



# Approval Pathway for Migraine and Headache Products

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# Disclaimer

- The views expressed in this presentation are those of the speaker and are not an official statement of the Food and Drug Administration.

# Approval Pathways

- Acute treatment of migraine
- Preventive treatment of migraine
- Acute treatment of cluster headache
- Treatment of cluster headache

# Acute Treatment of Migraine with and without Aura

ICHD-3 definition:

A. At least 5 attacks fulfilling B-D

B. Headache attacks lasting 4-72 hours

C. Headache has at least 2 of the listed 4 features:

Unilateral location, pulsating quality, moderate or severe pain intensity, aggravation by physical activity

D. During headache at least 1 of the following:

Nausea and/or vomiting; phonophobia and photophobia

Aura: at least 2 attacks with fully reversible visual, sensory, speech and/or language, motor, brainstem, retinal symptoms

# Acute Treatment of Migraine

Measurement of pain freedom:

- Based on a 4-point scale:
- 0=none; 1=mild; 2=moderate, 3=severe

Measurement of associated symptoms;  
most bothersome symptom (MBS)

- Binary measurement; yes/no at 2 hours post-dose

# Acute Treatment of Migraine

Co-primary endpoint: pain free and MBS free at 2 hours post dose

Secondary endpoints

- SPF at 24 or 48 hours ( no rescue medication, no relapse of pain)
- Incidence of pain relapse (return of HA within 48 hours when patient was pain-free at 2 hours)
- No headache pain at various time points

Clinical outcome assessment tools to assess changes in quality of life or function, with treatment

# Acute Treatment of Migraine

Safety data required (ICH E1 Guideline) :

- 300 patients for 6 months
- 100 patients for one year

Long term extension; can be open-label

Requirement to study pediatric patients

Guidance for Industry: Migraine: Developing Drugs for Acute Treatment (February, 2018)

# Preventive Treatment of Migraine

- Episodic Migraine definition:  $\leq 14$  headaches days/month
- Chronic Migraine definition:  $\geq 15$  headache days/month for  $>3$  months, with at least 8 identified as migraine



# Preventive Treatment of Migraine

Medication Overuse Headache definition:

- Headache occurring on  $\geq 15$  days/month in a patients with a pre-existing primary headache
- Regular overuse of acute headache medication for  $>3$  months.

# Preventive Treatment of Migraine

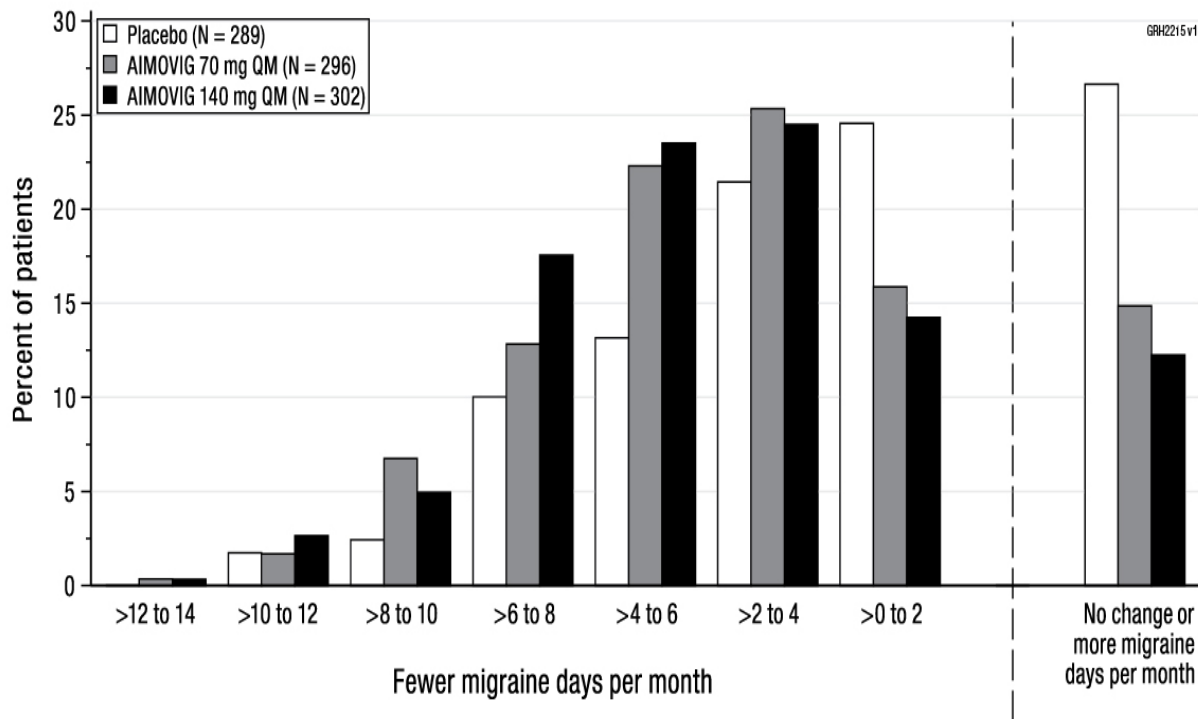
Primary endpoint: change from baseline in monthly migraine days or headache days over a 12 week period

Secondary endpoints:

- reduction in the use of rescue medication
- 50% responder rate

Distribution of effect

# Preventive Treatment of Migraine



# Acute Treatment of Cluster Headache (CH)

CH definition: Severe or very severe unilateral orbital, supraorbital and/or temporal pain lasting 15-180 minutes with either or both:

- One of the following: conjunctival injection, nasal congestion, eyelid edema, forehead/facial sweating or flushing, sensation of fullness in ear, miosis and/or ptosis
- A sense of restlessness

Frequency between one every other day and 8 per day

Primary outcome: pain relief at 15 minutes sustained to 1-2 hours

# Treatment of Cluster Headache

- Episodic CH definition: CH attacks occurring in periods lasting from 7 days to 1 year, separated by pain free periods lasting at least 3 months.
- Chronic CH definition: CH attacks occurring for more than 1 year without remission, or with remission periods lasting less than 3 months

## Treatment of Cluster Headache

- Less standardized approach
- Primary endpoint (episodic): reduction in weekly cluster headache attacks over 2, 3 or 4 weeks
- Primary endpoint (chronic): reduction in weekly cluster headache attacks from baseline over a 12 week period

# Summary

- Standardized approaches exist to study acute migraine and preventive treatment of migraine.
- We are working with sponsors to develop study designs for other headache types where there is less standardization, such as cluster headache.
- We have had a very productive 3 years, but we still have more work to do to provide more therapies to patients with migraine and headache disorders.