Review Article

Comparison of Efficacy and Adverse Effects of Triptans and Gepants – Anti-Migraine Drugs

Pakeezah Tabasum[1],Wajiha Fatima[2], FNU Adnan[3]
[1]MBBS, Department of Neurology, Peoples University of Medical and Health Sciences for Women, Nawabshah, Pakistan
[2,3]MBBS, Department of Neurology, Jinnah Sindh Medical University, Karachi, Pakistan

Author's Contribution
[1,2,3] *Conception of study*
[1,2,3] *Experimentation/Study Conduction*
[1,2,3] *Analysis/Interpretation/Discussion*
[1,2,3] *Manuscript Writing*
[1,2] *Critical Review*
[1,2,3] *Facilitation and Material analysis*

Corresponding Author
Pakeezah Tabasum,
MBBS Student,
Peoples University of Medical and Health Sciences for Women, Nawabshah, Pakistan
Email: pakeezahtabasum8@gmail.com

Article Processing
Received: 15/05/2025
Accepted: 01/08/2025

Cite this Article: Tabasum P, Fatima W, Adnan FNU. Comparison of Efficacy and Adverse Effects of Triptans and Gepants – anti-migraine drugs. SJRMC. 2025; S1:25.

Conflict of Interest: *Nil*
Funding Source: *Nil*

Access Online:

Abstract

Background: Migraine is the second leading cause of Years Lived with Disability (YLD) worldwide, affecting about 1.04 billion people. It is a unilateral neurological disorder, with 75% of cases occurring in women of reproductive age. Triptans, 5-HT1B/1D receptor agonists, have long been the mainstay of acute therapy, while the newer CGRP receptor antagonists, Gepants, offer alternative mechanisms and safer profiles for patients with cardiovascular risk.

Objectives: The objective of this narrative review is to compare the efficacy, safety, and adverse effects of triptans and gepants on acute treatment of migraines

Materials and Methods: A comparative review was conducted using electronic databases such as PubMed and Google Scholar. Keywords like "Triptans", "Gepants", and "Migraine" were searched for relevant articles. This short communication utilizes data from recent randomized control trials, meta-analysis, and observational studies. Key endpoints included clinical effects such as pain freedom, adverse effects.

Results: Triptans demonstrated higher efficacy and greater proportion of patients achieving pain freedom at 2 hours compared to gepants. Gepants were associated with fewer adverse effects and more favorable safety profiles, particularly in patients with cardiovascular diseases, as they do not cause vasoconstriction. Adverse event rates were higher for triptans than for gepants, with most events being mildly and rarely, leading to discontinuation

Conclusion: Triptans continue to offer superior efficacy in acute migraine relief as evidenced by high pain freedom rate. However, gepants with a more favorable safety profile and comparable real-world effectiveness, emerge as a viable and well-tolerated alternative, especially for patients with cardiovascular risk or triptan intolerance. Personalized treatment strategies that consider both efficacy and safety are essential for optimizing migraine care.

Keywords: Migraine Disorders, Serotonin 5-HT1 Receptor Agonists, Calcitonin Gene-Related Peptide
Keywords: Migraine Disorders (D008881), Triptans, Gepants, Rizatriptan, Zavegepant, Rimegepant

Introduction

Migraine is ranked as the second largest cause of disability globally. It also stands among the top ten diseases that cause Years Lived in Disability (YLDs) in 195 countries and territories of the world, with a prevalence rate of 1040 million (1000 million to 1090 million) and its count increase to 15.7% in ten years. This underscores its substantial impact on individual quality of life, productivity, and healthcare systems, highlighting the urgent need for effective, well-tolerated treatment options.[1,2]

Migraine can be described as a multi-factorial neurological disorder, characterized by recurrent unilateral headaches associated with nausea, vomiting, photophobia, and phonophobia. It can be with or without an aura. Aura is popularly known as a warning sign and is a sensory and perceptual disturbance preceding neurological problems like migraine and seizures. Among the people who experienced migraine, 75% of them are females, so in accordance with this, we can state that the significant impact of migraine is primarily experienced by women in their reproductive age (15 to 49 years).[3] Moreover, it has a potentially negative effect on the daily activities of a person, causing hindrance in productivity and participation in academics, professional, and even in social settings. Not only this, but migraine is also associated with a high amount of financial burden, with an annual total cost of $27 billion in the United States.[4]

The pathophysiology of migraine remains incompletely understood, but one widely accepted mechanism suggests that attacks are triggered by dilation and inflammation of cephalic and intracranial extracerebral arteries.[5-7] This vascular theory provides the rationale for using Triptans, which act as selective serotonin (5-HT1B/1D) receptor agonists, producing vasoconstriction of dilated vessels and inhibiting the release of trigeminal neuropeptides, thereby relieving headache symptoms.[8]

However, Triptans are limited by their vasoconstrictive properties, making them unsuitable for patients with cardiovascular disease. In contrast, Gepants, small-molecule calcitonin gene-related peptide (CGRP) receptor antagonists, act by blocking CGRP-mediated vasodilation and neurogenic inflammation without causing vasoconstriction.[9] This offers a safer alternative for patients in whom Triptans are contraindicated.

The rationale of this study lies in the clinical need to compare these two major drug classes. While Triptans are more established and often more efficacious in achieving pain freedom within two hours, Gepants provide a more favorable safety profile and sustained relief from migraine symptoms such as headache recurrence, nausea, photophobia, and phonophobia. Evaluating their relative efficacy and adverse effects is therefore essential to guide personalized treatment strategies, particularly in patients with comorbidities or Triptan intolerance. The objective of this narrative review is to compare the efficacy and adverse effects of Triptans and Gepants in acute migraine management.

Materials and Methods

This narrative review is based on a comparative review of the pharmacological

profile, clinical efficacy, safety outcomes of Triptans and Gepants, the two primary classes of anti-migraine medication. A structured and concise literature-based approach was adopted to synthesize existing data from original articles, randomized controlled trials, systematic reviews, meta-analyses, and observational studies published within the last five years. A comprehensive search was conducted using electronic databases, including PubMed and Google Scholar The search strategy included Boolean combination of keyword "Triptans", "Gepants", "Migraine", "Calcitonin gene-related peptide antagonist", "efficacy", "adverse effect".

Articles were screened based on their relevance to the comparison of the two drug classes in terms of therapeutic outcomes, mechanism of action, side-effect profile. Articles were included if they were published in English within the last five years, involved adult patients diagnosed with migraine, and provided comparative data on Triptans (such as sumatriptan, rizatriptan, or eletriptan) and Gepants (such as rimegepant, ubrogepant, zavegepant, or atogepant). Eligible studies comprised original research articles, randomized controlled trials, systematic reviews, or meta-analyses that reported outcomes related to efficacy—such as pain relief within two hours, sustained symptom relief, and recurrence—as well as safety, tolerability, and contraindications. Studies were excluded if they involved animal models, focused exclusively on pediatric populations, used non-FDA approved agents, or were purely mechanistic and non-comparative without clinical correlation.

Relevant findings from the selected studies were synthesized qualitatively, with particular attention given to endpoints such as onset of action, pain freedom rates, sustained relief of associated migraine symptoms (nausea, photophobia, phonophobia), adverse event profiles, and cardiovascular safety considerations. No statistical meta-analysis was performed; instead, results were narratively summarized, and a comparative table was included to highlight the key differences in mechanisms of action, efficacy, providing a clinically relevant overview for physicians considering personalized migraine treatment options. As this review is based solely on previously published literature, no ethical approval was required.

Results

The reviewed literature consistently described clear mechanistic differences between Triptans and Gepants. Triptans act as selective 5-HT1B/1D receptor agonists, producing vasoconstriction of dilated cranial vessels and inhibiting the release of trigeminal neuropeptides, thereby alleviating migraine pain.[5,8] In contrast, Gepants function as antagonists of the calcitonin gene-related peptide (CGRP) receptor, preventing CGRP-mediated vasodilation and neurogenic inflammation without causing vasoconstriction.[9] These mechanistic distinctions, identified across multiple studies, form the basis for differences observed in efficacy and tolerability outcomes between the two classes.

Gepants, including Zavegepant and Rimegepant, when compared with Triptans and found Triptans as more efficient than other antimigraine therapies in relieving pain

and other bothersome symptoms within 2 hours of administration of drug.[10] Furthermore, the Triptans group shows fewer adverse effects than Gepants, as mentioned in Table 1. Frequent use of Triptans associated with overuse of medication can lead to headache only.[5,11] Patients treated with Zavegepant show 2% more adverse effects when compared with placebo, such as taste disorder (including dysgeusia and ageusia), nausea, nasal discomfort and vomiting.[12] Whereas, a drug of Gepants, Rimegepant, causes nausea and UTI as a common adverse effect, and increased serum concentration of alanine aminotransferase or aspartate aminotransferase is also seen.[10] According to a study, Gepants are safely prescribed in individuals with contraindications to Triptans, e.g. those with cardiovascular disease or uncontrolled hypertension, patients who experience significant adverse effects from conventional migraine therapies, and those with history of medication overuse headache, making them a valuable addition to personalized migraine management strategies.[13] However, the pooled results of meta-analysis suggests Triptans are more effective in reducing pain intensity but due to its reduced tolerability profile, Gepants are considered a more favourable option.[14]

Table 1 *Clinical Effects, Efficacy, and Adverse effects of Triptans and Gepants*

Drug	**Mechanism**	**Clinical Effects**	**Efficacy**	**Adverse Effect**
Rizatriptan[8]	Serotonin receptors 5-HT1B and 5-HT1D	Stimulate serotonin (5-HT1B/1D) receptor to reduce inflammation and vasodilation	Provide long-term efficacy across multiple migraine attacks	Headache
Zavegepant[12]	Calcitonin gene–related peptide receptor antagonists	Blocks CGRP receptors, effective even in patients unresponsive to triptans	Provide relief from chronic and episodic migraine	dysgeusia and ageusia, nausea, vomiting, nasal congestion and abnormal taste.
Rimegepant[13]	calcitonin gene–related peptide receptor antagonists	Antagonize CGRP receptors with sustained effect and minimal cardiovascular risk	Provide relief from pain and other bothersome symptoms	Nausea and Urinary tract infection.

Discussion

The narrative review of Triptans and Gepants, particularly the newly approved Zavagepant and Rimegepant, reveals significant differences in efficacy and adverse effects, providing critical insight for clinical decision making in migraine management. Triptans have long been established as a main drug used in the treatment of acute migraine due to their ability to selectively bind to serotonin receptors (5-HT1B and 5-HT1D), thereby inducing vasoconstriction of dilated cephalic and intracranial arteries.[5] This mechanism directly targets the hypothesized pathophysiology of migraine, leading to rapid and effective relief of symptoms within 2 hours of administration. The tolerability and efficacy of Triptans, such as Rizatriptan, are well documented, making them the preferred choice for many clinicians.

On the other hand, Gepants represent a newer class of antimigraine drugs that target the Calcitonin Gene-Related Peptide (CGRP) receptor, a different pathway implicated in migraine pathogenesis. Gepants are CGRP receptor antagonists that block the binding of Calcitonin Gene-Related Peptide to its receptor, thereby inhibiting CGRP-mediated vasodilation and neurogenic inflammation in trigeminovascular system, which are key contributors to migraine pain.[15] Gepants like Rimegepants show excellent results as an acute and preventive treatment of migraine. They provide both acute relief and preventive benefit without causing vasoconstriction, making them safer for patients with cardiovascular.[15,16] Moreover, Gepants also help in those individuals who either do not respond to Triptans or cannot tolerate their side effects.[17] However, Gepants provide a novel mechanism of action and are effective in certain populations, their adverse effect profile raises concerns. Studies have shown that patients treated with Zavegepants report higher incidences of taste disorders, nausea, nasal discomfort and vomiting compared to placebo[12], while Rimegepant is associated with nausea, urinary tract infection, and deranged LFTs.[10]

The data suggests that while Gepants are beneficial for a subset of patients, Triptans remain the superior first-line treatment for most individuals due to their well-established efficacy and lower incidence of adverse effects. The frequent use of Triptans, however, must be monitored to prevent medication-overuse headache (MOH), a potential risk associated with long-term use. Nonetheless, the lower overall side effect burden of Triptans compared to Gepants makes them a more viable option for the majority of patients.

Conclusion

Triptans remain the most effective agents for achieving rapid pain freedom, particularly within two hours of administration, and continue to be the first-line choice for the majority of patients. However, their vasoconstrictive action limits use in individuals with cardiovascular risk factors or intolerance. Gepants, while demonstrating slightly lower efficacy in terms of immediate pain relief, offer a more favorable safety and tolerability profile, with particular advantages in patients who cannot use Triptans. Taken together, these findings suggest that Triptans and Gepants should not be viewed as competing options but rather as complementary therapies within a

personalized treatment approach. Clinicians should weigh efficacy against safety when selecting therapy, ensuring that management is tailored to individual patient comorbidities and treatment response.

References

1. Cen J, Wang Q, Cheng L, Gao Q, Wang H, Sun F. Global, regional, and national burden and trends of migraine among women of childbearing age from 1990 to 2021: insights from the Global Burden of Disease Study 2021. J Headache Pain. 2024;25:96.
2. James SL, Abate D, Abate KH, Abay SM, Abbafati C, Abbasi N, Abbastabar H, Abd-Allah F, Abdela J, Abdelalim A, Abdollahpour I. Global, regional, and national incidence, prevalence, and years lived with disability for 354 diseases and injuries for 195 countries and territories, 1990–2017: a systematic analysis for the Global Burden of Disease Study 2017. The lancet. 2018 Nov 10;392(10159):1789-858.
3. Croop R, Goadsby PJ, Stock DA, Conway CM, Forshaw M, Stock EG, et al. Efficacy, safety, and tolerability of rimegepant orally disintegrating tablet for the acute treatment of migraine: a randomised, phase 3, double-blind, placebo-controlled trial. The Lancet. 2019 Aug;394(10200):737–45.
4. Begasse de Dhaem O, Sakai F. Migraine in the workplace. eNeurologicalSci. 2022;27:100408.
5. Yang CP, Liang CS, Chang CM, Yang CC, Shih PH, Yau YC, et al. Comparison of New Pharmacologic Agents With Triptans for Treatment of Migraine. JAMA Network Open. 2021 Oct 11;4(10):e2128544.
6. Salahi M, Parsa S, Nourmohammadi D, Razmkhah Z, Salimi O, Rahmani M, Zivary S, Askarzadeh M, Tapak MA, Vaezi A, Sadeghsalehi H. Immunologic aspects of migraine: A review of literature. Frontiers in neurology. 2022 Sep 28;13:944791.
7. Goadsby PJ, Holland PR, Martins-Oliveira M, Hoffmann J, Schankin C, Akerman S. Pathophysiology of migraine: a disorder of sensory processing. Physiological reviews. 2017 Feb 8.
8. Karlsson WK, Ostinelli EG, Zhuang ZA, Kokoti L, Christensen RH, Al-Khazali HM, et al. Comparative effects of drug interventions for the acute management of migraine episodes in adults: systematic review and network meta-analysis. BMJ. 2024;386:e080107.
9. Wattiez AS, Sowers LP, Russo AF. Calcitonin gene-related peptide (CGRP): role in migraine pathophysiology and therapeutic targeting. Expert opinion on therapeutic targets. 2020 Feb 1;24(2):91-100.
10. Lipton RB, Croop R, Stock EG, Stock DA, Morris BA, Frost M, et al. Rimegepant, an Oral Calcitonin Gene–Related Peptide Receptor Antagonist, for Migraine. New England Journal of Medicine. 2019 Jul 11;381(2):142–9.
11. Gosalia H, Moreno-Ajona D, Goadsby PJ. Medication-overuse headache: a narrative review. The Journal of Headache and Pain. 2024 May 31;25(1):89.
12. Dhillon S. Zavegepant: First Approval. Drugs. 2023 Jun 25;83(9):825–31.
13. Anukoolwittaya P, Rattanawong W, Vongvaivanich K, Pongpitakmetha T, Thanprasertsuk S, Poonpedpun T, et al. Expert consensus on gepants for acute and preventive treatment of migraine in Thailand. J Headache Pain. 2025;26:131.
14. Iannone LF, Vaghi G, Sebastianelli G, Casillo F, Russo A, Silvestro M, et al. Effectiveness and tolerability of rimegepant in the acute treatment of migraine: a real-world, prospective, multicentric study (GAINER study). J Headache Pain. 2025;26(1):4.
15. Rissardo JP, Caprara AL. Gepants for acute and preventive migraine treatment: a narrative review. Brain sciences. 2022 Nov 24;12(12):1612.
16. Blair HA. Rimegepant: A review in the acute treatment and preventive treatment of migraine. CNS drugs. 2023 Mar;37(3):255-65.
17. Pellesi L, Jedie B, Barhum F, Al-Abdullah S, Martelletti P, Xiao Z. Head-to-head relief: ubrogepant, rimegepant, and zavegepant in migraine treatment. Pain Management. 2025 Apr 18:1-6.