وزارة الصحة
Ministry of Health
المديرية العامة لمستشفى خولة
Directorate General of Khoula Hospital

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Neurology Department

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Acronyms

EHF	European Headache Federation
CGRP	Calcitonin Gene-Related Peptide Antagonists
NSAID	Non- Steroidal Anti-Inflammatory Drug
MIDAS	Migraine Disability Assessment
ETNS	Electrical Trigeminal Nerve Stimulation
NVNS	Non- Invasive Vagus Nerve Stimulation
REN	Remote Electrical Neuromodulation
STMS	Single-Pulse Transcranial Magnetic Stimulation
HIT-6 score	Headache Impact Test– 6
MABs	Monoclonal Antibodies
CM	Chronic Migraine
EM	Episodic migraine
MRM	Menstrually Related Migraine
MOH	Medication Overuse Headache

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Chapter 1

1. Introduction

Migraine is a primary headache disorder, often manifesting as an acute or chronic neurological condition. It is classified this headache as pulsating, throbbing pain with varied efforts to construct consistently accepted diagnostic criteria. The International Society of Migraines described migraine as recurring with at least five episodes that persist for at least four to 72 hours when untreated or undertreated. The American Headache Society is also in synchrony with the definition and they define the headache as migraine when it occurs more than five attacks to include characteristics like unilaterality of pain, pulsation, aggravating factors like walking, as well as photophobia, phonophobia, nausea, and/or vomiting that must be present during the episodes of attack in the absence of any other etiological explanation .The classification of migrainous headache includes migraine with aura, migraine without aura, status migrainosus, complicated migraine, and other types of migraine. Migraine recurrence rates are high and therefore patients suffering from migraines should be offered abortive and preventive management. In light of the multiple pharmacologic alternatives for migraine management, the adverse effects associated with different treatment regimens, and their varying efficacy, it is vital to undertake ongoing evaluations and seek a tailored therapeutic strategy for our population suffering from migraine.

2. Purpose

The purpose of this guideline to:

a) Unify the treatment pathway for all patients experiencing poorly controlled acute episodic migrainous headaches.

b) Prevent transforming the headaches into medication overuse headache by introducing migraine specific treatment and treating chronic migraine headaches early on.

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3. Scope

This guideline applies to all neurologists who deal with patients with migraine headache

Chapter 2

4. Structure

It is the guideline of the DGKH to ensure proper standard care.

4.1 Goals of migraine treatment: The main aim of commencing pharmacological and non-pharmacological treatment is to improve a patient's quality of life by reducing the frequency, duration, and severity of headaches. Educating patients to reduce intake of recuse medication to prevent transforming headaches into medication overuse headaches and minimizing the adverse effects (see appendix 2).

4.2 Pharmacological strategies for migraine treatment: migraine can be treated using two strategies – abortive (acute) and prophylactic treatments as outlined below.

a) Abortive (acute) migraine treatment: Overview of mechanism of abortive therapies.

Migraines will have a recurrence 2/3 of the time within 28 hours of discharge from the emergency department, which is a crucial problem. Additionally, patients may progress to chronic migraine in the setting of poorly controlled episodic migraines making it crucial to properly control acute migraine attacks. Choosing an acute treatment for migraine attacks requires an individualized approach for each patient; a number of factors must be considered which are patient's profile, migraine characteristics, medication characteristics and availability of drug (see appendix 3). Abortive or acute treatments are usually more effective if they are given early in the course of the headache; a large single dose tends to work better than repetitive small doses. Triptans and NSAIDs are amongst the most common first-line medications in outpatient and emergent settings .They can be used up to 10 days/month alone or in combination. This limit is to prevent medication-overuse headaches.

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The severity of headache is the guide to which abortive treatment to be considered. In mild to moderate migraine attacks not associated with vomiting or severe nausea, simple analgesics (NSAIDs, paracetamol or combination analgesics are often tried first because they can be effective and are less expensive than migraine-specific agents. For attacks unresponsive to analgesics, the combined use of an NSAID with a triptan appears to be more effective than using either drug class alone. When mild to moderate attacks are associated with severe nausea or vomiting, an oral or rectal antiemetic drug can be used in conjunction with simple or combination analgesics. In cases of moderate to severe migraine attacks not associated with vomiting or severe nausea, oral migraine-specific agents are first-line, including oral triptans and the combination of triptan with naproxen. For those with contraindications to or who do not tolerate triptans, a calcitonin gene-related peptide (CGRP) antagonist or lasmiditan may be effective. When complicated by vomiting or severe nausea, severe migraine attacks can be treated with an antiemetic drug or non-oral migraine-specific medications including subcutaneous sumatriptan, nasal sumatriptan and zolmitriptan, or parenteral dihydroergotamine (see appendix 4).

Unfortunately, there are some unmet needs in acute treatment with triptan namely, non-responders, adverse effects, headache recurrence, and cardiovascular contraindications. Triptan failure can be as high as one-third of individuals with migraine. In such instances, the patient would fall into one of the categories, triptan non-responder, triptan resistant, or triptan refractory. A decision aid to define a patient as a responder or non-responder to a triptan is based on evaluating the response from two to four consecutive attacks. An attack is considered effectively treated if the patient's well-being, as defined above, is restored within 2 hours and for at least 24 hours. An individual with migraine is considered a triptan responder when the given triptan leads to effective acute attack treatment in at least three out of four migraine attacks. On the other hand, an individual with migraine is considered a triptan non-responder in the presence of failure of a single triptan (not matching the definition of triptan-responder).In addition, an individual with migraine is considered triptan-resistant in the presence of failure of at least 2 triptans; triptan refractory, in

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the presence of failure to at least 3 triptans, including subcutaneous formulation; triptan ineligible in the presence of an acknowledged contraindication to triptan use (See appendix 5). In such instances, it can consider switching the patient to one of the other classes of acute treatment, this includes selective serotonin (5-HT-1F) e.g Lamitidan, small molecules CGRP receptor antagonists .e.g rimegepant, ubrogepant, etc. Additionally, patients can consider trial noninvasive neuromodulation devices (ETNS, nVNS, REN, sTMS) if they do not respond to or tolerate drug treatments and those who wish to avoid medications.

b) Prophylactic (preventive) migraine treatment: overview of mechanism of prophylaxis therapies.

The main goal of prophylactic therapy is reduction of headache intensity, frequency and duration. Anti-migraine prophylaxis is initiated in patients who experience more than 4 migraine attacks per month, overuse acute/abortive medication and in headache with significant impact on quality of life. A variety of medications, including beta-blockers, calcium channel blockers, anticonvulsant, and antidepressants, have shown promise as preventative treatments for migraines.

i. What is next after failure of preventive treatments?

A patient should fail at least three preventive treatments, then one should consider newer classes of medications targeting CGRP pathway like monoclonal antibodies, gepants or botox injections. The monoclonal antibodies (mAbs) blocking calcitonin gene-related peptide (CGRP) or its receptor (CGRP/rec) are a major breakthrough in the prophylactic treatment of migraine. Erenumab, fremanezumab, and galcanezumab are also effective in individuals with more than two preventive medication failures because of efficacy or tolerability issues. Additionally, Erenumab had sustained efficacy in women with a history of menstrually related migraine (MRM). Erenumab is injected under the skin using a pre-filled syringe or pen. Patients can inject the medicine themselves after being trained. The recommended dose is 70 mg every 4 weeks as a single injection. Some patients may benefit from a dose of 140 mg every 4 weeks, given as either a single injection of 140 mg or two injections of 70 mg.In

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patients who have shown no response after 3 months of treatment, discontinuation should be considered. The reported adverse drug reactions for erenumab 70 mg and 140 mg were mostly mild or moderate in severity. This included; constipation, injection site reaction, muscle spasm, pruritus. Less than 2% of patients discontinued due to adverse events. Gepants can be considered in those patients who fail Anti-CGRP monoclonal antibodies or have needle phobia .Additionally , it has a short half-life therefore it can be considered in females of childbearing age. Page 7 Botox is approved for the treatment of chronic migraine in adults. Chronic migraine is defined as having at least 15 headache days a month, with at least eight of those featuring migraine symptoms. It is not an effective treatment for other types of headache including episodic migraine (headache on fewer than 15 days a month), tension-type headache and cluster headache. Most patients have at least two treatment cycles before deciding if Botox is effective. A good response to Botox is usually a 30-50% reduction in headache frequency. Injections are given every 12 weeks. Botox is usually given until your migraine has changed to episodic migraine for three months in a row, or that there is significant improvement in disability using quality of life questionnaires. If Botox doesn't improve migraine enough it may be stopped. Should the patient fail to respond to Botox injections or is needle phobic, then patient can be tried on non-pharmacologic interventions.

4.3 Non-pharmacological Strategies for Migraine Treatment:

Patients are always advised to avoid the triggers as this can reduce the headache frequency substantially. Pathophysiology-targeting non-pharmacological treatments may be useful for patients who cannot take, or have no response to, current pharmacological treatments (See appendix 6)

Chapter 3:

5. Responsibilities:

5.1Head of Neurology Department shall:

5.1.1 Ensure that all neurologists adhere to the guideline.

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5.2Director of Pharmaceutical care and medical supplies shall :

5.2.1 Ensure that all pharmacists adhere to the guideline.

5.3Ward In charge nurse shall:

5.3.1 Ensure that all staff nurses aware about this guideline.

Chapter 4

6 Document history and version control table

Version	Description	Name of Authors	Review Date
1	**Initial release**	Dr. Iman Al Lawati	**2027**
2			

7 References

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8 Annexes

8.1 Appendix (1) :Characteristics of Migraine Headache

Description: Recurrent headache attacks lasting 4-72 hours, with typical characteristics: unilateral, pulsating pain; moderate or severe intensity; aggravation by routine physical activity; and association with nausea and/or photophobia and phonophobia

A. ≥ 5 attacks fulfilling criteria B through D

B. Headache attacks either untreated or unsuccessfully treated lasting 4-72 hours

C. Headache has at least 2 of the following:
   1. Unilateral location
   2. Pulsating quality
   3. Moderate or severe pain intensity
   4. Aggravation by or causing avoidance of routine physical activity (e.g. walking or climbing stairs)

D. Headache accompanied by at least one of the following:
   1. Nausea and/or vomiting
   2. Photophobia and phonophobia

E. Not better accounted for by another ICHD-3 diagnosis

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8.2 Appendix (2): Goals of migraine treatment

Goals for Successful Treatment of Acute Migraine Attacks	Goals of Long-term Migraine Management
• Treat migraine attacks rapidly and consistently without recurrence • Restore patient's ability to function • Minimize use of back-up and rescue medications • Optimize self-care for overall management • Cause minimal or no adverse effects	• Reduce migraine frequency and severity • Reduce disability • Improve quality of life • Prevent headache • Avoid escalation of headache medication use • Educate and enable patients to manage their disease

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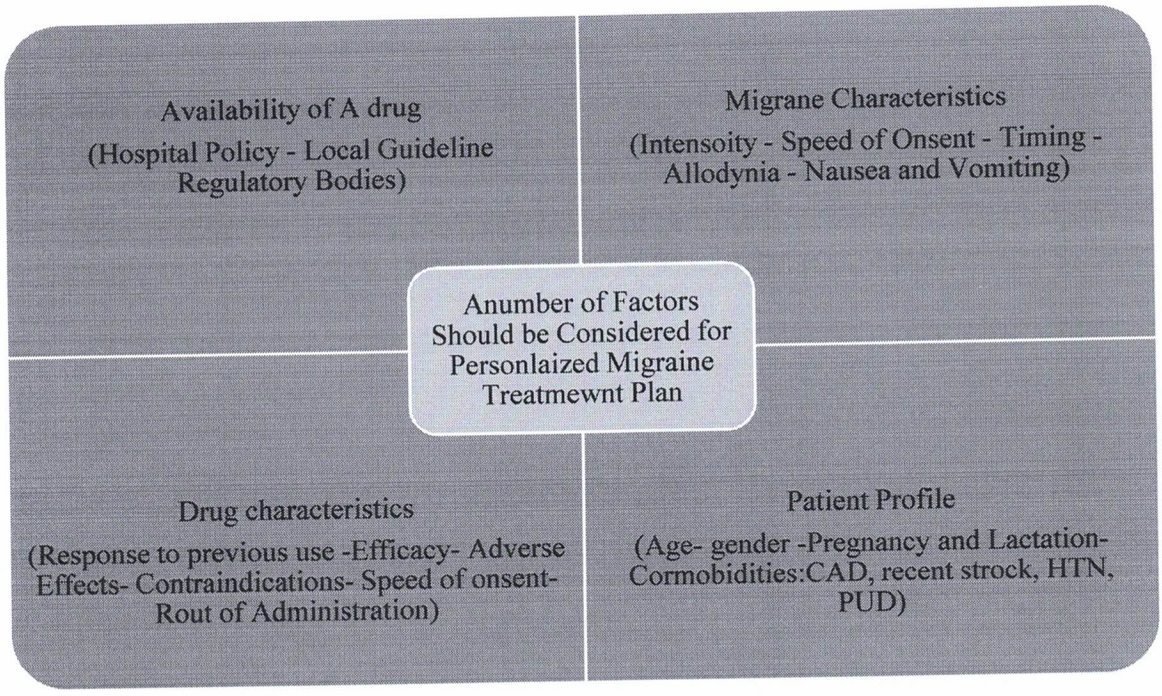
8.3 Appendix (3): Factors should be considered for personalized migraine treatment plan



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8.4 Appendix (4): Pharmacological treatment of Migraine

Dosing of each medication with level A evidence:

Class	Medication	Dose[a]*
Analgesics	Acetaminophen	1000 mg (for non-incapacitating attacks)
Ergots	DHE	2 mg NS; 1 mg pulmonary inhaler[b]†
NSAIDs	Aspirin	500 mg
	Diclofenac	50 or 100 mg
	Ibuprofen	200 or 400 mg
	Naproxen	500 or 550 mg
Opioids	Butorphanol	1 mg NS
Triptans	Almotriptan	12.5 mg
	Eletriptan	20, 40, or 80 mg
	Frovatriptan	2.5 mg
	Naratriptan	1 or 2.5 mg
	Rizatriptan	5 or 10 mg
	Sumatriptan	25, 50, or 100 mg; 10 or 20 mg NS; 4 or 6 mg SC
	Zolmitriptan	2.5 or 5 mg; 2.5 or 5 mg NS
Combinations	Acetaminophen/aspirin/caffeine	500/500/130 mg
	Sumatriptan/naproxen	85/500 mg

The severity of headache is the guide to which abortive treatment to be considered. In mild to moderate migraine attacks not associated with vomiting or severe nausea, simple analgesics (NSAIDs, paracetamol or combination analgesics are often tried first because they can be effective and are less expensive than migraine-specific agents. For attacks unresponsive to

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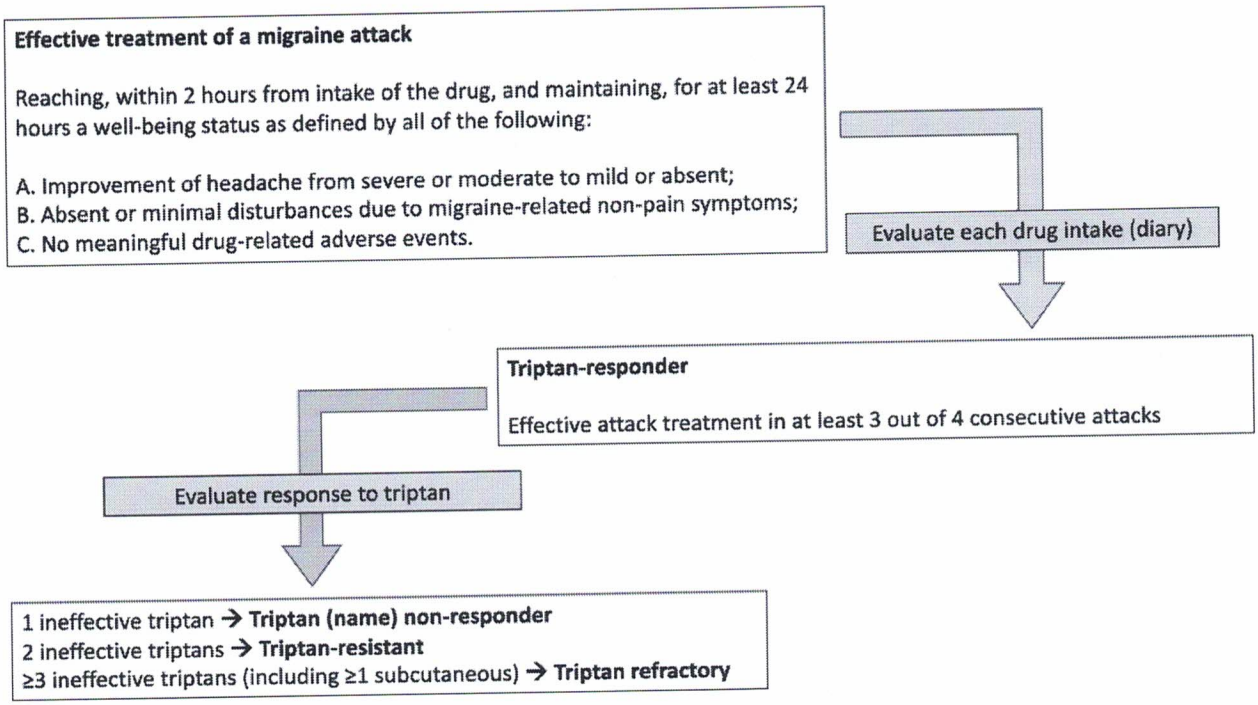
8.5 Appendix (5): Effective treatment of a migraine attack



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8.6 Appendix (6): Non-pharmacological strategies for migraine treatment

Diet[1]:	Lifestyle[2]:	Behavioural[1,3]:	Physical[3]:
High-dose nutraceutical supplements Nutritional and dietary interventions have been suggested although there is no clinical evidence	Managing migraine triggers such as caffeine, alcohol or lack of sleep	Relaxation techniques Stress management Cognitive behavioural therapy Biofeedback	Acupuncture

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8.7 Appendix(7): Abortive Treatment