

The Prudent Prescriber

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Pharm Reps \neq Rational Prescribing

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A New Approach for Preventing Migraine: Aimovig

Are mAbs the Answer?

My memories of treating migraineurs are not pleasant. The medications for both prevention and treatment often did not work well or caused hellacious side effects or both.

Enter Aimovig (erenumab), the first FDA approved monoclonal antibody (three more in the pipeline) indicated for the prevention of migraine headaches.

Mechanism of action of monoclonal antibodies (mAbs)

This class of drugs works by blocking the activity of calcitonin gene-related neuropeptide (CGRP). The peptide influences both neuronal modulation of pain and vascular activity.

Indications

The FDA has approved erenumab for prevention of episodic migraine headaches (4-14 migraine days per month) and for chronic migraineurs, who experience more than 14 headaches per month with at least 8 migraine days. It is approved for patients 18-65 years. Studies are now being carried out in children ages 12-17 years.

Administration and dosing

It is available in a prefilled auto-injection pen with 70mg of erenumab per ml. It is dosed at 70mg or 140mg per month, subcutaneously by patients at home.

Antibiotics do NOT

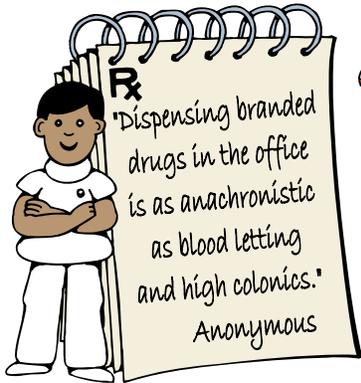


help acute bronchitis

β -blockers in post-MI save lives



Pill splitters save BIG



CHE?

Think:

- Ace
- Aldactone
- B-blocker
- Dig
- Diuretic



Avoid these expensive

"me-too" drugs:



- Intermezzo
- Vimovo
- Livalo
- Gralise
- Viibyrd
- Edarbi
- Daliresp



Treat patients > 60 years to 150/90



NOW AVAILABLE

ON THE

GENERIC MARQUEE

- Viagra \rightarrow sildenafil
- Effient \rightarrow prasugel
- Strattera \rightarrow atomoxetine
- Asacol HD \rightarrow mesalamine DR
- Pristiq \rightarrow desvenlafaxine

Efficacy

There are four industry sponsored, randomized, double blind, placebo controlled studies.

- * The largest study, STRIVE (NEJM November 30, 2017) randomized 955 patients (85% female, 87% white, median age 41 years) with episodic migraines to three groups: placebo, 70mg erenumab or 140mg erenumab, each given subcutaneously on a monthly basis for six months.
- * The primary endpoint was the change in the mean monthly migraine days from baseline over the last three months of the double-blind treatment phase of this study (months 4, 5, and 6). These patients had an average of 8.3 migraine days per month at baseline period.
- * Results: In the last three months of treatment, a reduction of 3.2 days of monthly migraine days was observed for patients on the erenumab 70mg dose and 3.7 days for those on the erenumab 140mg dose versus 1.8 days for placebo group. **So the average erenumab treated patient, who had over 8 days with migraines per month at baseline, had a net decrease of 1.4 to 1.9 migraine days per month—a modest response!**
- * The percentage of patients experiencing a 50% or greater reduction of mean monthly number of migraine days was 43.3% for erenumab 70mg and 50% for erenumab 140mg vs 27% for placebo. NNT, 4-6.
- * In the 70mg dose group versus the placebo group, there was a 0.9 day decrease in the number of days that patients took migraine specific medicines.
- * In a 12 week phase II randomized, double blind study of 483 episodic migraineurs treated with 70mg of erenumab or placebo monthly, **the average net decrease in migraines per month was 1.1 days in the erenumab group vs. the placebo group.**
- * Finally in a 12 week trial by Tepper et al, 667 chronic migraineurs (> 14 headaches/month) given 70mg of erenumab per month **had a net decrease of 1.1 headaches per month compared to the placebo group.**

Adverse events

- * At first blush, (about 3,000 patents), erenumab appears to be well tolerated. The dropout rate was low and the most common side effects were injection site irritation, constipation, and fatigue. These monoclonal antibodies have some vasoconstriction properties, so adverse cardiovascular effects need to be monitored. The long term safety of the CGRP monoclonal antibodies remains unknown. Migraine starts early in life and thus these patients might be exposed to this class of drugs over a long period of time. There have been three deaths in clinical trial participants who received CGRP monoclonal antibodies: a suicide, a death due to chronic obstructive pulmonary disease and a death that was labeled as an “arteriosclerosis event.”

Cost

- * List price for Aimovig will be \$575/month for the 70mg pen or \$6900 a year. It appears that the 140mg monthly dose would double the cost.

ICER

- * The Institute for Clinical and Economic Review's report concluded that at an annual net price of \$5,000, the price of the CGRP therapies aligns with the value to patients for whom other preventative treatments have failed. The drugs were not found to be cost-effective, however, if used to treat patients that had not already tried existing preventive treatments which are far less expensive.

My Take

- * I wish I could be as optimistic as Dr. Stuart Tepper, a professor of neurology at Dartmouth College. He commented on these new migraine directed mAbs, “They shake the ground under our feet. They will change the way we treat migraine.” CGRP antagonists are promising, but I’m not feeling any seismic activity.
- * The effect sizes in all these trials are small and not superior to topiramate or methysergide as preventive medications.
- * The STRIVE study excluded patients who had failed more than two classes of preventive medications; over 55% of the patients had never received any preventive medications. Thus STRIVE does not give us an evaluation of erenumab as a tool in hard-to-manage patients. The Liberty study, a 12 week trial involving 246 migraine patients

who had had previous exposure to 2–4 preventive treatments, compared the higher dose, 140mg of erenumab monthly versus placebo. 30.3% of the patients in the erenumab group had a 50% or more reduction in migraine frequency vs 13.7% of the placebo group. NNT equals 7.

- * STRIVE is a study of predominantly young, white women migraineurs. If your patient has different demographics, this study may not apply.
- * The greatest reduction in migraine days occurred in the first two months after treatment initiation which suggests that a clinical decision about whether the medication is effective can be made quickly.
- * The task will be to sort which of these four mAbs will work best for which niches of migraine patients, aura vs no aura, use with other preventive strategies, etc. The potential market is huge.

Pharmaceutical Outrages of the Month or Just How Stupid does Big Pharma Think We Are?

- ❖ Generic, twice a day amantadine still has a useful niche for some Parkinson's patients. Osmolex ER (tmax 7.5 hours, dosed once daily in the morning) and Gocovri (tmax 12 hours, dosed at bedtime) are new extended release versions of amantadine. Osmolex ER was brought to market by Osmotica Pharma, a company that focuses on transforming generic products into extended release medications. There were no new efficacy studies for Osmolex ER. Both drugs are touted as more tolerable without substantiation.

Prices:

Osmolex ER: \$18 per tab (kindly flat priced), \$540-\$1080/month.

Gocovri: \$47.50 per tab, \$2850/ month

Generic amantadine: \$0.85 per tab, \$51/month

I thought I was missing something, so I called a neurologist and asked about these two new drugs. His response, "I would never prescribe either of these drugs. I would look with disfavor on anyone who referred a patient on either of these drugs."

- ❖ Livalo (pitavastatin) at \$995/month is soon to lose its patent. Enter Zypitamag, (at only \$837/month), the magnesium salt of pitavastatin—every doctor's answer to the hypercholesterolemia problem. No new clinical trials. Recall that a month's worth of atorvastatin, simvastatin or lovastatin all cost less than \$10.
- ❖ Finally, Ximino, (a new extended release form of minocycline) for acne at \$840/ month joins other minocycline products, Solodyn (\$300/month), minocycline ER (\$300-\$420/month) and plain old 100mg tablets of minocycline at \$12/month.

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