US Food and Drug Administration Approval of Suzetrigine: A Breakthrough in Nonopioid Pain Management

To the Editor

Pain is an unpleasant sensory and emotional experience that significantly impacts morbidity, mortality, and health care system expenditures.[1] Acute pain is a sudden physiological response to noxious stimuli that may develop into a pathological condition.[2] Pain, particularly acute pain, is common after surgery and usually resolves within a short period of time. In the United States, millions of people are prescribed opioids for the management of acute pain, among other drugs. While opioids are popular and effective analgesics, their effects on the central nervous system increase the risk of dependence and addiction.

To provide safer and more effective pain management without the possibility of addiction, nonopioid analgesics that specifically block pain are under development. Suzetrigine (Journavx, Vertex Pharmaceuticals), a potent and selective nonopioid NaV1.8 inhibitor, was recently approved by the US Food and Drug Administration (FDA). It represents a significant advancement as the first new class of "nonopioid painkillers."[3]

The approval of suzetrigine was backed by data from 2 Phase-3 clinical trials conducted to measure the primary efficacy and safety of the drug over a 48-hour period with safety assessments lasting up to 14-day posttreatment.[3] The trials featured a randomized, double-blind, placebo- and active-controlled approach involving a total of 874 participants experiencing moderate-to-severe acute postoperative pain after abdominoplasty and bunionectomy. Pain intensity for each trial was measured using a patient-reported 11-point numeric pain rating scale. Patients were randomized to receive varying doses of suzetrigine, placebo, or hydrocodone bitartrate/acetaminophen.[4] For both studies, ibuprofen was permitted as a rescue medication. Participants who received high-dose suzetrigine had reduced acute pain over the 48-hour treatment period after abdominoplasty and bunionectomy compared to placebo while lower doses showed no effect.[4] Compared to hydrocodone, there was an apparent treatment effect; however, the studies were underpowered to compare the 2 agents. The reduction in pain compared to placebo is by inhibition of NaV1.8 sodium channels specific to nociceptors (pain-sensing receptors) only in peripheral nerves and not the brain or spinal cord, providing pain relief without the threat of addiction that accompanies opioids.[5]

Despite receiving Fast Track and Breakthrough Therapy designations from the FDA before its approval due to its promising potential to address significant unmet needs in pain management, suzetrigine is not completely devoid of adverse reactions. These include itching, muscle spasms, increased blood creatine phosphokinase (CPK) levels, headache, and rash.[5] Importantly, no adverse effects were reported on the central nervous system, cardiovascular system, or behavior in phase 3 trials. There was also no evidence of addiction or dependence. These findings position suzetrigine as a promising alternative to traditional opioid analgesics.[6] In conclusion, suzetrigine marks a pivotal advancement in pain management by offering effective relief without the risks associated with opioid use. Its approval redefines postoperative pain management, addressing a critical public health need while reducing addiction concerns. Although the side effect profile should be studied further, its unique mechanism and safety profile make it a groundbreaking option in the field of analgesics.

Muhammad Areeb Ul Haq, MBBS
Department of Medicine
Allama Iqbal Medical College
Lahore, Punjab, Pakistan
areebulhaq22@gmail.com

Sabrina Najeeb, MBBS
Department of Medicine
Karachi Metropolitan University
Karachi, Sindh, Pakistan

Wasi Junaid, MBBS
Department of Medicine
Karachi Metropolitan University
Karachi, Sindh, Pakistan

Rafia Chaudhry, MBBS
Department of Medicine
Karachi Metropolitan University
Karachi, Sindh, Pakistan

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