

## Migraine management in Saudi Arabia: An expert consensus

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## ABSTRACT

**الأهداف:** وضع بيان توافقي من قبل خبراء حول العلاج الوقائي للصداع النصفي في المملكة العربية السعودية، مع التركيز على استخدام الأجسام المضادة أحادية النسيلة لمستقبل الببتيد المرتبط بجين الكالسيتونين (CGRP mAbs)، في ضوء أحدث الإرشادات الدولية والممارسات السريرية المحلية.

**المنهجية:** أجريت دراسة قائمة على السجلات بأثر رجعي في قسم الأشعة في مستشفى في المنطقة الشرقية من المملكة العربية السعودية، من يناير 2019م إلى 2024م. أخذنا المرضى البالغين الذين أجريت لهم تصوير الدماغ لإجراء فحص الصرع مع إضافة تسلسل SWAN (تصوير الأوعية الدموية المرجح بالاستعداد) في الاعتبار. تم استبعاد حالات أورام المخ وما بعد الإصابة وما بعد الجراحة. تم توثيق ورم وعائي وريدي عندما ظهرت خضلة من الأوردة التي تم تصريفها إلى وريد أكبر (تمر عبر القشرة أو تصل إلى أسفل طبقة البطانة العصبية)، وظهرت بنية متفرعة منحنية ذات إشارة منخفضة على صورة SWAN. تم تحديد فائدة تسلسل SWAN في الكشف عن التشوه الوريدي فيما إذا كان الشذوذ المرتبط بتركيز ينتج عنه موجات غير طبيعية في تخطيط كهربية الدماغ. تمت مقارنة هذه الملاحظة بالتشوهات التي تم العثور عليها عن طريق الصدفة والتي شوهدت في مرضى الصرع مع تخطيط كهربية الدماغ الطبيعي (مجموعة المراقبة). تم تطبيق اختبار فيشر الدقيق وتم اعتبار القيمة  $p < 0.05$  ذات دلالة إحصائية للارتباط.

**النتائج:** استعرضت اللجنة التوصيات الدولية المحدثة والبيانات السريرية الأخيرة التي تدعم استخدام الأجسام المضادة CGRP كخيار علاجي من الخط الأول للوقاية من الصداع النصفي. تم التوافق على عدد من النقاط الأساسية، مثل معايير بدء العلاج، واختيار المرضى المناسبين، ودور الأجسام المضادة في الممارسة السريرية. وشددت التوصيات على أهمية بدء العلاج الفعال مبكراً للحد من عبء المرض وتحسين جودة الحياة.

**الخلاصة:** يوفر هذا البيان التوافقي من الخبراء دليلاً محدثاً حول العلاج الوقائي للصداع النصفي في المملكة العربية السعودية، ويؤيد دمج الأجسام المضادة CGRP كخيار من الخط الأول. تهدف هذه التوصيات إلى رفع مستوى رعاية مرضى الصداع النصفي وتلبية الاحتياجات غير الملباة في النظام الصحي المحلي.

**Objective:** To establish expert consensus on the preventive treatment of migraine in Saudi Arabia, with a focus on the use of calcitonin gene-related peptide monoclonal antibodies (CGRP mAbs), in light of the latest international guidelines and local clinical practice.

**Method:** A record-based study was performed retrospectively in Radiology department at our Hospital in Eastern region of Saudi Arabia, from Jan. 2019-2024. Adult patients for whom MRI brains were conducted for epilepsy work-up with added SWAN (susceptibility weighted angiography) sequence were considered. Brain tumor, post-injury, and post-surgery cases were excluded. A venous angioma was documented when a tuft of veins drained to a larger vein (traversing through cortex or reaching under ependymal layer), appeared low signal curvilinear branching structure on SWAN image. The usefulness of the SWAN sequence in

the detection of venous malformation determined if the visualized abnormality was found to be related to a focus resulting in abnormal waves on the brain electroencephalography. This observation was compared to the accidentally found such malformations that were seen in epileptic patients with normal EEGs (control group). Fisher's Exact test was applied and a  $p$ -value of  $<0.05$  was taken as statistically significant for an association.

**Results:** The expert panel reviewed updated clinical data and recent international guidelines recommending CGRP mAbs as first-line preventive treatment options. The panel reached consensus on key aspects of migraine management in Saudi Arabia, including treatment initiation criteria, patient selection, and the role of CGRP mAbs in clinical practice. The recommendations emphasize the need for earlier initiation of effective treatments to reduce disease burden and improve quality of life.

**Conclusion:** This expert consensus provides updated guidance on the preventive treatment of migraine in Saudi Arabia, supporting the integration of CGRP mAbs as a first-line option. These recommendations aim to enhance the standard of migraine care and address unmet needs in the local healthcare setting.

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Migraine is a common neurological disorder, affecting over 10% of people worldwide. It ranks as the second leading cause of disability globally.<sup>1</sup> In Saudi Arabia, the most recent estimates suggest that at least 25% of the population suffers from migraines, a rate significantly higher than the global average.<sup>2</sup> Migraine is more prevalent in women and is a highly disabling condition affecting patients, their families, and society.<sup>3,4</sup> The disease negatively impacts quality of life (QoL), including physical, emotional, and social aspects of daily life, such as family, work, and social relationships.<sup>5</sup> Additionally, migraine imposes a substantial economic burden and increases healthcare resource utilization.<sup>6</sup> In the United States (US), the annual cost burden has been estimated at over \$56 billion (inflated to 2013 US dollars), with over 60% of this figure attributable to direct costs.<sup>7</sup> Therefore, the availability of effective and safe treatments for migraine is essential to improve QoL and alleviate the burden of the disease.<sup>8</sup>

**Migraine Treatment.** Migraine treatment is categorized into acute and preventive therapies. Acute treatment is used for resolving migraine attacks, while preventive therapy is used to reduce the frequency, severity, and duration of migraine attacks. Despite the available evidence and guidelines on migraine treatment, it still remains underestimated, underdiagnosed, and undertreated in our region.<sup>9</sup>

Conventional preventive treatments for migraines include propranolol, timolol, tricyclic antidepressants (TCAs), and topiramate. However, despite these medications, most patients fail to achieve optimal long-term treatment outcomes. This issue may be attributed to treatment discontinuation due to side effects or failure to achieve the desired response. Consequently, there is a significant need for improved migraine management.

A new class of treatment, Calcitonin Gene-Related Peptide (CGRP) monoclonal antibodies (mAbs), has been approved as an effective and safe preventive option for migraine, with erenumab being the first CGRP mAb approved by the United States Food and

Drugs Administration (US FDA) in 2018.<sup>10</sup> Clinical trials of CGRP mAbs have demonstrated impressive safety and efficacy profiles, reshaping the migraine treatment landscape.<sup>11</sup> Four CGRP mAbs have been approved: erenumab, fremanezumab, galcanezumab, and eptinezumab.<sup>11</sup> In Saudi Arabia, only erenumab, galcanezumab, and eptinezumab have been approved.

A consensus statement published in 2021 by the American Headache Society (AHS) provided guidance on when to initiate the use of CGRP mAbs based on the available and clinical experience at that time.<sup>12</sup> The statement recommended that CGRP mAbs could be commenced after at least two oral preventive treatments proved unsuccessful.<sup>12</sup> Since then, new evidence has emerged regarding the efficacy, safety, and tolerability of CGRP mAbs along with extensive real-world experience gained through the use of CGRP mAbs, which led to an updating of the AHS statement in 2024.<sup>13</sup> In this updated position statement, CGRP mAbs are recommended as a first-line option for migraine prevention without requiring prior trials or failure of other conventional treatments.<sup>13</sup> The updated European headache federation (EHF) consensus was the first guidelines to endorse CGRP mAbs as a first-line option for migraine prevention.<sup>14</sup> This updated EHF guideline from 2022 states that, in individuals with migraine who require preventive treatment, CGRP mAbs should be included as a first-line treatment option.<sup>14</sup>

Despite the previously mentioned facts about the burden of migraine and the available data and updated guidelines for migraine treatments, there remains a need for optimum migraine management in Saudi Arabia, specifically regarding migraine preventive treatments. This expert consensus statement aims to provide an update on the management of migraine in Saudi Arabia, considering the available therapeutic agents of CGRP mAbs for migraine treatment and prevention.

**Methods.** An expert panel in neurology convened virtually to reach a consensus on the preventive treatment of migraine in Saudi Arabia. Ten neurologists and headache specialists from various regions of the Kingdom reviewed and discussed the latest available evidence on migraine management, including the use of CGRP mAbs. Afterward, a set of tailored questions was distributed to the experts via a web-based questionnaire. Panel members were asked to select the most accurate statement based on available evidence and their clinical practice. Statements that achieved at least 70% agreement among the panel members were considered

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**Table 2 -** Summary of the Expert Consensus Statements.

| Questions                                                                                                                                                                                                                                                                                                                                  | Statements                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <i>Question 1. When should migraine preventive treatments be offered to individuals with migraine?</i>                                                                                                                                                                                                                                     | Migraine preventive treatments should be offered to individuals with migraine in the following cases:<br><ul style="list-style-type: none"> <li>• Four or more migraines per month</li> <li>• Highly disabling migraine attacks (migraine with brainstem aura or hemiplegic migraine)</li> <li>• Two severe or disabling attacks not responding to acute migraine treatment, or acute treatment is contraindicated</li> </ul>                                                                                                                                                                                                                              |
| <i>Question 2. What are the different preventive treatment classes approved for the preventive treatment of episodic migraine patients and available in Saudi Arabia?</i>                                                                                                                                                                  | Preventive treatments approved for episodic migraine patients in Saudi Arabia include conventional treatment options, which are TCAs, BBs, anti-seizures, and the newer specific class, CGRP mAbs.                                                                                                                                                                                                                                                                                                                                                                                                                                                         |
| <i>Question 3. What are the different preventive treatment classes approved for the preventive treatment of chronic migraine patients and available in Saudi Arabia?</i>                                                                                                                                                                   | Preventive treatments approved for chronic migraine patients in Saudi Arabia are TCA, BBs, anti-seizures, and CGRP mAbs, in addition to onabotulinumtoxin A.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |
| <i>Question 4. What are the important factors for the optimal drug selection of preventive treatment?</i>                                                                                                                                                                                                                                  | Multiple important factors should be considered during the drug selection for optimal preventive treatment, including evidence of efficacy, patient preference, contraindications and allergies, tolerability and adherence, comorbid and coexistent illness, and cost and availability.                                                                                                                                                                                                                                                                                                                                                                   |
| <i>Question 5. When should the efficacy of migraine preventive treatments be evaluated after initiating treatment?</i>                                                                                                                                                                                                                     | The efficacy of migraine preventive treatments should be evaluated two to three months after treatment initiation.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |
| <i>Question 6. What are the parameters for defining successful migraine treatment for migraine patients?</i>                                                                                                                                                                                                                               | Several parameters are used to define migraine treatment success for migraine patients, including the following:<br><ul style="list-style-type: none"> <li>• 50% reduction with three months in the frequency of days with episodic migraine</li> <li>• 30% reduction with three months in the frequency of days with headache or migraine for chronic migraine</li> <li>• Significant decrease in attack duration based on patient's headache diary</li> <li>• Significant decrease in attack severity based on patient's headache diary</li> <li>• Reduction in migraine-related disability and improvements in functioning, such as MIDAS</li> </ul>    |
| <i>Question 7. Based on the clinical evidence regarding the efficacy and safety of the CGRP mAbs, at what stage can monoclonal antibodies targeting CGRP pathway be offered to individuals with migraine throughout the treatment lines?</i>                                                                                               | CGRP monoclonal antibodies targeting the CGRP pathway can be offered to individuals with migraine at any stage of treatment, particularly as a first-line treatment.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
| <i>Question 8. What are the clinical indications to consider for CGRP mAbs at an early stage of migraine treatment, such as first-line treatment?</i>                                                                                                                                                                                      | CGRP mAbs can be considered at an early stage of treatment in the following cases:<br><ol style="list-style-type: none"> <li>1) A high chance of developing side effects from oral preventive treatments based on history, comorbidities, or other oral medications</li> <li>2) A high chance of drug-drug interaction with other oral treatments</li> <li>3) A high chance of low adherence to oral treatment and/or an inability to take oral preventive treatments due to medical reasons (gastrointestinal reasons), social/religious reasons (fasting, nature of work), or the patient's preference not to take oral preventive treatments</li> </ol> |
| <i>Question 9. When should stopping treatment with CGRP mAbs be considered in individuals with migraine?</i>                                                                                                                                                                                                                               | CGRP mAbs treatment cessation should be considered in the following cases:<br><ul style="list-style-type: none"> <li>• The development of life-threatening or severe side effects or complications</li> <li>• The development of intolerable or disabling mild to moderate side effects</li> <li>• After 12 months of treatment with consistent benefits over the last three months of <math>\geq 75\%</math> reduction from baseline before starting CGRP mAbs treatment, as well as improvement in the migraine disability score (such as MIDAS)</li> </ul>                                                                                              |
| <i>Question 10. In individuals with migraine who failed one CGRP mAb, is switching to a different antibody an option?</i>                                                                                                                                                                                                                  | In individuals with migraine who failed one CGRP mAb, switching to a different CGRP mAb—either a CGRP receptor blocker or a CGRP ligand blocker—could be an option.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |
| <i>Question 11. Can treatment with CGRP mAbs be combined with other classes of preventive treatments, such as oral preventive treatments or onabotulinumtoxin A?</i>                                                                                                                                                                       | CGRP mAbs can be combined with other classes of preventive treatments, especially the combination of CGRP mAbs and onabotulinumtoxin A.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |
| <i>Question 12. In which individuals with migraine is caution suggested when considering treatment with CGRP mAbs?</i>                                                                                                                                                                                                                     | Caution is suggested when considering migraine treatment with CGRP mAbs in pregnant and nursing women, individuals with latex allergy, and individuals with a history of constipation or hypertension (with erenumab).                                                                                                                                                                                                                                                                                                                                                                                                                                     |
| <i>Question 13. Would the availability of a local clinical practice guideline for the diagnosis and treatment of migraine patients, as well as establishing a national registry for migraine, help clinical decision-makers and medical institutions make proper decisions that would improve the clinical care for migraine patients?</i> | The availability of a local clinical practice guideline for the diagnosis and treatment of migraine patients and establishing a national registry for migraine could help clinical decision-makers and medical institutions make proper decisions that would improve clinical care for migraine patients.                                                                                                                                                                                                                                                                                                                                                  |

**Table 1 -** Factors for optimal drug selection.

|                                                          |
|----------------------------------------------------------|
| Evidence of efficacy                                     |
| Medical professional experience                          |
| Tolerability                                             |
| Patient preference                                       |
| Headache subtype (episodic or chronic)                   |
| Comorbid and coexistent illnesses                        |
| Concomitant medications                                  |
| Physiological factors (e.g., heart rate, blood pressure) |
| Pregnancy or the potential for pregnancy among women     |
| Ease of use                                              |
| Response to previous treatments                          |

to have reached a consensus. A preliminary draft of the consensus recommendations was developed and shared with the panel again for their final approval.

**Results.** *Question 1. When should migraine preventive treatments be offered to individuals with migraine?*

Prophylactic treatment is a key aspect of migraine management, aimed at improving patients' QoL.<sup>15</sup> Such treatment can reduce a migraine attack's frequency, severity, and duration. Preventive treatment can also enhance the effectiveness of acute treatments during an attack.<sup>11,15</sup>

Since headache represents 1-4% of all emergency department visits and ranks among the top 20 reasons for outpatient visits, all migraine patients should be assessed to receive preventive treatment.<sup>16,17</sup> In practice, however, preventive therapy remains underutilized in migraine patients. In the US, data indicate that while 38% of migraine patients are eligible for prophylactic treatment, only 3-13% receive preventive therapy.<sup>17</sup>

Current guidelines recommend that migraine patients be considered for preventive treatment in the following cases:<sup>15</sup>

1. Acute migraine treatment is ineffective or contraindicated
2. The presence of medication-overuse headache
3. Highly disabling migraine attacks (migraine with brainstem aura or hemiplegic migraine)
4. Patient preference
5. Recurring migraine attacks that impair the patient's QoL
6. Frequent headaches of four or more episodes per month or eight or more headache days per month

The panel recommended that migraine preventive treatments should be offered to individuals with migraine in the following cases:

- Four or more migraines per month
- Highly disabling migraine attacks (migraine with

brainstem aura or hemiplegic migraine)

- Two severe or disabling attacks not responding to acute migraine treatment, or acute treatment is contraindicated

*Question 2. What are the different preventive treatment classes approved for the preventive treatment of episodic migraine patients and available in Saudi Arabia?*

The panel discussed different migraine preventive treatments that have been used in Saudi Arabia for many decades. These treatments are regarded as standard care and include B-blockers (BBs), anti-convulsants, antidepressants, and calcium channel blockers. Some of the conventional agents used for preventive migraine management in Saudi Arabia are prescribed off-label.

Regarding the CGRP mAbs class, the US FDA and the European Medicines Agency (EMA) have approved them all as preventive treatment for episodic migraine patients.<sup>14,18</sup> Currently, the Saudi Food and Drug Administration (SFDA) has approved three CGRP mAbs (galcanezumab, erenumab, and eptinezumab) for the prevention of episodic migraine.<sup>19</sup>

The panel agreed that the preventive treatments approved for episodic migraine in Saudi Arabia include conventional treatment options, like TCAs, BBs, anti-seizures, and the newer CGRP mAbs class.

*Question 3. What are the different preventive treatment classes approved for the preventive treatment of chronic migraine patients and available in Saudi Arabia?*

The panel discussed that although previous guidelines did not differentiate between episodic and chronic migraine management, recent clinical trials on migraine management are more defined. Botulinum toxin was approved for the preventive management of chronic migraines nearly a decade ago in the US and Canada.<sup>20</sup> Furthermore, CGRP mAbs had separate trials for chronic and episodic migraine and were approved for both indications.<sup>21</sup>

The SFDA drug list includes galcanezumab, erenumab, eptinezumab, and onabotulinumtoxin A for chronic migraine prevention.

The panel agreed that the preventive treatments approved for chronic migraine patients in Saudi Arabia are TCAs, BBs, anti-seizures, CGRPs mAbs, and onabotulinumtoxin A.

*Question 4. What are the important factors for the optimal drug selection of preventive treatment?*

The AHS guideline highlighted some essential factors to consider when undergoing preventive migraine agent selection (Table 1).<sup>12</sup> Optimal drug selection should be individualized and must account for several patient-related factors, such as patient preference,

tolerability, and comorbid conditions, in addition to the best available evidence and clinical experience.<sup>12,15,17</sup> Reproductive potential and family planning are also critical issues to discuss with female migraine patients of childbearing age.<sup>12</sup>

The panel recommended that multiple essential factors should be considered during the drug selection of optimal preventive treatment, including evidence of efficacy, patient preference, contraindications and allergies, tolerability and adherence, comorbid and coexistent illness, and cost and availability.

**Question 5. When should the efficacy of migraine preventive treatments be evaluated after initiating the treatment?**

The panel reviewed and discussed the concept that the efficacy of preventive treatment can be defined in terms of achieving a significant reduction in mean monthly headache days by at least 50% within 3 months. However, the duration and severity of the attack, the level of disability, and the extent of life impairment are other factors to be considered. Patient perspective must also be regarded seriously.<sup>12,15</sup>

Although most patients who are considered responders display a response within 3 months, it can take up to 6 months for a preventive agent to achieve its full therapeutic benefits.<sup>11,15,17</sup> Therefore, the AHS recommended that all preventive treatments be given an adequate trial (3 to 6 months) before treatment assessment.<sup>12</sup>

The CGRP mAbs are thought to have a rapid onset of action, and the effects can be visible within the first week of initiating treatment.<sup>14</sup> However, real-world data have revealed that response rates can increase over time in patients who do not display an adequate early response. Therefore, the EHF recommended that treatment with CGRP mAbs be first evaluated after at least 3 months of treatment. A decision to continue treatment for an additional period of 2 to 3 months might be considered in selected cases.<sup>14</sup>

The panel agreed that the efficacy of migraine preventive treatments should be evaluated in 2 to 3 months after treatment initiation.

**Question 6. What are the parameters used to define successful migraine treatment for migraine patients?**

The panel discussed that, for a preventive migraine treatment to succeed, it needs to reduce migraine attack frequency or days by at least 50% within 3 months for episodic migraine and 30% within 3 months for chronic migraine. Additional parameters include reduced attack duration or severity, enhanced response to acute treatments, improved ability to function, and reduced disability.<sup>11,12,15,17</sup>

The panel recommended several parameters to define migraine treatment success for migraine patients:

- 50% reduction with 3 months in the frequency of days with episodic migraine
- 30% reduction with 3 months in the frequency of days with headache or migraine for chronic migraine
- Significant decrease in attack duration based on the patient's headache diary
- Significant decrease in attack severity based on the patient's headache diary
- Reduction in migraine-related disability and improvements in functioning, such as MIDAS

**Question 7. Based on the clinical evidence regarding the efficacy and safety of the CGRP mAbs, at what stage can monoclonal antibodies targeting the CGRP pathway be offered to individuals with migraines throughout the treatment lines?**

Unlike the existing prophylactic treatments for migraine, CGRP mAbs are the first disease-specific preventive treatment for migraine.<sup>22</sup> Several clinical trials have proven their efficacy and unremarkable safety profiles.<sup>22</sup> Recent evidence supports CGRP mAbs having an efficacy that is at least comparable to the efficacy of the currently used preventive drugs, with excellent tolerability and ease of use.<sup>22,23</sup> The CGRP mAbs were recommended as a third-line treatment in the 2019 EHF guideline.<sup>24</sup> These treatments were initially considered following poor response, tolerability issues, lack of adherence, or after at least 2 other preventive treatment classes. However, the EHF guideline updated this recommendation in 2022 to favor the consideration of CGRP mAbs as a first-line treatment option, depending on patient condition and preferences.<sup>14</sup> As mentioned, the AHS guideline initially positioned CGRP mAbs after the failure of at least 2 other preventive treatments.<sup>12</sup> However, in their updated statement this year, the AHS positioned CGRP mAbs treatment as a first-line option for migraine prevention without the need for the previous trial or failure of the other conventional treatments.<sup>13</sup>

Our panel recommended CGRP mAbs be offered to individuals with migraine at any stage of the treatment course, particularly as a first-line treatment.

The panel agreed that monoclonal antibodies targeting the CGRP pathway can be offered to individuals with migraine at any stage of treatment, particularly as a first-line treatment.

**Question 8. What are the clinical indications for considering CGRP mAbs at an early stage of migraine treatment, such as first-line treatment?**

The panel discussed how CGRP mAbs were initially positioned by different regulatory bodies as a third-line treatment option after failing at least 2 oral preventive

agents due to poor response, tolerability, or compliance. However, the panel agreed that recent guidelines in favor of CGRP mAbs, owing to their efficacy, tolerability, and ease of use, mean they can be considered a first-line therapy.<sup>14</sup>

The panel agreed there are cases in which CGRP mAbs can be considered at an early stage of treatment. The clinical indicators include:

- 1) A high chance of developing side effects from oral preventive treatments based on history, comorbidities, or other oral medications.
- 2) A high chance of drug-drug interaction with other oral treatments.
- 3) A high chance of low adherence to oral treatment and/or an inability to take oral preventive treatments for medical reasons (gastrointestinal reasons), social/religious reasons (fasting, nature of work), or the patient's preference not to take oral preventive treatments.

**Question 9. When should stopping treatment with CGRP mAbs be considered for individuals with migraine?**

All available evidence is based on expert opinion. For CGRP mAbs, the EHF recommendation is to consider stopping CGRP mAbs treatment after 12–18 months based on patient response, tolerability, and preference.<sup>8</sup> Treatment should be stopped earlier if patients develop side effects that are intolerable or life-threatening.<sup>14</sup>

However, real-world data have revealed a worsening of symptoms for a few months after CGRP mAbs treatment discontinuation.<sup>25</sup> A follow-up study of patients after erenumab discontinuation found over 50% experienced early disease worsening.<sup>22</sup> A follow-up of three randomized controlled samples of participants on galcanezumab revealed a gradual reduction of effect upon treatment cessation, without signs of rebound headache four months post-treatment for most patients with episodic and chronic migraine.<sup>26</sup>

The panel agreed that CGRP mAbs treatment cessation should be considered in the following cases:

- The development of life-threatening side effects, complications or severe side effects
- The development of intolerable or disabling mild to moderate side effects
- After 12 months of treatment with consistent benefits over the last three months of  $\geq 75\%$  reduction from baseline before starting CGRP mAbs treatment, as well as improvement in the migraine disability score (such as MIDAS)

**Question 10. In individuals with migraine who failed one CGRP mAb, is switching to a different**

**antibody an option?**

The panel discussed a retrospective cohort study that included patients treated with one anti-CGRP after failing another, which revealed that switching non-responder patients from one anti-CGRP to another could provide some benefit.<sup>27</sup> Another multicenter retrospective study found that switching from erenumab to another CGRP mAb (galcanezumab or fremanezumab) in previously non-response patients resulted in a superior response.<sup>28</sup>

In line with the recent research on switching, the panel recommended that, for individuals with migraine who failed one CGRP mAb, switching to a different CGRP mAb—either a CGRP receptor blocker or a CGRP ligand blocker—could be an option.<sup>14</sup>

The panel agreed that, for individuals with migraine who failed one CGRP mAb, switching to a different CGRP mAb—either a CGRP receptor blocker or a CGRP ligand blocker—could be an option.

**Question 11. Can treatment with CGRP mAbs be combined with other classes of preventive therapies, such as oral preventive treatments or onabotulinumtoxin A?**

The panel discussed that no available evidence in the literature supports the efficacy and safety of combining CGRP mAb with oral preventive treatments. However, there is some evidence that may support the benefit of combining CGRP mAbs and onabotulinumtoxin A with no added side effects. The latest EHF guideline urges clinicians to weigh the benefits of combination versus the risks and follow an individualized treatment approach.<sup>28</sup>

Our panel agreed that CGRP mAbs can be combined with other classes of preventive treatments, especially between CGRP mAbs and onabotulinumtoxin A.

**Question 12. In which individuals with migraine is caution suggested when considering treatment with CGRP mAbs?**

The panel discussed and reviewed the available literature regarding women planning to conceive, as well as pregnant and lactating women. The panel agreed these women should be advised against using a preventive treatment due to the potential adverse events on the newborn or the developing fetus.<sup>12</sup> Caution is suggested when considering migraine treatment with CGRP mAbs in pregnant and nursing women due to the lack of data on this vulnerable population.<sup>12,14</sup>

Since real-world surveys have found that over 50% of patients on erenumab have developed some degree of constipation, its use should be cautiously considered in patients with a history of constipation or hypertension.<sup>29</sup> Erenumab should also be avoided in patients with known latex allergy.<sup>30</sup>

The panel recommended caution when considering migraine treatment with CGRP mAbs in pregnant and nursing women, individuals with latex allergy, and individuals with a history of constipation or hypertension (with erenumab).

**Question 13.** *Would the availability of a local clinical practice guideline for the diagnosis and treatment of migraine patients, as well as establishing a national registry for migraine, help clinical decision-makers and medical institutions make proper decisions that would improve clinical care for migraine patients?*

There is a need to create local guidelines that can act as a reference for streamlining migraine treatment practices. Such guidelines could assist clinicians and policymakers in making informed decisions about migraine management.

The panel agreed that the availability of a local clinical practice guideline for the diagnosis and treatment of migraine patients and establishing a national registry for migraine could help clinical decision-makers and medical institutions make proper decisions that would improve clinical care for migraine patients.

**Discussion.** This consensus statement reflects the collective expertise of neurologists and headache specialists across Saudi Arabia and offers an updated framework for the preventive management of migraine, particularly in the context of recent therapeutic advancements. The panel's recommendations align with and localize international guidelines, with a particular emphasis on the role of CGRP monoclonal antibodies (mAbs) in improving patient outcomes.

Preventive migraine treatment remains underutilized both globally and in Saudi Arabia despite evidence of its impact on reducing attack frequency, severity, and disability. The panel highlighted the need to proactively assess all migraine patients for potential prophylactic therapy, particularly those experiencing four or more monthly migraine attacks, those with disabling symptoms, or those with poor response to acute treatments. These recommendations underscore a shift towards earlier and more individualized preventive strategies.

The introduction of CGRP mAbs as the first migraine-specific preventive agents marks a significant development in migraine management. Their safety, efficacy, and patient-friendly administration routes make them a compelling option, particularly for patients with contraindications to oral treatments or adherence challenges. Importantly, the panel supported international updates—such as those from the American Headache Society and European Headache Federation—that advocate for the use of CGRP mAbs

as first-line therapy. This is a notable shift from earlier positioning of these agents as third-line options.

Real-world data also support the use of CGRP mAbs across various stages of treatment. The panel acknowledged scenarios where early initiation of CGRP mAbs may be clinically appropriate, including patients with intolerance or contraindications to conventional therapies. Additionally, the consensus supports flexible strategies such as switching between CGRP mAbs in cases of inadequate response and combining them with other preventive agents like onabotulinumtoxin A when necessary.

However, the panel emphasized the need for careful monitoring and reevaluation of treatment efficacy, recommending a trial period of 2–3 months before assessing benefit. Criteria for successful treatment included a  $\geq 50\%$  reduction in attack frequency for episodic migraine and  $\geq 30\%$  for chronic migraine, along with improvements in severity, duration, and functional outcomes.

Notably, the absence of a national migraine registry in Saudi Arabia was identified as a critical gap. Establishing these tools could enhance evidence-based decision-making, standardize care, and support long-term planning for migraine services.

**Conclusion.** The landscape of migraine management and treatment still has many gaps that need to be addressed. Preventive therapy is clearly underutilized in migraine patients who could benefit from it. All migraine patients should be evaluated for receiving prophylactic therapy. The emergence of CGRP mAbs as a disease-specific treatment introduces a new modality that has proved to be effective, well tolerated, and more convenient for patients. Recent guidelines now endorse CGRP mAbs as a first-line treatment option for episodic and chronic migraines. The creation of local clinical practice guidelines for migraine management in Saudi Arabia could assist clinicians and medical institutes in making informed decisions, thereby improving clinical care and treatment outcomes for migraine patients.

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## References

1. Stovner LJ, Hagen K, Linde M, Steiner TJ. The global prevalence of headache: an update, with analysis of the influences of methodological factors on prevalence estimates. *J Headache Pain* 2022; 23: 34.
2. Al Jumah M, Al Khathaami AM, Kojan S, Hussain M, Thomas H, Steiner TJ. The prevalence of primary headache disorders in Saudi Arabia: a cross-sectional population-based study. *J Headache Pain*. 2020; 21:11.

3. Burch RC, Buse DC, Lipton RB. Migraine: Epidemiology, Burden, and Comorbidity. *Neurol Clin* 2019; 37: 631-649.
4. Aguilar-Shea AL, Membrilla Md JA, Diaz-de-Teran J. Migraine review for general practice. *Aten Primaria* 2022; 54: 102208.
5. Ruiz de Velasco I, González N, Etxeberria Y, Garcia-Monco JC. Quality of life in migraine patients: a qualitative study. *Cephalalgia Int J Headache* 2003; 23: 892-900.
6. Eltrafi A, Shrestha S, Ahmed A, Mistry H, Paudyal V, Khanal S. Economic burden of chronic migraine in OECD countries: a systematic review. *Health Econ Rev* 2023; 13: 43.
7. Newman L, Vo P, Zhou L, Lopez Lopez C, Cheadle A, Olson M, et al. Health Care Utilization and Costs in Patients With Migraine Who Have Failed Previous Preventive Treatments. *Neurol Clin Pract* 2021; 11: 206-215.
8. Bentivegna E, Onan D, Martelletti P. Unmet Needs in Preventive Treatment of Migraine. *Neurol Ther* 2023; 12: 337-342.
9. Unmet Needs of Patients Living with Migraine in the Gulf Cooperation Council (GCC) Countries | Pain and Therapy [Internet]. [cited 2024 Oct 18]. Available from: <https://link.springer.com/article/10.1007/s40122-024-00576-8#citeas>
10. Buse DC, Rupnow MFT, Lipton RB. Assessing and managing all aspects of migraine: migraine attacks, migraine-related functional impairment, common comorbidities, and quality of life. *Mayo Clin Proc* 2009; 84: 422-435.
11. Peters GL. Migraine overview and summary of current and emerging treatment options. *Am J Manag Care* 2019; 25: S23-S34.
12. Ailani J, Burch RC, Robbins MS, Board of Directors of the American Headache Society. The American Headache Society Consensus Statement: Update on integrating new migraine treatments into clinical practice. *Headache* 2021; 61: 1021-1039.
13. Charles AC, Digre KB, Goadsby PJ, Robbins MS, Hershey A, American Headache Society. Calcitonin gene-related peptide-targeting therapies are a first-line option for the prevention of migraine: An American Headache Society position statement update. *Headache* 2024; 64: 333-341.
14. Sacco S, Amin FM, Ashina M, Bendtsen L, Deligianni CI, Gil-Gouveia R, et al. European Headache Federation guideline on the use of monoclonal antibodies targeting the calcitonin gene related peptide pathway for migraine prevention - 2022 update. *J Headache Pain* 2022; 23: 67.
15. Silberstein SD. Preventive Migraine Treatment. *Contin Minneap Minn* 2015; 21: 973-989.
16. Cerbo R, Villani V, Bruti G, Di Stani F, Mostardini C. Primary headache in Emergency Department: prevalence, clinical features and therapeutical approach. *J Headache Pain* 2005; 6: 287-289.
17. Kumar A, Kadian R. Migraine Prophylaxis. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 [cited 2024 Oct 18]. Available from: <http://www.ncbi.nlm.nih.gov/books/NBK507873/>
18. Rashid A, Manghi A. Calcitonin Gene-Related Peptide Receptor. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 [cited 2024 Oct 18]. Available from: <http://www.ncbi.nlm.nih.gov/books/NBK560648/>
19. Drugs List | Saudi Food and Drug Authority [Internet]. [cited 2024 Oct 18]. Available from: <https://www.sfda.gov.sa/en/drugs-list>
20. Becker WJ. Botulinum Toxin in the Treatment of Headache. *Toxins* 2020; 12: 803.
21. Mohanty D, Lippmann S. CGRP Inhibitors for Migraine. *Innov Clin Neurosci* 2020; 17: 39-40.
22. Vandervorst F, Van Deun L, Van Dycke A, Paemeleire K, Reuter U, Schoenen J, et al. CGRP monoclonal antibodies in migraine: an efficacy and tolerability comparison with standard prophylactic drugs. *J Headache Pain* 2021; 22: 128.
23. Lampl C, MaassenVanDenBrink A, Deligianni CI, Gil-Gouveia R, Jassal T, Sanchez-Del-Rio M, et al. The comparative effectiveness of migraine preventive drugs: a systematic review and network meta-analysis. *J Headache Pain* 2023; 24: 56.
24. Sacco S, Bendtsen L, Ashina M, Reuter U, Terwindt G, Mitsikostas DD, et al. European headache federation guideline on the use of monoclonal antibodies acting on the calcitonin gene related peptide or its receptor for migraine prevention. *J Headache Pain* 2019; 20: 6.
25. Al-Hassany L, Lyons HS, Boucherie DM, Farham F, Lange KS, Marscholke K, et al. The sense of stopping migraine prophylaxis. *J Headache Pain* 2023; 24: 9.
26. Kuruppu DK, North JM, Kovacic AJ, Dong Y, Pearlman EM, Hutchinson SL. Onset, Maintenance, and Cessation of Effect of Galcanezumab for Prevention of Migraine: A Narrative Review of Three Randomized Placebo-Controlled Trials. *Adv Ther* 2021; 38: 1614.
27. Iannone LF, Buralassi A, Vigani G, Tabasso G, De Cesaris F, Chiarugi A, et al. Switching anti-CGRP(R) monoclonal antibodies in multi-assessed non-responder patients and implications for ineffectiveness criteria: A retrospective cohort study. *Cephalalgia Int J Headache* 2023; 43: 3331024231160519.
28. Overeem LH, Peikert A, Hofacker MD, Kamm K, Ruscheweyh R, Gendolla A, et al. Effect of antibody switch in non-responders to a CGRP receptor antibody treatment in migraine: A multi-center retrospective cohort study. *Cephalalgia Int J Headache* 2022; 42: 291-301.
29. Holzer P, Holzer-Petsche U. Constipation Caused by Anticalcitonin Gene-Related Peptide Migraine Therapeutics Explained by Antagonism of Calcitonin Gene-Related Peptide's Motor-Stimulating and Prosecretory Function in the Intestine. *Front Physiol* 2021; 12: 820006.
30. Sangalli L, Brazzoli S. Calcitonin Gene-Related Peptide (CGRP)-Targeted Treatments—New Therapeutic Technologies for Migraine. *Future Pharmacol* 2023; 3: 117-131.