ACCOUNTABLE HEALTH PARTNERS

UR MEDICINE

2020

Pharmacy Pearls

New Agents for Acute Treatment of Migraine in Adults

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For many years, acute migraine treatment options have not changed; recently, however, multiple new agents have entered the market increasing the options for patients with migraine.

Three *new* medications available for acute treatment of migraine are: Reyvow, Ubrelvy, and Nurtec ODT

Medications for Acute Treatment of Migraine

Drug	Generic Available?	Estimated Cash Price*	Clinically Relevant Drug Interactions
sumatriptan (Imitrex)	Yes	$92	
naratriptan (Amerge)	Yes	$132	
rizatriptan (Maxalt, Maxalt MLT)	Yes	$194 (PO)/$250 (ODT)	Max 15 mg/day with propranolol
sumatriptan SQ	Yes	$208	
zolmitriptan (Zomig, Zomig ZMT)	Yes	$290 (PO)/$292 (ODT)	Max 5 mg/day with cimetidine
eletriptan (Relpax)	Yes	$314	Avoid with CYP3A4 inhibitor(s)
almotriptan (Axert)	Yes	$442	Max 12.5 mg/day with CYP3A4 inhibitor(s)
sumatriptan nasal	Yes	$455	
zolmitriptan nasal (Zomig)	No	$597	
frovatriptan (Frova)	Yes	$608	
lasmiditan (Reyvow)	No	$770	
rimegepant (Nurtec ODT)	No	$1019	Many- run interaction screen before prescribing
ubrogepant (Ubrelvy)	No	$1038	Many- run interaction screen before prescribing

*Average cash price based on www.Goodrx.com – actual price varies based on dose, pharmacy, days' supply, and patient's insurance

Efficacy Comparison

In 2018, the FDA released industry guidance for efficacy endpoints that should be incorporated into clinical trials for agents being tested for acute migraine treatment

- Primary endpoints: pain-free at 2 hours post-dose and relief of patient's most bothersome symptom (nausea, photophobia, or phonophobia) at 2 hours post-dose
- Secondary endpoints: pain-free at various time points post-dose, proportion of patients requiring additional medication (second dose or rescue medication within 24 hours of initial treatment), sustained pain-free at 24 hours post-dose, pain relapse within 48 hours of initial dose

Medications approved since FDA clinical trial guidance in 2018 measure pain freedom at 2 hours; clinical trials of sumatriptan did not specify pain freedom specifically (measured "response" which varied among trials from reduction in headache to pain freedom). Results below are summarized from different clinical trials and cannot be directly compared to each other; NNTs are compared to placebo (ranges are due to differences between doses)

Drug	NNT Response at 2 hrs	NNT Photophobia relief at 2 hrs	NNT Phonophobia relief at 2 hrs	NNT Nausea relief at 2 hrs
5-HT1B/1D Agonists ("Triptans")- cause vasoconstriction and reduce inflammation				
sumatriptan PO (Imitrex)	5-6	4-8	4-8	7-8
CGRP Antagonists ("Gepants")- block CGRP, which appears to mediate trigeminovascular pain transmission				
rimegepant (Nurtec ODT)[2]	10	11	9	17
ubrogepant (Ubrelvy)[3]	11-14	7-11	9-14	13-15
5-HT1F Agonist ("Ditan")- decreases trigeminal system stimulation without causing vasoconstriction				
lasmiditan (Reyvow)[4]	6-14	6-13	8-13	77-143

Review of New Acute Migraine Treatment Agents: Reyvow, Ubrelvy, Nurtec ODT

Role in Acute Migraine Management: not well-defined at this time; given the short-term, single-attack design of these trials, long-term data are needed to determine safety and tolerability of these agents. Additionally, efficacy compared to triptans is unknown. At this time, we continue to recommend treatment selection found in our AHP migraine best practices, found here.

Mechanism of Action: Reyvow has the same mechanism of action as the triptans but is more selective. It lacks vasoconstrictor activity. Ubrelvy and Nurtec ODT are CGRP receptor antagonists which appear to mediate trigeminovascular pain transmission.

Lasmiditan (Reyvow)- approved 10/2019

C-V controlled substance

MOA: Selective 5HT-1F receptor agonist that lacks vasoconstrictor activity

Dose: 50, 100, or 200 mg taken once (no benefit with taking a second dose for the same migraine attack); may increase dose for subsequent attacks up to 200 mg; max 1 dose in 24 hours

Dose adjustments: use is not recommended in severe hepatic impairment

Common ADEs: Somewhat poorly tolerated; dizziness (up to 17%, dose-related and lasts 1.5-2 hours), parasthesia, somnolence, fatigue, nausea

Precautions: May cause CNS depression which can lead to driving impairment; patients should avoid driving or operating machinery for at least 8 hours after taking

Ubrogepant (Ubrelvy)- approved 12/2019

MOA: Calcitonin gene-related peptide (CGRP) receptor antagonist

Dose: 50 or 100 mg, may be repeated ≥2 hours after initial dose; max 200 mg/24 hours

Dose adjustments: max 100 mg/24 hours for CrCl 15-29 mL/min and severe hepatic impairment; avoid use for CrCl <15 mL/min

Common ADEs: drowsiness, nausea, dry mouth

Drug-drug interations: CYP3A4 and P-gp substrate highly affected by CYP3A4 and P-gp inhibitors and inducers- recommend checking drug interactions prior to prescribing

Rimegepant (Nurtec ODT)- approved 2/2020

MOA: Calcitonin gene-related peptide (CGRP) receptor antagonist

Dose: 75 mg once; max 75 mg/24 hours

Dose adjustments: avoid use for CrCl <15 mL/min and severe hepatic impairment

Common ADEs: nausea, hypersensitivity reaction

Drug-drug interactions: CYP3A4 and P-gp substrate highly affected by CYP3A4 and P-gp inhibitors and inducers- recommend checking drug interactions prior to prescribing