Drug	MOA	Pharmacokinetics	Uses	Adverse effect
A) ACUTE ATTACK **1. ABORTIVE THERAPY**				
Drug used on : **a. ERGOTS** (Non-Selective) **Ergotamine tartarate** **Dihydroergotamine**	**Agonism at 5HT1.** **At presynaptic** trigeminal nerve endings→ ↓release of vasodilating peptides ↓excessive firing of these nerve endings. **At blood vessels** → ↓vasodilation & stretching of the pain endings by ↓ transmitter release in the perivascular space **Partial** agonist effect on α-adrenoceptors → vasoconstriction	**Ergotamine tartarate:** Oral absorption → low bioavailability. Sublingual →Low bioavailability. Rectal suppository →Better bioavailability. Elimination →Extensive hepatic 1st pass metabolism. Excretion →90% of metabolites in bile Traces unmetabolized → **urine & feces.** T1/2 2 hrs, **BUT**, vasoconstriction → 24 hr (↑tissue binding). Present in all forms. **Dihydroergotamine:** More rapid hepatic clearance. Present in → nasal spray, inhaler & injections.	Frequent, moderate attack. Infrequent severe attack. **Dihydroergotamine** → severe recurrent attack. **Contraindications:** **Pregnancy** & miscarriage. **Heart disease.** **Hypertension.** Liver and kidney diseases. Fever, sepsis. For **prophylaxis** of migraine. With TRIPTANES. With β-blocker.	N & V, abdominal pain & diarrhea. Feeling of cold and numbness of limbs, tingling **Hallucination.** **Pericardial distress…** Prolong use → rebound headache due to vasodilatation followed by vasoconstriction. Prolong use & high dose → **paraesthesia & gangrene**.
b. TRIPTANES (Selective) **Sumatriptan** → **N**asal spray, **&** injectable Oral bioavailability low / Subcutaneous bioavailability is 97%, peaks after 2 min & t1/2 nearly 2 hours **Naratriptan**→ Oral**ly** Oral bioavailability 70%, peaks after 2 hrs & $t_{1/2}$ nearly 6 hours (longer duration) ZOLMITRIPTAN→nasal spray, and injectable forms Oral bioavailability 40%, peaks after 2 hrs & $t_{1/2}$ nearly 3 hours	**Agonism at 5HT1.** **At presynaptic** trigeminal nerve endings→ ↓release of vasodilating peptides ↓excessive firing of these nerve endings **At meningeal** , dural , cerebral vessels → ↓vasodilation & stretching of the pain endings.	**Contraindications:** **-Peripheral vasospastic diseases.** **-Uncontrolled hypertension.** **-History of ischemia.** **-Cerebrovascular disorders.** **-In concurrent use with ergots or others inducing vasospasm.** **-In concurrent use with MAO Is, lithium, SSRIs, ….→(5HT)=not given with antidepressant drugs** -Renal or hepatic impairment **(specially with *NARA →RIZOTRIPTAN)***	**-To abort attacks in patients with frequent, moderate or infrequent but severe attacks.** **- In cluster headache**	-Mild pain & burning sensation at the site of injection. -Paraesthesia, tingling , warmth, heaviness. -Flushing / Dizziness. -Hypertension. **-Vasospasm** **-Ischemic heart; Angina →M.I** **-Arrhythmias** **In zolmitriptan:** **-Chest and neck tightness.** **-Somnolence**

2.Rescue therapy

1] Analgesics: NSAIDs / Aspirin< Acetaminophen,Non-opioid: **μ** agonist; Tramadol - *act on 5HT & NE receptors*,Sedatives; Butalbital

2] Antiemetics:

A) Dopamine Antagonists : Domperidone ,**Promethazine**, **$5HT_3$ antagonists :** Ondanseteron - Granisetron **,H_1 antagonist** : Meclizine

Others; Steroids

B)PREVENT RECURRENCE

- ↓recurrence frequency, severity, duration & / or disability
- ↑responsiveness to abortive therapy
- if the patient usually suffers from the recurrence attack he should take preventive therapy to reduce the recurrences. Full effect of therapy needs several weeks to manifest & should continue for 6 months & can be repeated.

a.Antiepileptics:
Block Na channel & augment GABA at GABA-A receptors →**Gabapentin**
Topiramate; weight loss & dysthesia.
Valproic; weight gain, hair loss, polycystic ovary→ **not** given to **young females**.

b.Antidepressants:
Pizotifen,
TCA.
SSRIs.

c.Antihypertensives:
β blockers; Propranolol, **atenolol**, **metoprolol**, Not in young & anxious nor in elderly & depressed, diabetic.
Ca Channel Blockers:
Cinnarazine, **flunarizine**, **verapamil**.
ACEIs: angiotensin converting enzyme inhibitor→ **lisinopril**.
ARB: angiotensin II receptor blocker →**candesartan.**

d.Antispastic muscle relaxants:
Tizanidine, Botulinum toxins