REPORT AT A GLANCE: **ACUTE PAIN**

KEY FINDINGS

Intervention	Comparators	Evidence Rating	US Price	Health-Benefit Price Benchmark
suzetrigine (Journavx™, Vertex Pharmaceuticals)	• No systemic treatment • Opioid analgesics • Non-steroidal anti-inflammatory drugs (NSAIDs)	**"P/I"** promising but inconclusive for all comparators	$232.50 for a one-week course	ICER expects the treatment to be cost-saving from a lifetime perspective because of cost offsets due to fewer patients developing opioid use disorder (OUD).

"It has been a long time since we have had a new class of drugs for acute pain. Suzetrigine has a different mechanism of action from prior oral therapies, and this creates options for treatment alone or in combination with existing medications. The overall value of this new drug is linked to the risk of a one-week course of opioids leading to opioid use disorder. If the risk is not zero and suzetrigine proves to be safe, we believe that suzetrigine will likely be a cost-effective, and perhaps a cost-saving, alternative from a long-term perspective. However, we note the skepticism about the evidence base from members of the Midwest CEPAC. Longer term data will help define the appropriate role of suzetrigine in practice, but a pain medicine with a new mechanism of action will create options for patients and clinicians."

– ICER's Chief Medical Officer David Rind, MD

THEMES AND RECOMMENDATIONS

- All stakeholders have a responsibility and an important role to play in ensuring that all patients with acute pain are treated appropriately and equitably. ICER repeatedly heard from multiple stakeholders about inadequate management of acute pain in Black Americans, as well as evidence that this inadequate management may be tied to both implicit and explicit bias.
- Manufacturers should set prices that are aligned with net benefit. Vertex deserves recognition for appropriately pricing suzetrigine. However, the manufacturer should also conduct additional research on suzetrigine to answer open questions.
- Clinicians and clinical societies should advocate for broader patient access to multimodal pain management.

Clinical Analyses

KEY CLINICAL BENEFITS STUDIED IN CLINICAL TRIALS

Acute pain is ubiquitous though it frequently does not require specific treatment. A retrospective cross-sectional study using two nationally representative datasets from 2019 estimated that 80.2 million patients in the US annually experience pain requiring prescription medication treatment for less than three months.

In the postoperative setting, many patients are treated with opioid analgesics to manage their pain. Opioids can have important side effects including sedation, respiratory depression, confusion, falls, and constipation, but a primary concern with opioid prescriptions for acute pain is the risk of developing persistent opioid use and/or opioid use disorder (OUD). This risk is uncertain and can vary widely, in part based on the definition used and underlying patient and medication risk factors. It is estimated that approximately 108,000 people in the US died from opioid overdoses in 2022 and that nearly 15,000 of those deaths involved prescription opioids. An analysis from 2017 found that annual health care costs from OUD were nearly $35 billion, criminal justice costs (including lost productivity of those incarcerated) were $23 billion, and other lost productivity was more than $92 billion.

Given concerns about opioids, safer analgesic medications could be beneficial. Generally, however, nearly all other systemic analgesics used for acute pain are either nonsteroidal anti-inflammatory drugs (NSAIDs) or acetaminophen, and use of more than one pain medication to allow for greater analgesia with fewer side effects is typically recommended. Suzetrigine (Journavx®; Vertex Pharmaceuticals) is an oral small-molecule inhibitor of the voltage-gated sodium channel $Na_v1.8$ that has been studied for the treatment of acute post-surgical pain and represents a new class of analgesic medication. The drug is administered every 12 hours. Suzetrigine was approved by the Food and Drug Administration (FDA) on January 30, 2025.

In this report, we assess suzetrigine as a treatment for moderate-to-severe acute pain. Suzetrigine is also being studied for chronic pain but, while that may be a later indication for the drug, it is currently only approved by the FDA for acute pain and, as such, this report focuses only on that indication. The evidence for suzetrigine comes primarily from two similar Phase III randomized trials comparing it to placebo and to the opioid hydrocodone 5 mg in combination with acetaminophen 325 mg (HB5/APAP325; often known by the trade name, “Vicodin”); one trial included patients after bunionectomy and the other after abdominoplasty. Across the two trials, 873 patients received suzetrigine, 879 patients received HB5/APAP325, and 439 patients received placebo. Patients treated with suzetrigine had greater and faster reductions in pain than those treated with placebo. Suzetrigine appeared to have similar efficacy to HB5/APAP325 for abdominoplasty, but slower onset of clinically meaningful pain relief for bunionectomy. Adverse effects of suzetrigine were similar to placebo and nausea appeared less common than with HB5/APAP325.

We also conducted a network meta-analysis to compare suzetrigine to higher-dose oral opioids and to NSAIDs, both with or without acetaminophen. This was done in part because opioid dosing in pivotal trials (1 tablet every 6 hours) was lower than is typically prescribed post-surgery. Confidence intervals were widely overlapping, making it hard to come to definite conclusions about relative efficacy. Rates of development of OUD after short-term administration of opioids for acute pain are also uncertain, as are rates of NSAID adverse effects (e.g., acute kidney

Clinical Analyses

injury, gastrointestinal bleeding, acute coronary syndrome) when used in the post-operative setting.

We have some uncertainties that are inherent when pain scores are imputed after rescue medication. We note, however, that the FDA's review of the imputation methods via sensitivity analyses yielded results that were similar to the primary analysis of the pivotal trials. Additionally, as noted above, the dosing of HB/APAP used in the clinical trials was lower and less frequent than many patients would be treated with postoperatively. We have concerns about as-yet-unknown harms of suzetrigine as we would for any drug with a new mechanism of action; we are particularly concerned about possible acute renal injury given the results of a study in people with diabetes, and have some concerns as to whether there could be an increased risk for cardiac arrhythmias given inhibition of $Na_v1.8$.

The above uncertainties inform our ratings that the evidence for suzetrigine for the treatment of acute pain in comparison with no systemic treatment, in comparison with opioid analgesics, and in comparison with NSAIDs are all promising but inconclusive (P/I). Our reasoning for these ratings differs for each comparison and is discussed in detail in Section 3.3 of the Final Evidence Report along with consideration of which patients might be more appropriate for early treatment with suzetrigine. As safety data become available with real world use, assessment of net benefit is likely to change.

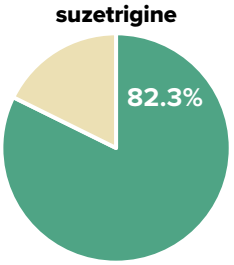
Economic Analyses

LONG-TERM COST EFFECTIVENESS

We conducted an economic analysis that modeled the long-term cost-effectiveness of one week of treatment with suzetrigine compared with HB5/APAP325 using a wholesale acquisition cost (WAC) for suzetrigine of $15.50 per tablet or $232.50 for a one-week course. The model was primarily driven by risks of OUD from this short course of an opioid analgesic. Due to the lifetime costs and harms of OUD, and assuming a wide range of estimates of OUD risk, treating with suzetrigine would be slightly cost-saving relative to opioid therapy while producing greater health benefits ("dominant"). We estimate that suzetrigine, at its WAC price, would meet commonly used cost-effectiveness thresholds if a one-week course of treatment with opioids results in an excess of at least two in 10,000 cases of OUD over the subsequent three years.

POTENTIAL BUDGET IMPACT

Assuming a 20% uptake of suzetrigine each year, 82.3% of patients could be treated over five years at the WAC price before reaching the ICER potential budget impact threshold of $735 million per year.



Percent of eligible patients with acute pain that could be treated in a given year before crossing the ICER potential budget impact threshold

Public Meeting Deliberations

VOTING RESULTS

ICER's Virtual Public Meeting: Voting Results on Clinical Effectiveness and Contextual Considerations

ICER assessed, and the independent appraisal committee voted on the evidence for the net health benefit of suzetrigine in adults with acute pain not adequately controlled with non-systemic therapies:

- Half of the panelists (7-7) found that current evidence is **adequate** to demonstrate a net health benefit of suzetrigine plus non-systemic therapies in comparison to non-systemic therapies alone.
- The majority of panelists (12-2) found that current evidence is **not adequate** to demonstrate a net health benefit of suzetrigine plus non-systemic therapies in comparison to oral opioid analgesics plus non-systemic therapies.
- The panelists unanimously (14-0) found that current evidence is **not adequate** to demonstrate a net health benefit of suzetrigine plus non-systemic therapies when compared to oral NSAIDs plus non-systemic therapies. Appraisal committee members cited the lack of evidence comparing suzetrigine to NSAIDs, and the mixed results of the Phase III trials when explaining their votes.

Panel members also weighed potential benefits and disadvantages beyond the direct health effects and weighed special ethical priorities. Voting highlighted the following as particularly important for payers and other policymakers to note:

- There is substantial unmet need despite currently available treatments.
- This condition is of substantial relevance for people from a racial/ethnic group that have not been equitably served by the healthcare system.

ICER's Virtual Public Meeting: Voting Results on Long-Term Value for Money

The FDA approved suzetrigine for acute pain on January 30, 2025. The manufacturer announced a US price of approximately $232.50 for a one-week course of treatment for acute pain.

After reviewing the clinical evidence and considering the treatments' other potential benefits, disadvantages, and contextual considerations noted above, the Midwest CEPAC evaluated the long-term value of suzetrigine at its current pricing:

- Nine panelists found that suzetrigine at its current pricing represents "**intermediate**" long-term value for money, with one panelist voting "**high**" long-term value for money. Four panelists found that suzetrigine represents "**low**" long-term value for money, citing the lack of long-term data on safety and mixed results of the Phase III trial .

About ICER

The Institute for Clinical and Economic Review (ICER) is an independent, non-profit research institute that conducts evidence-based reviews of health care interventions, including prescription drugs, other treatments, and diagnostic tests. In collaboration with patients, clinical experts, and other key stakeholders, ICER analyzes the available evidence on the benefits and risks of these interventions to measure their value and suggest fair prices. ICER also regularly reports on the barriers to care for patients and recommends solutions to ensure fair access to prescription drugs. For more information about ICER, please visit www.icer.org.