakeholders should strive to decrease the stigma around OUD and enhance awareness that it is a chronic disease that requires long-term treatment.
- Manufacturers should align the price of extended-release medications with their added benefits to patients, and once that is done, payers should eliminate barriers to access these treatments for OUD.
- Regulators and government policymakers should consider eliminating restrictions on prescribing extended-release treatments, and avoid legislative action favoring one OUD treatment over the others.

Clinical Analyses

ICER EVIDENCE RATINGS

How strong is the evidence that these extended-release treatments improve outcomes in patients with OUD?

✓	**CAM2038:** Evidence is still limited but provides moderate certainty of comparable or better clinical outcomes compared to buprenorphine/naloxone.
?	**Sublocade:** No judgment can be made because clinical trials have not directly compared it to buprenorphine/naloxone.
?	**Probuphine:** Evidence of improved outcomes compared to buprenorphine/naloxone is promising but inconclusive because the clinical trial population may not reflect the general population being considered for use of this treatment.
↔	**Vivitrol:** Produces outcomes equivalent to those associated with buprenorphine/naloxone.

HARMS

For all treatments, rates of serious adverse events were generally low and similar to those experienced with buprenorphine/naloxone and placebo. The most common adverse events reported in the trials were injection/implant site pain, gastrointestinal issues, headaches, and insomnia.

SOURCES OF UNCERTAINTY

Lack of Comparisons Among Treatments: Differences in trial designs, population selection, and outcomes precluded formal comparisons among the four extended-release treatments for OUD.

Trial Population: Patients with psychiatric comorbidities were generally excluded from the trials despite the high prevalence among patients with OUD.

Outcomes: There is uncertainty regarding what rate of opioid-free urine samples constitutes a meaningful measure of success.

Economic Analyses

LONG-TERM COST-EFFECTIVENESS

Do these treatments meet established thresholds for long-term cost-effectiveness?

NO

Extended-release treatments for OUD resulted in at most small clinical benefits compared to sublingual buprenorphine/naloxone, but at substantially higher costs. Therefore, at current prices, **these treatments exceed the commonly cited thresholds for cost-effectiveness** of $50,000–$150,000 per quality-adjusted life year gained.

VALUE-BASED PRICE BENCHMARKS

What is a fair price for these treatments based on their value to patients and the health care system?

	Current List Price	Price to Achieve $100,000–$150,000 per QALY threshold	Discount Required to Reach the Value-Based Price
CAM2038	Not yet available	$4,100–$5,300 per year	-
Probuphine	$4,950 per six-month implant	$1,700–$2,300 per six-month implant	53% to 65% off list price

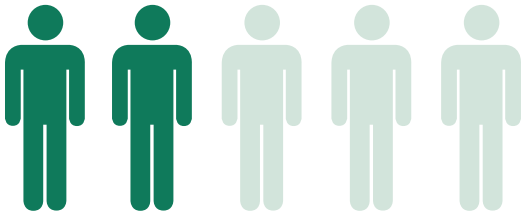
- While there is no announced price yet for **CAM2038**, ICER calculated the treatment's value-based price benchmark range to be between $4,100 and $5,300 per year.
- Even assuming a small clinical benefit with **Probuphine**, its current list price would need to be discounted by 53%–65% to reach ICER's value-based price benchmark range.
- **Vivitrol's** value-based price is equivalent to the price for buprenorphine/naloxone — which would require Vivitrol's list price to be discounted by 69% — since Vivitrol was assessed as producing equivalent outcomes.
- ICER did not calculate a value-based price for **Sublocade** because the evidence was viewed as insufficient to compare it to buprenorphine/naloxone.

Economic Analyses (continued)

POTENTIAL SHORT-TERM BUDGET IMPACT

How many patients can be treated with CAM2038 before crossing ICER's $991 million budget impact threshold?

Although an annual value-based price range of $4,100-$5,300 for CAM2038 would align with commonly cited thresholds for long-term cost-effectiveness, **only up to 40% of the eligible population in the US could be treated each year** before exceeding ICER's budget impact threshold of $991 million.



The short-term budget impact was only calculated for CAM2038 because the other treatments are already approved and available.

Voting Results

The New England CEPAC deliberated on key questions raised by ICER's report at a public meeting on November 8, 2018. The results of the votes are presented below. More detail on the voting results is provided in the full report.

CLINICAL EVIDENCE

A majority of the panel found that the evidence was not adequate to demonstrate that any of the extended-release treatments provides superior net health benefit over buprenorphine/naloxone, nor was the evidence adequate to distinguish between the four extended-release treatments.

LONG-TERM VALUE FOR MONEY

Consistent with ICER's value assessment framework, because the incremental cost-effectiveness ratios for Probuphine, Sublocade, and Vivotrol all exceed $175,000 per QALY, these three interventions were each deemed "low value" without a formal vote from the panel.

Because no price was available for the yet-to-be approved CAM2038, an incremental cost-effectiveness ratio could not be calculated and therefore a value vote was not taken.

OTHER BENEFITS AND CONTEXTUAL CONSIDERATIONS

During their deliberation, panel members weighed the therapies' other benefits and contextual considerations. The panel expressed concern that opioid use disorder can be particularly severe and can represent a high lifetime burden of illness. The panel underscored how the reduced complexity of CAM2038, Sublocade, and Vivitrol may allow the successful treatment of many patients for whom other available treatments have failed, significantly improving patient outcomes. The panel also noted that less frequent dosing schedules and doctors' visits could lead to improved patient privacy and reduced stigma.

On the other hand, the panel emphasized the significant uncertainty about the magnitude and durability of long-term benefits for CAM2038, Sublocade, and Vivitrol.

Policy Recommendations

The New England CEPAC Panel participated in a moderated policy discussion that included physicians, patient advocates, manufacturer representatives, and payer representatives. None of the resulting policy statements should be taken as a consensus view held by all participants. For a more detailed discussion, please see the full report.

FOR ALL STAKEHOLDERS

- Decrease stigma by aligning efforts around education that enhances awareness that OUD is a chronic disease requiring long-term treatment.

FOR MANUFACTURERS

- Align the price of extended-release medications with their clinical value.

FOR PAYERS

- If prices are aligned with clinical value, create coverage criteria that present no barriers to access. In particular, prior authorization criteria for Sublocade and similar extended-release treatments should be flexible enough to support evidence-based individualized treatment decisions.

FOR REGULATORS AND GOVERNMENT POLICYMAKERS

- Consider eliminating restrictions on prescribing extended-release formulations of buprenorphine.
- Avoid legislative action favoring one extended-release treatment for OUD.
- Coordinate treatment for individuals leaving the correctional system and ensure continuity of care.

FOR RESEARCHERS

- Work with clinicians and manufacturers to identify clinical characteristics that would better predict which patients would benefit most from each approach to treat OUD.

About ICER

The Institute for Clinical and Economic Review (ICER) is an independent nonprofit research institute that produces reports analyzing the evidence on the effectiveness and value of drugs and other medical services. ICER's reports include evidence-based calculations of prices for new drugs that accurately reflect the degree of improvement expected in long-term patient outcomes, while also highlighting price levels that might contribute to unaffordable short-term cost growth for the overall health care system.

ICER's reports incorporate extensive input from all stakeholders and are the subject of public hearings through three core programs: the California Technology Assessment Forum (CTAF), the Midwest Comparative Effectiveness Public Advisory Council (Midwest CEPAC) and the New England Comparative Effectiveness Public Advisory Council (New England CEPAC). These independent panels review ICER's reports at public meetings to deliberate on the evidence and develop recommendations for how patients, clinicians, insurers, and policymakers can improve the quality and value of health care. For more information about ICER, please visit ICER's website (www.icer-review.org).