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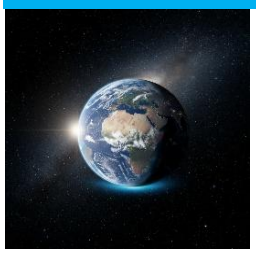

Journal of Education, Health and Sport. eISSN 2391-8306.

Journal Home Page
https://apcz.umk.pl/JEHS/index

CHODOR, Michal, KRYS, Zuzanna and MICHALIK , Zuzanna. Advances in Acute Migraine Therapy: Triptans Compared with CGRP Receptor Antagonists. Journal of Education, Health and Sport. 2026;89:70058. eISSN 2391-8306. https://doi.org/10.12775/JEHS.2026.89.70058

The journal has had 40 points in Minister of Science and Higher Education of Poland parametric evaluation. Annex to the announcement of the Minister of Education and Science of 05.01.2024 No. 32318. Has a Journal's Unique Identifier: 201159. Scientific disciplines assigned: Physical culture sciences (Field of medical and health sciences); Health Sciences (Field of medical and health sciences).
Punkty Ministerialne 40 punktów. Załącznik do komunikatu Ministra Nauki i Szkolnictwa Wyższego z dnia 05.01.2024 Lp. 32318. Posiada Unikatowy Identyfikator Czasopisma: 201159. Przypisane dyscypliny naukowe: Nauki o kulturze fizycznej (Dziedzina nauk medycznych i nauk o zdrowiu); Nauki o zdrowiu (Dziedzina nauk medycznych i nauk o zdrowiu).
The authors declare that there is no conflict of interests regarding the publication of this paper.
Received: 21.03.2026. Revised: 06.04.2026. Accepted: 06.04.2026. Published: 10.04.2026.

Advances in Acute Migraine Therapy: Triptans Compared with CGRP Receptor Antagonists

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Abstract:

Introduction and purpose: Migraine is one of the most common and disabling neurological disorders. Attacks significantly decrease quality of life and daily functioning; therefore, effective treatment is crucial. Triptans have remained the standard therapy for many years, while calcitonin gene-related peptide (CGRP) receptor antagonists (gepants) represent an alternative. The aim of this review is to compare their effectiveness and safety.
Materials and Methods: This review evaluates the efficacy and safety of acute migraine therapies, focusing on triptans and gepants. Literature was searched in PubMed/MEDLINE, Scopus, and Google Scholar.

State of Knowledge: Both therapies are effective in treating migraine pain and associated symptoms. Triptans act as selective 5-$HT_1B/_1D$ receptor agonists with rapid onset. However, their vasoconstrictive effects limit use in patients with cardiovascular disease. Gepants inhibit the CGRP pathway and do not cause vasoconstriction, suggesting a better safety profile, although with a slower onset.

Summary: Triptans remain first-line therapy, while gepants are a suitable alternative.

Individualized treatment is essential.

Key words - migraine; triptans; gepants; acute migraine therapy

1. Introduction

1.1 Epidemiology and clinical significance

Migraine is one of the most common neurological disease in the world and it poses a crucial problem for public health. Globally about 1 billion people suffer from this type of headache, which constitutes about 15% of the world's population [2]. Women tend to have migraine about 2-3x times more often than men. Peak of incidence falls between the age of 15-49[1].

The Global Burden of Disease analysis showed that although migraine occurs almost twice less frequently than tension headaches, it accounts for 90% of disability caused by headaches [1]. This disproportion results from the higher severity of disability caused by migraine headaches compared to tension headaches (0.441 vs. 0.037) and the fact that people affected by migraine experience symptoms most of the year. In 2023, headaches were attributed to 45.5 million years lived with disability (YLD), of which 40.9 million YLD were caused by migraine [1]. According to data published by the WHO, migraine significantly reduces quality of life, affects professional and social functioning, and generates significant indirect and direct costs [2].

Migraine burden shows significant gender differences. Women suffer from almost twice as much YLD disability and are significantly more likely than men to be ill, while also experiencing symptoms for a greater proportion of the time than men. With age, the percentage of time spent experiencing symptoms increases in both sexes. Age-standardized prevalence rates and YLD index have remained relatively stable for 30 years [1]. The long-standing burden of migraine, its chronic and recurrent nature, and its prevalence make it a major public health problem, emphasising the need for effective management and prevention strategies.

1.2 Definition of migraine

Migraine is a primary headache disorder. Pain episodes last from 4 to 72 hours and are often accompanied by additional symptoms such as nausea and sensitivity to light and sound.

Typically, pain is described as moderate to severe, throbbing, localised unilaterally, intensifying during exertion.

An attack may be preceded by visual or sensory sensations called a migraine aura [3]. Other prodromal symptoms may appear, including fatigue, irritability, yawning, sighing, neck or back stiffness, or mood changes [35]. The first symptoms are most often observed during puberty, when attacks tend to be shorter but are associated with stronger abdominal symptoms [2].

Despite extensive research, the exact cause is still unknown. Currently, the cause is believed to be the release of pain-inducing and pro-inflammatory substances in the area of the blood vessels and nerves of the head. Examples of factors that trigger a headache attack include eating certain foods, consuming alcohol, stress, sleep disturbances, weather changes, menstrual changes [2, 36].

Migraine without aura: criteria from International Classification of Headache Disorders 3rd Edition (ICHD-3):

Criterion	Description
A	At least 5 attacks fulfilling criteria B–D
B	Headache lasting 4–72 hours
C	At least 2 of the following characteristics: • Unilateral location • Pulsating quality • Moderate or severe pain intensity • Aggravation by or avoidance of routine physical activity
D	At least 1 of the following symptoms: • Nausea and/or vomiting • Photophobia and phonophobia
E	Not better explained by another ICHD-3 diagnosis

Migraine with aura: criteria from International Classification of Headache Disorders 3rd Edition (ICHD-3):

Criterion	Description
A	At least 2 attacks fulfilling criteria B and C
B	One or more of the following fully reversible aura symptoms: 1. visual 2. sensory 3. speech and/or language 4. motor 5. brainstem 6. retinal
C	At least three of the following six characteristics: 1. at least one aura symptom spreads gradually over ≥5 minutes 2. two or more aura symptoms occur in succession 3. each individual aura symptom lasts 5-60 minutes[1] 4. at least one aura symptom is unilateral[2] 5. at least one aura symptom is positive[3] 6. the aura is accompanied, or followed within 60 minutes, by headache
D	Not better accounted for by another ICHD-3 diagnosis

1.3 Pathophysiology of migraine, role of CGRP:

Initially vasodilation was assumed to be the primary cause of migraine [25]. Progression in understanding the process of migraine attacks shows that it is rather the effect of neurogenic inflammation and other mechanisms [26]. The most commonly cited causes include activation of the trigeminal vascular system, release of vasoactive neuropeptides (especially CGRP), and cortical spreading depression (CSD) [21, 26, 27, 31-34].

Stimulation of trigeminal nerve fibers leads to the release of inflammatory mediators such as calcitonin gene-related peptide (CGRP), substance P, and neurokinin A. Their action leads to meningeal vasodilation, neurogenic inflammation, and the transmission of nociceptive stimuli to the brainstem and higher cortical structures. It is suggested that these are responsible for sustaining the symptoms of the attack [21].

The phenomenon that explains the occurrence of migraine aura is the aforementioned cortical spreading depression (CSD), which consists of a temporary inhibition of cerebral cortex activity caused by a wave of depolarization of neurons and glial cells. This depolarization also leads to the excitation of afferent fibers of the trigeminal nerve which starts the episode [21].

CGRP performs many functions in the body, including vascular, digestive, sensory, vestibular and haematopoietic functions, as well as immunomodulatory effects and the perception of pain stimuli [27]. It exists in two forms: the alpha form, which is involved in the pathogenesis of migraine and is found mainly in the sensory neurons of the trigeminal system, and the beta form. The CGRP receptor consists of the CLR and RAMP1 proteins and a G-protein-coupled receptor; its activation leads to the activation of adenylate cyclase and an increase in cAMP, producing effects dependent on the type of cell to which it is bound [28]. CGRP is found primarily in C- and Aδ-type sensory fibers. It causes cerebral vasodilation and abnormal activation of the trigeminal-vascular system responsible for pain transmission. Additionally, CGRP induces neuroinflammation by stimulating mast cell degranulation and the release of IL-1 from satellite glial cells [29, 30, 31]. As a result, these processes lead to the development and maintenance of a state of hypersensitivity in the pain system [32]. CGRP inhibition has become an important target in migraine therapy. Direct blocking of CGRP or its receptor is possible through the use of monoclonal antibodies and gepants. It was initially thought that triptans relieved migraine pain mainly through vasoconstriction via 5-HT1B and 5-HT1D receptors. However, it turned out that many CGRP neurons in the trigeminal ganglion possess 5-HT1B, 5-HT1D and 5-HT1F receptors. Therefore, serotonin receptor agonists, such as triptans and lasmiditan, may act similarly to gepants by inhibiting the release of CGRP and other neurotransmitters from primary trigeminal neurons, thereby reducing activation of the trigeminal-vascular system and migraine pain [33, 34].

1.4 Importance of effective treatment to stop attack.

The main goal of migraine treatment is to quickly and permanently relieve pain and accompanying symptoms. The appropriate selection of treatment and the timing of its implementation are of great importance, as early intervention limits the development of central sensitization. Triptans – 5-$HT_1B/_1D$ agonists – despite their side effects, have been used successfully for this indication for many years [11, 16, 24].

In recent years, a new class of drugs has been introduced – Gepants [6]. Their action is directed at blocking the receptor for calcitonin gene-related peptide (CGRP).These drugs are also effective in interrupting migraine attacks, with a different safety profile than triptans. This offers the prospect of their implementation in patients with contraindications to the use of vasoconstrictive drugs [6].

Medication overuse headache (MOH) is a complication that can occur with the frequent use of medication, particularly triptans, non-steroidal anti-inflammatory drugs, or combination analgesics. According to the International Classification of Headache Disorders, it occurs in patients who overuse the medication form for more than 15 days a month for more than three months. The mechanism involves changes in pain-modulation pathways. This can result in chronification of the migraine and reduce the effectiveness of the treatment [3, 22, 23].

2. Aim of the study and research questions.

The study reviewed current clinical trials and systematic reviews evaluating the effectiveness of these therapies in interrupting migraine attacks. The analysis primarily covers the assessment of primary endpoints used in clinical trials for the treatment of acute migraine attacks, such as complete pain relief within two hours of drug administration, maintenance of analgesic effect in the hours following treatment, as well as the frequency of pain recurrence and the occurrence of adverse events [4-11,14-16].

The aim of the study is also to determine the potential place of CGRP receptor antagonists in current migraine attack treatment regimens and to assess their significance as a therapeutic alternative for patients in whom the use of triptans is ineffective or contraindicated [14, 15, 24].

RESEARCH QUESTIONS:

Based on the above assumptions, the following research questions were formulated:

1. How effective are CGRP receptor antagonists in interrupting migraine attacks compared to triptans?
2. What are the differences in the duration and persistence of action between the analyzed groups of drugs?
3. Is the safety profile of gepants more favorable than that of triptans?
4. Can gepants be an alternative for patients who have contraindications to the use of triptans?
5. Where do CGRP receptor antagonists stand in relation to current strategies for acute migraine attacks?

3. Materials and methods.

3.1 Research strategy.

This narrative review was conducted to identify studies evaluating the efficacy and safety of therapies used in the acute treatment of migraine attacks, with a particular focus on triptans and calcitonin gene-related peptide (CGRP) receptor antagonists. The literature search was conducted using PubMed/MEDLINE, Scopus, and Google Scholar electronic databases. No restriction regarding the publication date was applied during the literature selection process. This decision was made due to the different times of introduction of the two drug groups into clinical practice. Limiting the search to only the most recent publications could have resulted in the underrepresentation of studies concerning the earlier-introduced therapies. Therefore, studies published across all available years were considered to ensure a comprehensive and balanced comparison of both drug groups.. A combination of the following keywords related to acute migraine treatment, CGRP, triptans and gepants was used: “migraine”, “acute migraine treatment”, “triptans”, “sumatriptan”, “rizatriptan”, “zolmitriptan”, “eletriptan”, “CGRP receptor antagonists”, “calcitonin gene-related peptide”, “gepants”, “ubrogepant”,

“rimegepant”, “zavegepant”, “atogepant”, “randomized controlled trial”, “efficacy”, “safety”. Boolean operators were applied to construct search strings analogous to those used in contemporary scoping and systematic reviews of acute migraine treatment.

3.2 Inclusion and exclusion criteria.

The analysis included publications meeting the following criteria: (1) clinical trials (randomized controlled trials, RCTs) or systematic reviews and meta-analyses; (2) Publications on acute treatment of migraine attacks; (3) Studies involving adult patients (≥18 years) diagnosed with migraine; (4) Articles published in English; (5) Studies evaluating the efficacy or safety of triptans or CGRP receptor antagonists.

Publications meeting at least one of the following criteria were excluded from the analysis: (1) Studies on migraine prevention rather than acute attack treatment; (2) Articles of an expert opinion, commentary, or letter to the editor nature; (3) Studies conducted exclusively on animal models or in laboratory conditions; (4) Studies involving small groups of patients without randomization or of limited methodological quality; (5) Publications that did not include data on clinical efficacy or treatment safety.

3.3 Endpoints analyzed.

The analyzed studies included the most commonly used endpoints for the efficacy of acute migraine treatment.

Primary endpoints:

- Complete pain relief 2 hours after administration of the drug (pain freedom at 2 hours).
- Absence of the most bothersome symptom (MBS) within 2 hours.

Secondary endpoints:

- Sustained pain freedom within 24 hours - Time for headache resolution.
- Frequency of migraine pain recurrence within 24–48 hours.

- Effect of treatment on accompanying symptoms such as nausea, photophobia, and phonophobia.

Safety endpoints:

- Frequency of adverse events.
- Type of adverse events reported.

4. Characteristics of the analyzed drug groups

4.1. Triptans

Triptans are selective agonists of serotonin 5-HT_1B and 5-HT_1D receptors, which are first-line acute medications for mild to severe migraine attacks [8,9,16]. Their effective anti-migraine action results from several synergistic mechanisms:

- vasoconstriction (which opposes the vasodilation typical of a migraine attack) [18]
- inhibition of neuropeptide release (including CGRP - calcitonin gene-related peptide) which results in reduced swelling, limitation of the local inflammatory response, and decreased sensitivity of pain receptors [17,18,19],
- inhibition of pain conduction within the trigeminal-spinal system - weakening the activation of second-order neurons in the trigeminal spinal nucleus and reducing central sensitization, which leads to a reduction in the intensity of migraine pain [17,18].

The above mechanisms lead to: immediate pain relief and reduction of clinical symptoms (nausea, photophobia, improvement in patient functioning) [8,9].

The most commonly used products:

- sumatriptan – this was the first product to be launched on the market; it is available in subcutaneous, intranasal, and oral forms; it has a rapid onset of action, especially the subcutaneous form; it is effective in acute migraine attacks and in migraine attacks with clinical symptoms such as nausea [16,20],
- rizatriptan - a drug available in oral form (tablets that dissolve in the mouth), it has a fast onset of action of about 30 minutes and is effective in 2-hour pain freedom [9,20],

- zolmitriptan - a preparation available in nasal form, which has an advantage compared to others during vomiting, has good penetration into the CNS and is characterized by fast action [16],
- eletriptan - has a lower percentage of pain recurrence, which gives it an advantage over other drugs and is often chosen as a second option after sumatriptan due to its beneficial effect on patients who do not respond to other triptans [9,16],

Contraindications associated with the action of triptans mainly result from their vasoconstrictive effect. The main and absolute contraindications are cardiovascular diseases, especially stable and unstable coronary artery disease, previous myocardial infarction, and confirmed coronary vasospasm (e.g., Prinzmetal angina). 5-HT_1B receptors are present in the smooth muscles of the coronary arteries, which is why triptans cause them to contract and may lead to potential ischemia [11,18]. Cerebrovascular diseases, such as history of ischemic stroke/TIA, documented cerebrovascular disease, and peripheral artery disease, are also associated with this effect [8,11]. Triptans may also lead to a temporary increase in blood pressure, which increases the risk of cardiovascular complications in patients with unstable or severe hypertension [8,11].
Due to the increased risk of CNS ischemia, they are also contraindicated in patients with hemiplegic migraine and migraine with aura involving brainstem symptoms [11,12]. In order not to increase the vasoconstrictive effect, triptans should not be taken with other drugs from this group and/or with ergotamine; the required interval between these drugs should be at least 24 hours [11].
Triptans are drugs metabolized in the liver, mainly by monoamine oxidase A (MAO-A) and, to a lesser extent by cytochrome P450, they should not be used concomitantly with MAO-A inhibitors (this applies in particular to sumatriptan, rizatriptan, and zolmitriptan) due to the possibility of increased drug concentration [4,11]. This leads to another conclusion that severe liver failure is a contraindication for taking triptans, as they impair liver function, e.g., by reducing clearance and increasing systemic exposure to the drug, which may cause the effects of triptans to accumulate and lead to more severe side effects [4,8].

4.2. Gepants

Gepants are CGRP receptor antagonists which act mainly by temporarily and reversibly blocking the interaction between CGRP and its receptor, leading to a reduction in inflammatory swelling and counteracting pathological pain transmission [6,7,19]. Unlike triptans, they do not cause vasoconstriction and act independently of the serotonin response [6,7]. As gepants are composed of small molecules, which allows them to be administered orally, quickly reach therapeutic concentrations, and limit side effects from the central nervous system, as they act mainly at the systemic level [4,6,15]. These drugs are an acute treatment alternative to triptans, but can also be used as a prevention of chronic migraine by reducing the number of attacks [6,10,15].

Most commonly used:

- ubrogepant - a drug registered for the treatment of acute migraine attacks, effective in patients with a history of failure to respond to triptan therapy and with cardiovascular conditions [5,10,15],
- rimegepant - a drug used for both acute treatment and prophylaxis, characterized by good tolerability and convenient dosing (in prophylactic dosing, it should be taken every other day) [6,10,15],
- atogepant - used in the prevention of episodic migraine, administered orally once a day, which increases patient comfort, and is an alternative to monoclonal antibodies [15],
- zavegepant - characterized by its rapid onset of action, which is made possible by its intranasal form, which is also an alternative for people with migraine with clinical symptoms such as vomiting, it is a relatively new drug that is becoming a competitor to intranasally administered triptans [8,15],

Due to the fact that gepants do not cause vasoconstriction, their contraindications are different and narrower compared to triptans [6,7,15]. They are mainly based on the fact that these drugs are metabolized by CYP3A4, which makes them contraindicated in severe liver failure, particularly ubrogepant and atogepant [4,6,15]. Concomitant use of gepants with ketoconazole, clarithromycin, or HIV protease inhibitors may lead to drug interactions and cause accumulation of gepants in the body, which is additionally associated with increased side effects [4,8,15]. This effect may be related to the inhibition of CYP3A4 activity by these drugs [4]. This also means avoiding drugs that induce CYP3A4, such as rifampicin, which may reduce the effectiveness of gepants [4,15].
Due to the lack of sufficient clinical studies, administration to pregnant and/or breastfeeding women is not recommended [8,15]. A rare contraindication is hypersensitivity to the active pharmaceutical ingredient, specifically rimegepant, which may cause an allergic reaction [8,15].

5. Comparison of clinical efficacy

5.1. 2-hour pain freedom

A common criterion for assessing the clinical efficacy of triptans and gepants is the so-called 2-hour pain freedom, which is a freedom from pain 2 hours after administration of the drug. Based on meta-analyses and scientific studies, it can be concluded that both groups of drugs fulfill this criterion [9,10,20]. However, when comparing the two groups, triptans show higher

efficacy at this time point than gepants, with higher rates of both complete pain relief and reduction in pain intensity after 2 hours compared to ubrogepant or rimegepant, as demonstrated in a meta-analysis of 64 randomized clinical trials (over 46,000 patients) [9,10,20]. Gepants (in particular ubrogepant and rimegepant) show significant efficacy in the treatment of acute migraine attacks, as confirmed by a study showing that their effect on 2-hour pain freedom after administration was significantly higher compared to the placebo group [5,10,15]. In a real-world study of rimegepant, approximately 44-50% of patients achieved pain freedom within 2 hours, with earlier administration of the drug increasing the efficacy of the therapy [5,15]. In summary, triptans are faster acting and more effective in relieving pain 2 hours after administration, but gepants provide moderate and stable efficacy [9,10,15].

5.2. 24-hour pain relief

An important clinical parameter is the maintenance of the analgesic effect for 24 hours [9,10]. Studies have shown that patients using gepants were more likely to maintain pain relief for 24 hours compared to patients taking triptans [10,15]. This may be due to the pharmacokinetics of gepants, which block CGRP receptors, ensuring more stable inhibition of the pain cascade [17,19]. Triptans, on the other hand, have a faster onset of action but a short-lived therapeutic effect, which may lead to a shorter pain-free interval [20].

5.3. Migraine recurrence

An equally important clinical aspect to consider is migraine recurrence [9,10]. Patients using gepants experience a lower recurrence rate, which is most likely due to a more direct effect on the CGRP pathway, which is responsible for maintaining neurogenic inflammation during migraine attacks [17,19]. In contrast, triptans have a shorter duration of action, resulting in faster recurrence of migraine attacks in some patients [20].

5.4. Effect of drugs on accompanying symptoms

Migraine is a syndrome of symptoms that include headache, nausea, vomiting, photophobia, phonophobia and hypersensitivity to smells [3,17]. Studies on triptans and gepants have shown that they not only effectively reduce headache pain, but also improve associated symptoms [9,10,15]. This is due to their agonistic effect on serotonin receptors 5-HT_1B and 5-HT_1D, whose activation leads to the inhibition of the release of pro-inflammatory neuropeptides such as CGRP and to a direct effect on these receptors, which play a key role in the development of neurogenic inflammation and in the genesis of migraine symptoms [17,18,19]. Triptans act quickly to relieve headache within the first 2 hours after administration, but also have an effect on photophobia and/or phonophobia [9,20]. They inhibit gastrointestinal symptoms such as nausea and vomiting, which is highly important for patients who find it difficult to take oral medication and carry out their daily activities [11,20]. The best effects of triptans are observed when they are taken in the early stages of a migraine attack, before full central sensitization occurs within the trigeminal-vascular system [17,18]. As for gepants, they show superiority and faster relief of pain and accompanying symptoms than placebo [5,10,15]. The improvement includes both sensory symptoms, such as sensitivity to light and sound as well as gastrointestinal symptoms [5,15].Both triptans and gepants are effective in relieving the

symptoms associated with acute migraine attacks, but their mechanisms of action are different [6,7,17]. Gepants directly block the release of CGRP, while triptans act by activating serotonin receptors and inhibiting the release of neuropeptides [6,18,19]. As a result, both groups contribute to improving the overall condition of the patient during a migraine attack, although gepants may have a more favorable tolerance profile [8,15].

6. Comparison of drug safety

The use of triptans in the treatment of migraine has provided a good understanding of their safety profile [8,11,16]. The most characteristic adverse effects of this class of drugs include paresthesia, tingling, dizziness, a sensation of warmth, drowsiness, weakness, nausea, and a feeling of heaviness or tightness in the chest. These symptoms are commonly referred to as "triptan sensations" [8,11].

Symptoms such as chest pain or a sensation of heaviness in the chest may be related to the agonistic effect of triptans on 5-HT_1B/5-HT_1D serotonin receptors, which can lead to vasoconstriction [17,18]. Despite these symptoms, there was no relationship found between the use of triptans and increased risk of ischemic heart disease; however, the appearance of such symptoms requires caution and appropriate clinical evaluation [8,16].

For this reason, the use of triptans is contraindicated or requires special caution in patients with ischemic heart disease, uncontrolled hypertension, peripheral vascular disease, and in individuals with a history of cerebrovascular events [8,11].
Gepants, unlike triptans, do not affect serotonin receptors, and their mechanism of action involves CGRP receptor antagonism [6,7,19]. Consequently, they do not exhibit vasoconstrictive effects. For this reason, the advantage of gepants over triptans appears particularly significant in the population of patients with an increased cardiovascular risk [7,10,15].

At the same time, the available research findings indicate that it is necessary to maintain caution when using this class of drugs in this patient population. This is because the full long-term safety profile of gepants still requires further study [8,15]. Regardless of the choice of therapy, an individualized approach to each patient and appropriate monitoring of treatment are essential [8,11].

7. Discussion

Migraine is a chronic neurological disorder whose pathophysiology is associated with the activation of the trigeminal-vascular system and the release of neuropeptides such as CGRP [17,18,19,21]. The groups of migraine medications analyzed in this study—such as triptans and a newer form of therapy targeting CGRP receptors, including gepants—base their action precisely on such mechanisms [6,7,18,19].

Practical significance of the results

From a clinical perspective, based on the mentioned studies, triptans represent one of the primary therapeutic options for treating acute migraine attacks [9,11,20,24]. Their practicality is based on high efficacy and rapid onset of action [9,20,24]. At the same time, newer medications, such as gepants, represent a significant alternative for patients in whom the use of triptans is contraindicated or ineffective [6,7,10,15,24]. It has also been demonstrated that gepants effectively reduce symptoms accompanying migraine attacks, such as nausea, vomiting, photophobia, and phonophobia, which contributes to an improvement in patients' quality of life [5,10,15]. Based on these data, it is possible to identify patient groups for whom specific treatment strategies may have a particularly beneficial effect [8,10].

The impact of gepants on the medication overuse headache risk

Medication overuse headache (MOH) is a chronic headache caused by the overuse of pain relievers to treat migraines. It is diagnosed when medications are taken for at least 10–15 days a month for more than 3 months [23]. The cited articles suggest that CGRP receptor antagonists, known as gepants, may be associated with a lower risk of inducing MOH [22,23]. Studies show that repeated administration of gepants does not lead to the development of sensitization within the trigeminal-vascular system or to cutaneous allodynia, which are recognized mechanisms underlying MOH. In preclinical models, blocking the
CGRP pathway may even limit the mechanisms leading to the development of MOH [23]. However, it should be noted that clinical data in this regard are limited and typically involve short observation periods. Therefore, long-term studies are needed to unequivocally determine this mechanism of gepants [22].

Potential sponsorship bias

When interpreting the results of these studies, the possibility of sponsorship bias must also be taken into consideration. Some clinical trials of gepants were funded by pharmaceutical companies involved in the development of these drugs; while they were conducted in accordance with methodological standards, the funding may influence aspects of study design, data presentation and interpretation of results [6,7,9,15]. Therefore, it is essential to critically appraise both individual trials and meta-analyses when evaluating the efficacy and safety of new migraine therapies [9,10,15].

8. Conclusions:

Migraines represent a significant public health problem due to their recurrent nature, substantial impact on patients' quality of life, and daily functioning. An effective treatment option allows patients to maintain proper social and professional functionality despite the chronic nature of the disease.

The analysis of literature indicates that triptans remain the first-line treatment option in acute migraine attacks. They have a rapid onset of action and are highly effective within the first 2 hours after taking the medication. We have to acknowledge that triptans are short-term acting medications, so the pain can recur. Gepants are a promising alternative for patients with contraindications for using triptans. The key feature of gepants is their longer-lasting anti-pain effect, which improves patient comfort and reduces the recurrence of pain. Another notable effect of gepants is their ability to inhibit the mechanisms that lead to medication-overuse headaches (MOH); by comparison, triptans do not have this effect.

Both medication groups are highly effective in relieving the symptoms associated with acute migraine attacks, such as nausea, photophobia, and vomiting. However, gepants are preferred in patients who are prone to side effects from triptans, as they have a more favorable tolerability profile. In terms of safety, the main disadvantage of triptans is their vasoconstrictive effect, which makes them contraindicated in patients with an increased cardiovascular risk; in this case, gepants, which do not affect blood vessels, serve as an alternative treatment. Despite all the advantages of the safety profile of gepants, treatment with them is currently expensive, which is why triptans remain the more cost-effective option in patients who tolerate them.
The influence of pharmaceutical companies on scientific research into these classes of drugs should also be mentioned. This highlights the need for a critical evaluation of the scientific literature, even when methodological standards are applied.

Both triptans and gepants play an important role in the treatment of acute migraine attacks. The therapy choice should be based on the patient's clinical condition, safety and toleration of the pharmacotherapy. Further studies are needed to improve treatment strategies.

Disclosure section

Funding Statement:

This research received no external funding.

Institutional Review Board Statement:

Not applicable, as this study is based on a review of previously published literature.

Informed Consent Statement:

Not applicable.

Data Availability Statement:

No new data were created or analyzed in this study. Data sharing is not applicable to this article.

Conflict of Interest Statement:

The author declares no conflicts of interest.

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All authors have read and agreed to the published version of the manuscript.

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During the preparation of this work, the authors used Chat GPT for the purpose of improving language and readability, formatting the text, and verifying bibliographic styles. After using this tool, the authors reviewed and edited the content as needed and take full responsibility for the substantive content of the publication.. After using this service, the authors reviewed and edited the content as needed and take full responsibility for the substantive content of the publication.

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