

General

Suzetrigine for Vaso-Occlusive Pain in Sickle Cell Disease: A Three-Patient Case Series

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Keywords: Sickle cell disease, Vaso-occlusive crises, Suzetrigine, Neuropathic pain, Multimodal analgesia

<https://doi.org/10.52965/001c.162149>

Orthopedic Reviews

Vol. 18, 2026

Background

Sickle cell disease (SCD) is characterized by recurrent vaso-occlusive crises and chronic pain, often requiring multimodal analgesia that frequently includes opioids. Given the risks associated with long-term opioid therapy, there is a growing need for effective non-opioid alternatives. Suzetrigine, a selective NaV1.8 sodium channel inhibitor, represents a novel analgesic approach targeting peripheral nociceptive signaling.

Methods

We present a case series of three patients with sickle cell-related pain treated with suzetrigine as part of a multimodal pain management strategy. The cohort included one patient with sickle cell trait (HbAS), one with hemoglobin SC disease, and one with hemoglobin SS disease. Clinical outcomes, including pain control, healthcare utilization, and medication use, were evaluated.

Results

Two of three patients reported subjective improvement in pain control with suzetrigine, including reduced reliance on opioid medications and no emergency department visits or hospitalizations during the observation period. Both patients were on minimal opioid therapy. In contrast, the third patient, who was maintained on chronic opioid therapy, did not experience improvement and required hospitalization for pain management. No adverse effects related to suzetrigine were observed in any patient.

Conclusion

Suzetrigine may be a non-opioid adjunct for managing sickle cell-related pain, particularly in opioid-naïve or opioid-intolerant patients. However, its efficacy may be limited in opioid-tolerant individuals. Larger studies are needed to better define its role in the management of vaso-occlusive pain and chronic pain in SCD.

INTRODUCTION

Sickle cell disease (SCD) is a hereditary hemoglobinopathy caused by a mutation in the β -globin gene (HBB), resulting in the production of hemoglobin S (HbS) and the characteristic sickling of red blood cells under conditions of stress, hypoxia, or dehydration.^{1,2} The disease affects millions worldwide and is particularly prevalent among individuals of African, Middle Eastern, and South Asian descent.¹⁻³ Clinically, SCD is marked by chronic hemolytic anemia, progressive end-organ damage, and recurrent vaso-occlusive episodes, which are the hallmark of the condition.¹⁻³

Pain is the most common and debilitating manifestation of SCD.⁴ Vaso-occlusive crises occur when sickled erythrocytes obstruct the microvasculature, leading to ischemia,

inflammation, and severe acute pain.^{4,5} These episodes frequently require emergency care and hospitalization, significantly impairing quality of life and contributing to substantial healthcare utilization. In addition to acute pain, many patients experience chronic pain syndromes related to ongoing tissue injury and central sensitization, making effective and sustained analgesic management a clinical priority.^{4,6,7} Traditional treatment strategies include a multimodal approach using non-opioid and opioid analgesics; however, long-term opioid therapy carries risks of tolerance, dependence, opioid use disorder, and adverse effects.^{8,9}

Below, we present a case series of three patients with chronic pain related to sickle cell disease who were treated with suzetrigine as part of a multimodal pain management strategy. The cohort includes one patient with sickle cell trait, one with hemoglobin SC disease, and one with he-

moglobin SS disease. We describe each patient's clinical course, incorporation of suzetrigine into their treatment regimen, and the associated outcomes following therapy. The same dosing guidelines were prescribed to the patients which included: 100mg loading dose on an empty stomach followed by subsequent twice daily 50mg every 12 hours. The therapy is indicated for short-term, maximum 14 days.

CASE SERIES

Patient 1 is a 34-year-old African American female with hemoglobin electrophoresis demonstrating HbS 41.8% and HbA 55.1%, consistent with sickle cell trait (HbAS). She presented for evaluation of recurrent pain episodes primarily involving the bilateral lower extremities and lower back, often triggered by physical exertion.

Her medical history is notable for asthma and prior hospitalizations for pneumonia. At baseline, she managed pain with OTC nonsteroidal anti-inflammatory medications and acetaminophen and only rarely required opioid medications. She denied prior complications such as stroke, acute chest syndrome, kidney dysfunction, or prior blood transfusion.

Suzetrigine was incorporated into her outpatient pain management regimen, with hydrocodone and tramadol available for breakthrough pain. During the observation period, her pain episodes were managed in the outpatient setting. No adverse reactions were reported during her trial. Per chart review, the patient was on Hydrocodone and Tramadol for pain control related to diffuse joint pain complaints and discomfort. During her time on suzetrigine, she did not need to utilize opioid therapy.

PATIENT 2

Patient 2 is a 34-year-old female with hemoglobin electrophoresis demonstrating HbS 51.1% and HbC 44%, consistent with hemoglobin SC disease. She experienced recurrent vaso-occlusive pain episodes primarily involving the right hip, the left knee, and the left calf.

Her medical history is notable for immune thrombocytopenia diagnosed in 2024, splenomegaly, avascular necrosis of the right hip, and stage 2 sickle cell retinopathy. The patient reported sensitivity to opioid medications and previously used tramadol 100 mg as needed but rarely took it due of excessive sedation. Her baseline pain regimen primarily consisted of nonsteroidal anti-inflammatory medications, including naproxen, and she reported that ketorolac provided the most effective relief during pain episodes.

Suzetrigine was initiated as part of her pain management regimen. During the observation period, she received supportive therapy including intravenous fluids and ketorolac during infusion clinic visits. No adverse effects related to suzetrigine were documented.

PATIENT 3

Patient 3 is a 37-year-old man with a history of chronic pain related to Hemoglobin SS disease. His SCD is complicated by a history of secondary hemochromatosis from prior blood transfusions. His chronic pain regimen consists of oxycodone-acetaminophen 10-325mg three times a day as needed for acute pain and methocarbamol 750mg twice a day as needed. He also utilizes ibuprofen 600mg for mild pain complaints.

The patient reported worsening pain despite normal hemoglobin and reticulocyte levels. He did not want to increase his current opioid requirements. Suzetrigine was prescribed to help with his acute vaso-occlusive crises. The patient went through the 2-week medication regimen. He denied noticing any benefit or changes in his pain while on suzetrigine. The patient went to the emergency room and required admission for pain control while on suzetrigine.

The patient outcomes are summarized in [Table 1](#).

DISCUSSION

Suzetrigine, a selective sodium channel inhibitor, represents a novel non-opioid analgesic approach aimed at modulating peripheral nociceptive signaling. By selectively inhibiting NaV1.8 channels expressed on peripheral sensory neurons, suzetrigine reduces the transmission of pain signals without directly engaging central opioid pathways.^{10, 11} This mechanism offers the potential for effective analgesia while minimizing the risks associated with opioid therapy, including respiratory depression, tolerance, and dependence. As suzetrigine is currently being investigated and utilized across a variety of pain conditions, it is important to better understand its clinical utility and identify which pain syndromes may derive the greatest benefit from this therapy.¹²

In this report, suzetrigine was incorporated into the pain management regimens of three patients: one with sickle cell trait and two with sickle cell disease. All patients tolerated the medication without documented adverse effects.

The first patient reported subjective improvement in pain control with a reduction in opioid use. Notably, no hospitalizations occurred during the observation period. Although intermittent outpatient supportive therapies, including intravenous fluids and ketorolac, were still required, the absence of emergency department visits suggests that pain was effectively managed in the outpatient setting.

The second patient had a history of opioid intolerance and rarely used tramadol due to sedation, highlighting a clinical scenario in which non-opioid analgesic options may be particularly beneficial. At follow-up, she reported minimal pain and noted improvement in symptoms following the initiation of suzetrigine.

In contrast, the third patient had a history of chronic pain and was maintained on long-term opioid therapy. Suzetrigine was introduced as part of a multimodal strategy to improve pain control during acute vaso-occlusive crises. However, the patient did not experience meaningful im-

Table 1.

Outcome Measure	Patient 1	Patient 2	Patient 3
Pre Treatment Mean Pain (NRS)	6.5/10	3/10	2.5/10
Post Treatment Hospital Visits	0	0	1
Pre Treatment Hospital Visits (In the past 3 months)	0	0	3
Post Treatment Clinic visits/Therapy visits	7	1	1
Patient reported improvement with suzetrigine therapy	Yes	Yes	No

provement in symptoms and required hospitalization for pain management in the subsequent month. There were no changes to his baseline opioid regimen. This case suggests that suzetrigine may have limited efficacy in patients who are opioid-tolerant or maintained on higher-dose opioid therapy.

Recent clinical studies evaluating suzetrigine in acute postoperative pain have demonstrated clinically meaningful reductions in pain intensity compared with placebo, along with a favorable safety profile and no evidence of respiratory depression or opioid-related adverse effects.¹³ Although these studies were conducted in surgical pain models, they provide proof of concept that selective NaV1.8 inhibition can produce effective analgesia.

This case series is of particular interest as it represents one of the earliest descriptions of suzetrigine use in the management of sickle cell-related pain, including vaso-occlusive crises. Patients with sickle cell disease frequently require repeated treatment for acute pain episodes, and strategies that reduce reliance on opioid-based regimens remain an important clinical priority. In this series, two of three patients reported improvement in pain control with the addition of suzetrigine, while one patient did not experience benefit and required hospitalization.

Given the small sample size, no definitive conclusions can be drawn. However, the differential responses observed may suggest that suzetrigine is more effective in opioid-naïve or opioid-intolerant patients, with potentially diminished benefit in those with established opioid tolerance.

Furthermore, the role of NaV1.8 inhibition in the pathophysiology of vaso-occlusive pain remains unclear, and additional studies are needed to better define its therapeutic utility in this population.

CONCLUSION

This case series evaluates suzetrigine as a novel non-opioid adjunct in the management of sickle cell-related pain, including vaso-occlusive crises. In our cohort, suzetrigine was well tolerated and associated with subjective improvement in pain control in two of three patients, particularly in those who were opioid-intolerant or not on chronic high-dose opioid therapy. However, the lack of efficacy observed in an opioid-tolerant patient underscores the need for careful patient selection and suggests that its benefit may be limited in certain populations. While these findings are preliminary, they support further investigation into NaV1.8-targeted therapies as part of multimodal pain management strategies. Larger, prospective studies are needed to better define the clinical utility, optimal patient population, and role of suzetrigine in managing both chronic pain and acute vaso-occlusive episodes in patients with sickle cell disease.

Submitted: April 19, 2026 EDT. Accepted: May 05, 2026 EDT.

Published: May 22, 2026 EDT.

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