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January 13, 2025

Sarah K. Emond, MPP
President
Institute for Clinical and Economic Review
14 Beacon Street, Suite 800
Boston, MA 02108

Re: Vertex Pharmaceuticals public comments on the ICER draft evidence report concerning its investigational treatment suzetrigine for moderate-to-severe acute pain

Vertex Pharmaceuticals Incorporated appreciates the opportunity to respond to the Draft Evidence Report for the ICER evaluation of suzetrigine, its investigational, oral, selective $Na_V1.8$ pain signal inhibitor for the treatment of moderate-to-severe acute pain.

There is significant unmet need for safe and effective medicines for the treatment of moderate-to-severe acute pain. The current treatment of acute pain generally consists of nonsteroidal anti-inflammatory drugs (NSAIDs) and acetaminophen, which have limited efficacy in moderate-to-severe pain, and opioids, which are effective for moderate-to-severe pain but have tolerability concerns and carry the risk of addiction. Specifically, opioids stimulate the reward pathway in the brain which can lead to misuse, addiction, and opioid use disorder (OUD).[1]

We are encouraged that the draft evidence report reflects the importance of suzetrigine as a new option for pain treatment that has the potential to reduce opioid use and the negative downstream consequences. We would like to share some clarifications and additional considerations.

Phase 3 studies have demonstrated that suzetrigine is an effective treatment for moderate-to-severe acute pain based on the efficacy data with and without rescue imputation.

ICER has stated they have uncertainty in assessing the efficacy of suzetrigine due to the absence of public data on the use of rescue medication in the Phase 3 trials and has asked for clarity on how pain scores were imputed after rescue medication use.

Suzetrigine was studied as a monotherapy with the use of rescue medications in two randomized, double-blind, placebo-controlled, pivotal Phase 3 trials, one after an abdominoplasty surgery (N=1,118) and one after a bunionectomy surgery (N=1,073).[2] In both Phase 3 randomized, controlled trials, ibuprofen was permitted as rescue medication, if needed, as is conventional in trials of acute pain with an opioid comparator. To assess the efficacy of suzetrigine as a monotherapy, the pre-specified study analyses utilized an immediate pre-rescue ibuprofen Numeric Pain Rating Scale (NPRS) score to replace (impute) NPRS scores for 6 hours after rescue. An additional ad hoc analysis without imputation of NPRS scores after ibuprofen rescue was conducted to assess the efficacy of suzetrigine plus ibuprofen (if used) compared to placebo plus ibuprofen (if used). This ad-hoc analysis was presented at the most recent American Society of Anesthesiologists (ASA) meeting in October 2024.

Suzetrigine showed statistically significant superior efficacy as a monotherapy and when used with ibuprofen as rescue in pain reduction compared to placebo as measured by the time-weighted sum of the pain intensity difference as recorded on the NPRS from 0 to 48 hours (SPID48) in both the abdominoplasty and bunionectomy trials.[2] Suzetrigine had a more rapid onset of clinically meaningful pain relief (defined as ≥2-point reduction in NPRS from baseline) compared to placebo in both the abdominoplasty and bunionectomy trials. While suzetrigine was not superior to hydrocodone bitartrate/acetaminophen (HB/APAP) in both trials, efficacy outcomes of SPID48 and time to meaningful pain relief were comparable to HB/APAP. ICER mentioned the time to 2-point reduction in NPRS as the "time to onset" for suzetrigine, however we note that this is the time to "clinically meaningful pain relief". The time to first perceptible pain relief is instead the time to 1-point reduction in NPRS from baseline which represents the "minimum clinically important difference".[3, 4]

ICER has also suggested there is uncertainty in suzetrigine's safety profile due to the novel mechanism of action. Suzetrigine is a potent and selective inhibitor of $Na_V1.8$ (≥31,000 fold selective over all other Na_V subtypes).[5-7] $Na_V1.8$ is selectively expressed in nociceptive neurons within the peripheral nervous system and has a critical role in transmitting nociceptive signals along peripheral sensory nerves. By selectively inhibiting $Na_V1.8$ channels, suzetrigine inhibits transmission of nociceptive signals to the spinal cord and brain, thus inhibiting pain signals in the peripheral nervous system. Suzetrigine selectively inhibits $Na_V1.8$ without off-target effects on other Na_Vs expressed in the body, including in other organs. Cardiac events due to the inhibition of $Na_V1.8$ are unlikely given $Na_V1.8$ is not normally expressed in the heart.[8] No drug-related cardiac safety events with suzetrigine were observed in the acute pain studies or in the Phase 2 study in diabetic peripheral neuropathy in which patients were treated for 12 weeks.[2, 9, 10] Additionally, since there is no $Na_V1.8$ expression in the human brain and suzetrigine is highly selective for the $Na_V1.8$ channel, there is no evidence of addictive potential or dependence with suzetrigine based on this mechanism of action, combined with nonclinical and clinical safety assessments.[7]

The results from multiple studies in acute and chronic pain with suzetrigine support the safety profile. In particular, in the acute pain Phase 3 studies of abdominoplasty and bunionectomy, suzetrigine led to lower overall incidence of adverse events than placebo or HB/APAP. Notably, those in the suzetrigine arm had lower incidence of vomiting and nausea than those in the HB/APAP arm, which is of particular importance given these adverse events are a common concern with opioid use.

Overall, suzetrigine has shown a compelling combination of efficacy and safety in its Phase 3 studies. The results from the Phase 3 studies demonstrate that suzetrigine is superior to placebo and similar in efficacy compared to HB/APAP, with a favorable safety profile and no evidence for addiction or abuse potential, for the treatment of adults with moderate-to-severe acute pain.

Clarification that HB/APAP is the most frequently used opioid, with the 5 mg/ 325 mg dosage being the most commonly prescribed for acute pain in the United States.

Dosing of HB/APAP was consistent with the CDC Clinical Practice Guidelines for prescribing opioids for pain (i.e., immediate-release opioid, lowest effective dose). A retrospective cross-sectional study using two robust, nationally representative datasets showed that among the 41

million people receiving opioids for acute pain in the United States, HB/APAP 5/325mg is the most frequently used dosage, making this the most relevant opioid comparator in clinical trials.[11]

Both the short-term adverse effects associated with opioid use and the broader impact of opioid misuse on society are important considerations for the evaluation of any therapy that may reduce the use of opioids.

We are encouraged that ICER has incorporated the impact of OUD in this review and reinforce that short-term opioid prescriptions carry significant risks. Numerous studies have quantified the risk of opioid misuse and OUD due to prescription opioids for the management of acute pain, as well as the increased risk of illicit drug use.[12-15] A systematic review of new persistent opioid use found that 8.3% of opioid naive individuals who received opioids for the management of post-surgical acute pain develop persistent opioid use. A study conducted by the CDC found that as few as 2 days of opioids can increase the risk of long-term opioid use, with the risk rising rapidly over the course of one week.[16] A recent analysis of a large US claims database estimated the 1-, 2-, and 3-year incidence rate of diagnosed OUD among opioid naive patients exposed to prescription opioids for acute pain management at 0.21%, 0.32%, and 0.43%, respectively.[12] The average duration of the initial opioid prescription in this study was 5-days, highlighting that short-term opioid use for acute pain carries substantial risk of OUD.[11]

While the impact of OUD has been incorporated in this review, we believe that the shorter-term adverse effects from opioid use should also be considered. Opioid-related adverse events (ORADEs) are a common short-term complication associated with the use of opioids and have been associated with worse patient outcomes.[17-19] Patients with ORADEs in the hospital setting experience higher odds of inpatient mortality and 30-day readmission, prolonged length of stay, and increased cost of hospitalization.[17] Nausea and vomiting are common ORADEs and are significant factors in complications such as pulmonary aspiration, dehydration, and electrolyte imbalance.[20] Patients prescribed opioids who have nausea or vomiting claims had significantly more hospitalizations, emergency department visits, and physician office visits, amounting to 2.7 times higher adjusted 30-day healthcare costs relative to patients prescribed opioids who did not have nausea or vomiting claims.[18] The inclusion of these known side effects of opioids is important for the economic evaluation of any therapy with the potential to reduce the use of opioids and particularly in calculations of potential budget impact.

ICER's review considered some societal costs associated with OUD, however we believe that it is important to consider the totality of societal costs of the opioid epidemic. The total economic burden of the opioid epidemic in the United States in 2018 was estimated by the Society of Actuaries to be approximately $160 billion, of which approximately 38% ($60 billion) was attributed to healthcare costs.[21] The remaining 62% ($100 billion) were costs associated with mortality (lost lifetime earnings), criminal justice, child and family assistance, education, and lost productivity, highlighting the societal burden of the opioid epidemic. Other studies have estimated the economic toll of the opioid crisis to be over a trillion dollars.[22, 23] Given the substantial societal burden relative to direct healthcare costs of opioids, it is important to consider the impact of opioids on not only patient productivity losses and criminal justice costs, but also costs associated with lost lifetime earnings due to mortality, child and family assistance, and education. Even if not included in the formal economic analysis, this context is a critical component to the potential impact of a non-opioid alternative treatment option for moderate-to-severe acute pain.

Thank you for the opportunity to comment on ICER's draft evidence report.

Sincerely,

Jaime Rubin Cahill, MA, MPH
Head of Health Economics and Outcomes Research
Vertex Pharmaceuticals Incorporated

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Recovery Mobile Clinic
REDEEM. MOTIVATE. COMMIT.

January 13, 2025

Sarah K. Emond, MPP President and Chief Executive Officer Institute for Clinical and Economic Review

Dear Ms. Emond:

I appreciate the opportunity to comment on the Draft Evidence Review on the treatment of acute pain as posted on December 9, 2024. As a Nurse Practitioner who was formerly involved in integrative pain management and the current President and Founder of the Recovery Mobile Clinic, a mobile clinic to treat addiction, I know well the challenges of opioid addiction and the potential pitfalls of prescription opioids. As a result, the development of novel therapies used to treat pain and reduce our overreliance on prescription opioids offers tremendous opportunity to improve the delivery of healthcare in the United States, prevent opioid addiction occurring post surgically, and save lives.

My name is Jordana Latozas, and I currently serve as the President and Founder of the Recovery Mobile Clinic based in Michigan. As a healthcare provider who saw that transportation barriers often affected my patients' ability to maintain sobriety and treatment of substance use disorders and mental health, so I launched the Recovery Mobile Clinic in 2020. The clinic has grown to over 34 weekly clinics in southeast Michigan, treating around 500 patients a week. Prior to this, I was an acute care nurse practitioner with 15 years of experience providing postsurgical analgesic support to patients. Frequently, this involved giving patients prescription opioids to manage their pain.

Occasionally, despite my intentions to treat patients with non-addictive approaches, I was unable to do so because of structural preferences for using prescription opioids. In the United States, this happens frequently as opioids remain today the status quo in treating acute pain patients. Prescription opioids continue to be the standard of care for a variety of reasons, including:

· Institutional familiarity with narcotic-based pain approaches;

· Lack of awareness among practitioners and patients of non-addictive approaches;

· Payer preferences for lowest cost treatment options (i.e. generic prescription opioids); and

· Inadequate incentives for using non-addictive approaches.

This paradigm has undoubtedly contributed to the current state of the opioid epidemic in the United States where:

· 200 Americans die every day from an opioid related drug overdose: a 74 percent increase in just 6 years;

· 90 percent of acute pain patients receive opioids to manage their pain;

· Millions of patients become newly dependent opioid users every year after being prescribed an opioid to manage their pain; and

· 125 million opioid prescriptions are dispensed annually.

For some, opioid prescribing can have dangerous repercussions. Research shows that approximately 10 percent of patients who are prescribed an opioid to manage their acute pain will continue to take opioids months after their acute pain incident. A subset of these patients will develop an opioid use

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disorder and, when they are no longer able to obtain their pills through the healthcare system, will turn to the streets for other, illegal forms of opioids. Some of these patients will overdose. And some will die.

I see this every day in my clinics.

As a healthcare professional, I know that one way to change this paradigm is to fundamentally change the way that we treat pain in the United States and to reduce our reliance on prescription opioids to manage pain. To do that, healthcare professionals need more tools at our disposal. Currently, non-opioid pain options include nerve blocks, use of non-steroidal anti-inflammatory drugs (NSAIDs), acetaminophen, and other off-label products. Nerve blocks, in particular, are difficult as they are administered by a healthcare professional rather than self-administered by a patient in the same manner that opioids or NSAIDs are.

I understand that there are a variety of products in development that offer promise and the opportunity to treat acute pain without the need for prescription opioids. To the extent these products are approved by the Food and Drug Administration (FDA) and deemed safe and effective, they would become useful tools in our fight to improve pain care in the country and in preventing opioid misuse occurring after surgery.

I am excited by the prospects of these products become part of our healthcare lexicon and arming healthcare professionals with new, potentially impactful tools in helping patients after surgery. Such products would provide a meaningful tool in an opioid addiction prevention strategy and they are badly needed.

I look forward to a day when I see fewer patients in my clinics who initiated an opioid use habit after being prescribed an opioid. Before we get there, we need to improve the way that we treat pain and we need to arm healthcare professionals with the tools they need. If approved, these non-addictive products could bridge that gap and reduce rates of postsurgical opioid use, misuse, dependence, and addiction.

It is potentially a very exciting time in the fight against the opioid epidemic.

Thank you so much for your consideration of these comments.

Sincerely,

Jordana Latozas RN, ACNP, President/Founder

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TO: Institute for Clinical and Economic Review

FROM: Stephen Thomas, PhD
Professor of Health Policy and Management and Dir., Center for Health Equity
University of Maryland
College Park, Md

DATE: January 2, 2025

RE: Public Comment Letter

I am writing in response to the recent draft evidence report regarding acute pain treatment. I appreciate the opportunity to provide comments and contribute to the conversation about advancing equitable, evidence-based healthcare solutions.

As a Professor of Health Policy and Management and Director of the Center for Health Equity at the University of Maryland, my research emphasizes evidence-based science integrated with an understanding of how social contexts shape attitudes and behaviors, particularly among underserved, poorly served, and never-served communities. Recognizing the profound inequities in health outcomes, I developed the **Health Advocates In-Reach and Research (HAIR)** program. This initiative transforms barbershops and beauty salons—trusted spaces in African American communities—into hubs for health education and public health services.

Through my work with the HAIR program, I have witnessed firsthand how systemic health disparities exacerbate the devastating effects of the opioid epidemic in minority communities. The epidemic's uneven impact is alarming. For instance, the Centers for Disease Control and Prevention reported a 44% increase in opioid-related deaths among Black Americans in 2022. Furthermore, a recent analysis by KFF highlights persistent inequities in opioid overdose rates, which remain disproportionately high in Black communities, even as overdose rates decline in other groups.

While opioids have their place in acute pain management, it is imperative to expand access to effective non-opioid alternatives. Preventing addiction before it starts by promoting non-addictive, evidence-based treatments should be a national priority. Current disparities in healthcare access only magnify the need to make non-opioid options available, particularly in communities that bear the brunt of the opioid epidemic.

The development and approval of novel, non-opioid pain management drugs represent an opportunity to close the gap between the treatments of the past and the innovations of tomorrow. By prioritizing equity and accessibility, we can address the root causes of the opioid crisis and create a healthcare system that serves everyone.

It is never too late to act. By encouraging the adoption of non-addictive treatments, we can take a decisive step toward ending the opioid epidemic and fostering a healthier future for all communities.

Thank you for your attention to this critical issue, and I welcome the opportunity to engage further in advancing equitable, evidence-based solutions.

January 13, 2025

Sarah K. Emond, MPP
President and Chief Executive Officer
Institute for Clinical and Economic Review

Dear Ms. Emond:

Thank you for the opportunity to comment on the Draft Evidence Review on the treatment of acute pain as posted on December 9, 2024. I am excited at the prospects of novel therapeutics coming to market for the treatment of acute pain which could significantly obviate the need for prescription opioids.

My name is Sterling Elliott, and I am a seasoned institutional pharmacist by training. My specific expertise is in the area of surgery and teaching patients to effectively manage postsurgical pain with a specific emphasis on functional recovery. In my practice, I aim to help patients reduce their reliance on opioids for postsurgical analgesic support. My work is done in close partnership with Northwestern University's Department of Orthopaedic Surgery where I serve as an Assistant Professor of Orthopaedic Surgery at the Feinberg School of Medicine.

As a general rule, patients today receive opioids to manage postsurgical pain. This is just as true today as it was 20 years ago. According to the latest data from the Centers for Disease Control and Prevention, there were 125 million opioid prescriptions dispensed last year in the United States. This represents a nearly 50 percent decrease in just over a decade. However, 90 percent of acute pain patients continue to receive opioids.

Opioid overprescribing carries other significant challenges, including the opportunity for unused pills to be diverted in the community. Some estimates show that as many as 80 percent of patients report having leftover prescription opioid pills after surgery. These pills frequently sit in medicine cabinets where they are available for diversion in our communities. As a result, the Substance Abuse and Mental Health Services Administration estimates that more than half of Americans who misuse prescription opioids do not have a prescription. Instead, these individuals obtain these pills from family, a friend, or on the secondary market.

A minority of these patients will continue to take prescription opioids months after their acute pain incident. This occurs in approximately 10 percent of patients who are prescribed opioids after surgery, though it is more prevalent among previously opioid-naïve patient populations.

As a clinician, I know that my options for treating postsurgical pain are limited. Typically, non-opioid pain management typically consists of utilizing a combination of non-steroidal anti-inflammatory drugs (NSAIDs) in combination with acetaminophen and some off-label products. Accordingly, the prospects of novel therapeutics used to provide postsurgical analgesic support without the risk potential of traditional, generic prescription opioids is very enticing – particularly given my clinical focus.

Across the country, when it comes to treating acute pain, clinicians are being told to do more with less. State opioid prescribing limitations make treating acute pain patients harder. Clinicians are limited in what – and how much – they are able to prescribe a patient. At a time when we continue to lose 200 Americans every day to an opioid-related drug overdose, such efforts to reign in prescribing make sense. However, as a clinician, we need more tools at our disposal.

Novel therapies that are FDA-approved and that carry an indication for providing postsurgical analgesic support can fill this void and provide clinicians with important new tools in treating patients. Such therapies offer clinicians the opportunity to further reduce opioid prescribing practices. In the process, such therapies offer the opportunity to reduce postsurgical opioid misuse across the country, reduce community diversion of narcotic pills, and save lives.

Such a class of products would fill both a clinical and patient need. This is especially true now when patients are increasingly aware of the risks of prescription opioids.

Thank you for your consideration of these comments. I look forward to your final report.

Sincerely,

Sterling Elliott, PharmD, BCMTMS

ACPA:

The American Chronic Pain Association (ACPA) is a non-profit, 501(c) (3) organization. Our Mission is to facilitate peer support, education, hope, and motivation for individuals living with pain and those treating pain conditions. We strive to raise awareness among the health care community, policymakers, and the public at large about issues of living with physical and emotional pain. Our vision is to motivate those with pain conditions to seek quality care, to optimize healthcare office visits, and to prevent chronic disease.

The ACPA supports companies that are patient focused and dedicated to research that brings safer drugs to people living with pain. While opioids have a place for some patients with severe pain, exploring novel mechanisms that provide safer and more effective pain management beyond opioids is needed. Studies have shown that nonopioid therapies can provide effective pain management with significantly lower risks of addiction and overdose compared to opioids. We respect and support Vertex's dedication to developing safe and effective pain therapies, while also helping to combat the opioid crisis.

CAREGIVER ACTION NETWORK CAN

caregiveractionnetwork.org

As the President and CEO of the Caregiver Action Network (CAN), the nation's leading family caregiver organization, I am increasingly concerned about the impacts of the opioid epidemic, not just on caregivers themselves, but on the important populations they serve.

CAN works to improve the quality of life for tens of millions of family caregivers. These Americans care for loved ones with chronic conditions, disabilities, or diseases. Far too often, opioids and other prescription drugs find themselves abused by patients or diverted into the hands of others who become addicted themselves.

I understand that ICER is undergoing an independent review of an innovative non-opioid, non-addictive treatment for acute pain. This has the potential to revolutionize the care industry by helping get seniors off addictive opioids and to keep these dangerous drugs out of America's homes. ICER has an ability to help make these novel treatments mainstream for Americans, including to our most vulnerable seniors.

Pain is a condition we are all familiar with, but it is also an area where there have been limited developments in the treatment of pain in over 20 years. Although current therapies are often effective for pain management, so many have limitations due to side effects, and/or addictive potential.

Seniors remain an underreported and often forgotten casualty of the opioid crisis. A 2022 study from Northwestern Medicine found that between 1999 and 2019, opioid-related overdose deaths increased 1,886% in U.S. adults ages 55 and older, from 518 deaths in 1999 to 10,292 deaths in 2019.

So many of these deaths stem from abuse of opioids prescribed for acute pain after surgeries or falls. ICER can help turn these numbers around.

Sincerely,

Marvell Adams Jr.
Chief Executive Officer
Caregiver Action Network

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Re: Acute Pain: An Assessment of Suzetrigine
Public Comments of Draft Evidence Report

To Whom It May Concern at Institute for Clinical and Economic Review,

I am the founder of For Grace, a nonprofit organization dedicated to improving care and wellness for women challenged by chronic pain. Since 2002, we have strived to empower women to be better consumers for their pain care, sensitize the general public to gender pain disparities and enlighten public policy makers about pain as a major health issue to improve life outcomes for all women in chronic pain.

I have been a woman in pain since 1982, when I developed Complex Regional Pain Syndrome from a ballet injury. It took me nearly 14 years to get a proper diagnosis along with treatment, while in the meantime I was bedridden for 10 years and unable to speak for five years due to the ravages of the disease. Though now more functional, I use a wheelchair for distances and am still dealing with high-impact chronic pain on a daily basis.

The draft evidence report addresses the potential value and effectiveness of suzetrigine for acute pain – and I personally can attest to the importance of this new class of pain control drug, one that would have been beneficial to me in two instances I detail below.

Four decades ago when I developed CRPS, it took a number of months before the disease fully took hold. The current theory is that CRPS initiates locally in the body via an auto-immune mechanism. If allowed to continue its course without effective intervention, CRPS will eventually bed in the CNS generating neuro-inflammation which expresses in high-levels of constant neuropathic pain. Due to it now becoming a centralized pain syndrome, a new injury anywhere in the body can cause CRPS to develop there. As such, it is referred to as “The Suicide Disease.”

If a drug like suzetrigine had been availed to me during my acute pain phase, before CRPS fully set up as a disease, its course may have been mitigated during its early development. At that time, it was critical that something act as a barrier to the constant, unrelenting cycling of pain signals between my local injury and the CNS. Suzetrigine, especially due to its intrinsic effectiveness on neuropathic pain, might have been an ideal intervention, one that could have saved me a lifetime of pain and disability.

The other instance was rather recent. In August 2024, I developed a severe case of shingles, one that my doctors said was the worst they'd ever seen. Emanating from a dormant virus in the nerve tissue, the resulting rash, blisters and discomfort can be overwhelming. For me, it was easily the worst neuropathic pain I've ever experienced, and that's saying a lot from the 40+ year CRPS survivor.

To manage the pain, I resorted to dusting off a ten year old bottle of Vicodin I'd stowed away for an emergency. Taking two to three 5 mg tablets daily cut the pain to the point where I could be comfortable as the virus moved through its progression. Once that bottle was exhausted, my pain doctor wrote me a new prescription.

But once I submitted the script to my pharmacy, I was told they were out of Norco and was offered an anti-depressant as an alternative. This reluctance was clearly due to the fall-out of the opioid crisis that has swept through the US for the last decade. I declined, and suffered accordingly.

If my doctor's prescription had been for suzetrigine instead of Norco, it would have been filled without hesitancy. An effective and safe alternative to opioids for acute pain would be one that doctors would prescribe, pharmacies would fill and insurance companies would pay for without concern.

Those suffering from pain, whether it be acute or chronic, are in urgent need of interventions that are effective and have a better safety profile than opioids. Too many have had their acute pain turn into life-upending chronic pain needlessly – and have had acute pain problems inappropriately under-treated.

It is my fervent hope that this new class of pain medication, along with other emerging therapies, will provide promise and hope for better days ahead for a community whose desperate need for better outcomes has been overlooked for far too long.

Grace and Gratitude,
Cynthia Toussaint
Founder & Director, For Grace: Women In Pain
forgrace.org

January 13, 2025

Sarah K. Emond, MPP
President and Chief Executive Officer
Institute for Clinical and Economic Review

Dear Ms. Emond:

Thank you for the opportunity to comment on your organization's recently published Draft Evidence Report on acute pain. I hope that these comments can inform your organization's work as to the value and need for additional therapeutic options to treat acute pain in the United States.

My name is [redacted]. I live in [redacted] and I have been in recovery from opioid use disorder (OUD) for the last eight years. I have a long history of trauma that has made me predisposed to addiction. I abused drugs and alcohol as early as my early teens. However, it was only after I was prescribed narcotics to a tonsillectomy that I developed an opioid use disorder.

After running out of my prescribed opioids, I sought another doctor who would continue to prescribe me oxycodone and methadone in exchange for cash. This was necessary as I did not have insurance coverage. It was remarkably easy back then. Eventually, this doctor was caught and prosecuted for his prescribing habits, which made it more difficult for me to obtain prescription opioid pills. When this happened, I turned to heroin. I used heroin for six years and, when fentanyl became an increasingly large part of the nation's heroin supply, I overdosed over a dozen times.

I am lucky to be alive today.

Eventually, I found my way into recovery and have been sober for the last eight years. Today, I work to give back to others who are struggling and who have experienced the same journey as I have – from being prescribed opioids legally, to obtaining the same opioids illegally, and then, to heroin and other forms of opioids. I am the [redacted] in [redacted] provides peer support and a safe haven for those with a mental health condition or suffering from addiction.

The sad reality about my journey is how common it is. I understand that millions of Americans become newly persistent opioid users after being prescribed an opioid to manage an acute pain incident. Today, prescription opioids remain the standard of care for acute pain treatment. As many as 90 percent of acute pain patients continue to receive opioids to manage their pain and between 6 and 20 percent of these patients will continue taking opioids months after their incident.

I understand that the majority of opioid-related overdose deaths in this country occur due to heroin or fentanyl. The Centers for Disease Control and Prevention have been very clear on that. However, many addicts – like myself – do not develop an opioid use disorder through illicit forms of opioids. The habit is developed because they are exposed to opioids legally and, when that opioid supply dries up, they turn to the street for other, more easily obtainable forms of opioids, like heroin or fentanyl. I know this because I was one of these people and I talk to these people in my work every day.

I am encouraged that this reality may soon be coming to an end. That there may yet be a light at the end of the tunnel in the form of other, non-addictive forms of acute pain management. This is

an exciting day for patients who may soon have choices when it comes to managing their acute pain. The development of these products could be lifesaving for people like me who fell into the traps of addiction after being prescribed an opioid for an acute pain incident.

I understand that there is a pipeline of non-opioid therapeutics that may soon become available for acute pain patients. I, for one, will celebrate that day when the status quo in acute pain management changes. I foresee a time in the very near future where patients are unnecessarily prescribed opioids for acute pain. Instead, patients and their healthcare providers will have a conversation about what makes sense for them and make informed decisions about a care pathway. In the process, I am confident that patients will choose the non-addictive option. In the process, we will be preventing millions of cases of newly persistent opioid use in the country and saving lives.

I look forward to celebrating that day.

Thank you so much for your consideration of these comments.

Sincerely,

[redacted]

Throughout my life, I have had plenty of surgeries which required the use of opioids to help manage pain. While each surgery has differed, what has remained consistent is the lack of alternative treatment options and, at times, the adverse impact that opioids have had on my health.

After my first surgery it quickly became apparent to me that opioids are addictive. While I never became dependent on opioids, I felt the indescribable pull of the opioids that have impacted so many and knew I needed to taper off them as soon as possible. I also experienced unsettling changes in my mental health and dealt with side effects including nausea, constipation, vomiting and horrible sweating that made it all the more difficult to recover from my surgery.

As ICER evaluates new types of drugs that act like opioids but are not habit forming, I am hopeful that patients will soon have access to additional, valuable treatment options. As someone who understands the dangerous nature of opioids, I could not be more excited. There is a true opportunity here to change lives, including mine.

Access to non-addictive, non-opioid pain management treatment options that do not put patients and their health at risk of further decline is imperative. While certainly there is a place for opioids, patients like me should have options to the pain treatments they need to stay healthy.

While I am thankful that my most recent doctor was able to answer all my questions about opioids, I know that so many other patients do not have the knowledge to avoid an accidental addiction to pain killers. Addiction can be stopped before it ever starts.

I am offering you evidence as a patient who managed to survive countless rounds of opioids following various surgeries. There is a need for new types of medication to offer pain relief without addictive qualities. Please consider the true value of this acute pain treatment innovation on individual patients and society at-large.

Sincerely,

[redacted]

IRAQ AND AFGHANISTAN
VETERANS OF AMERICA

January 11, 2025

To whom it may concern:

As the CEO of the Iraq and Afghanistan Veterans of America (IAVA), the nation's leading post-9/11 generation veterans advocacy organization representing 425,000 members and supporters nationwide, I feel it's important for me to weigh in on the Institute for Clinical and Economic Review's (ICER) draft evidence report on the effectiveness and value of a new treatment option for acute pain.

I am pleased to see ICER's draft evidence report acknowledges the potential value and cost savings of this type of treatment innovation and role in curbing the opioid epidemic. As the generation of veterans that came of age amidst the opioid epidemic, post-9/11 veterans are uniquely interested in alternative ways to treat their pain.

A non-addictive, non-opioid treatment for acute pain also has the potential to change the landscape for millions of veterans across America who fought our most recent wars, because it will save lives. According to a 2022 study, U.S. veterans have been heavily impacted by the opioid overdose crisis, with data showing that from 2010-2019 overdose mortality rates increased by 53%. We should all want to do what we can to change that tragic statistic.

Military service can not only make you a combat veteran who might someday struggle to recover from your wartime wounds, but the training alone can come with painful consequences. Veterans and those still serving deserve the greatest amount of options as they work to rebound from the havoc that defending our nation can wreak on our bodies. And, if there's an opportunity to avoid opioid reliance in the process, we should take it.

Thank you for considering my perspective not only as the CEO of IAVA, but as a U.S. Army and Iraq War veteran myself. Together we can improve the lives of my generation of veterans and generations to come.

Best regards,

Allison Jaslow
CEO, Iraq and Afghanistan Veterans of America
Iraq War Veteran

MAPDA | MOTHERS FOR AWARENESS AND PREVENTION OF DRUG ABUSE

To whom it may concern at the Institute for Clinical and Economic Review (ICER),

As a former member of Congress and the co-founder and CEO of Mothers for Awareness and Prevention of Drug Abuse (MAPDA), I write to you today regarding your recent report supporting the importance of expanding treatment options for acute pain management, particularly for innovative non-opioid alternatives. This issue is deeply personal to me knowing firsthand the harrowing toll opioid dependency takes on families across America – not only as a former legislator but as a mother whose family has been directly impacted by substance abuse.

The devastating statistics speak for themselves: in 2021, 50,000 American seniors experienced an opioid overdose. Recent Kaiser Family Foundation data shows that opioid deaths are actually increasing for people 65 and older, while falling in other age groups. These aren't just numbers – they represent real people and real families, whose tragedies could potentially be prevented through better access to alternative pain management options.

During my 15 years in Congress, I witnessed how the opioid crisis tears through communities with devastating efficiency. In my current role at MAPDA, we believe "the greatest gift is a conversation" in helping prevent drug abuse and overdose. I'm extending that conversation to ICER today because we stand at a critical crossroads where your evaluation of non-opioid pain management alternatives could save thousands of lives.

A significant gap exists in our current pain management approach. While traditional opioids remain necessary in certain cases, we desperately need more options that can effectively manage pain while minimizing risks. Their prevalence in our healthcare system has created a deadly pipeline to opioid use disorder (OUD). This gap is particularly concerning for our most vulnerable populations, including:

- Seniors managing multiple medications who face increased risks of dangerous drug interactions
- Individuals with a history of substance use disorder who need effective pain management without triggering relapse
- Those of all ages who are particularly susceptible to drug misuse due to predisposed genetic vulnerabilities which are invisible until their first opioid prescription

Household and disposal safety is another concern I've seen repeatedly in my advocacy work. Many of the overdose cases we encounter at MAPDA involve prescription medications obtained from home medicine cabinets or shared amongst friends and family. By supporting the development and implementation of non-opioid treatments, we can ensure effective pain management while reducing the risk of medication abuse within households and communities.

Having worked extensively in public policy, I understand the rigorous evaluation process required for new treatments. However, I urge ICER to consider several crucial factors in moving forward:

1. The specific needs of our most vulnerable populations, particularly seniors who are

increasingly falling victim to opioid-related incidents
2. The broader societal impact of reducing opioid presence in households, where one prescription can impact multiple lives
3. The incalculable value – both in dollars and human lives – of preventing opioid dependency before it begins

Every month we see countless new families struggle with opioid abuse and overdose. I've learned that incremental progress is the key to turning the tide and saving lives. Supporting innovative pain management alternatives represents a crucial step forward in this ongoing battle.

Thank you for your consideration of this important public health crisis.

Sincerely,

Mary Bono
Former Member of Congress
Co-founder, CEO, & Chair of the Board
Mothers for Awareness and Prevention of Drug Abuse (MAPDA)

January 13, 2025

Sarah K. Emond, MPP
President and Chief Executive Officer
Institute for Clinical and Economic Review

Dear Ms. Emond:

On behalf of Voices for Non-Opioid Choices ("Voices"), a national nonpartisan, nonprofit organization dedicated to preventing opioid addiction, thank you for the opportunity to comment on the Draft Evidence Review on the treatment of acute pain as posted on December 9, 2024. Voices and our members advocate for policies to prevent opioid addiction in the United States through encouraging access to and use of non-opioid treatments. To the extent that novel therapies are approved by the Food and Drug Administration (FDA), access to such therapies could go a long way towards preventing opioid addiction that occurs after an acute pain incident.

Voices was founded in April 2019. At the time, 115 Americans were dying every day from an opioid-related drug overdose. Today, we lose more than 200 Americans every day to an opioid-related drug overdose. An increase of more than 70 percent in just six years.

While the latest data from the Centers for Disease Control and Prevention (CDC) show that rates of opioid-related drug overdoses are decreasing in the United States, there are still some causes for concern, including:

- Anne Milgram, the Administrator of the Drug Enforcement Agency (DEA), attributes "less potent fentanyl" as the main reason we are seeing decreases in opioid-related overdose deaths, while the CDC does not opine on why rates are decreasing.
- Decreases in opioid-related overdose deaths are not universal and some groups – including older Americans – are seeing increases in rates of opioid-related overdoses; and
- Rates of opioid-related overdose deaths are still historically high.

The country's response to the opioid addiction crisis has largely focused on strategies to prevent opioid-related overdose deaths rather than preventing opioid addiction in the first place. So, while the investments made to ensure the availability of naloxone in communities around the country, support our nation's healthcare workforce dealing with increased incidence of opioid use disorder (OUD, and providing additional resources for first responders on the front lines of this epidemic are laudable, they do little to prevent individuals from using, abusing, or becoming addicted to opioids in the first place.

This is a missed opportunity, and more work is needed in this area.

Voices, and our 200 members from around the country, know that there is an opportunity to prevent addiction before it starts, particularly for opioid-naïve and acute pain patients. One way to prevent opioid use, misuse, dependence, and addiction is to minimize potentially unnecessary exposure to prescription opioids after surgery.

In the United States, 90 percent of acute pain patients still receive prescription opioids today to manage postsurgical pain. Approximately 10 percent of these patients – or more than 4 million Americans – will become newly persistent opioid users following a surgical procedure. Some of these Americans will transition away from prescription opioids and turn to other illicit forms of opioids. Some will overdose. And some will die.

We can do better by these patients and improve the pain care landscape in the United States. An opportunity currently exists to treat acute pain patients with non-addictive approaches. Multimodal pain protocols involve prioritizing a combination of non-addictive pain approaches to give patients the proper analgesic support, while reducing our overreliance on prescription opioids. Multimodal protocols continue to evolve in the United States and they must continue to be made widely available to patients and providers.

Additionally, clinicians need more tools at their disposal to treat acute pain patients. The majority of states in this country limit the amount of prescription opioids that a provider may give to a patient. While this is a laudable step intended to reduce exposure to such narcotics, it does little to give clinicians other tools they require in place of opioids.

This is why innovations in the non-opioid acute pain management space are so exciting – such approaches offer the opportunity to improve the clinical practice of pain management and to do so without fear of the repercussions that may come with exposure to prescription opioids.

Innovation in the non-opioid pain management space is an exciting prospect. It is exciting for patients, families, caregivers, and healthcare providers who, for too long, have been left without choices when it comes to pain management decisions. To the extent that such products are viewed favorably by the decisionmakers at the FDA, Voices believes that such approaches represent a viable path forward to patients and providers and will go a long way towards facilitating conversations between patients and their providers about preferences for postsurgical pain management.

Thank you for your consideration of these comments. Please let us know if you have any questions, comments, or concerns. We look forward to working with you and your organization on these important issues.

Sincerely,

Chris Fox
Executive Director

To Whom It May Concern:

My name is Robert Kent and as former General Counsel with the White House Office of National Drug Control Policy (ONDCP), I have actively followed the work of the Institute for Clinical and Economic Review (ICER) over the years.

I was pleased to see an open assessment and comment period on new medications for acute pain that might lessen our country's dependence on addictive opioids. While at ONDCP, I was on the frontlines of the epidemic and worked to respond to the effects of overuse of opioids by eliminating the DEA-X-waiver to make buprenorphine easier to access, worked to increase access to methadone nationwide, and made lasting investments into harm reduction services.

Additionally, I served in a similar capacity in New York State as the General Counsel for the New York State Office of Addiction Services and Supports (OASAS) and led OASAS' efforts to implement New York State's Heroin and Opioid Task Force recommendations, which were focused on addressing the negative impacts of over-reliance on opioids.

I mention my background, not to gloat, but to show ICER how important this topic has been to me over the years. The opioid epidemic is one of the most serious health emergencies to have happened in the United States. While there may not be a panacea to solving this crisis, there are logical and important steps that can be taken as a society. One such step would be the use of alternatives to opioids to manage pain.

One of the most important things to happen in recent years is the development of new pharmaceuticals that are non-addictive. That means patients can go into the operating room, have surgery, and have a medication option that is non-habit forming. Closing the gap between existing treatments and these newly developed drugs will help stanch the bleeding of the epidemic, offer patients a more seamless recovery, and help reduce America's reliance on opioids.

ICER has an opportunity to give favorable review to these new classes of drugs and I am pleased to give my full endorsement.

Sincerely,

Robert Kent
Virginia