

OREGON DUR BOARD NEWSLETTER[©]

AN EVIDENCE BASED DRUG THERAPY RESOURCE

© COPYRIGHT 2001 OREGON STATE UNIVERSITY. ALL RIGHTS RESERVED

Volume 3, Issue 3

Also available on the web and via e-mail list-serve at
http://pharmacy.orst.edu/drug_policy/drug_policy.html

September 2001

Selected New Drugs Reviewed

By Kathy Sentena, Pharm.D., OSU Primary Care/Managed Care Pharmacy Resident

ALMOTRIPTAN (AXERT[®])

Almotriptan was approved in May of 2001 for the abortive treatment of migraine headaches. Almotriptan is a selective serotonin agonist, similar to sumatriptan, naratriptan, rizatriptan and zolmitriptan.

Almotriptan is metabolized primarily by the CYP3A4 enzyme system. As with other triptans, it is recommended that almotriptan not be taken with other serotonin receptor agonists, ergotamine-type medications, MAO-inhibitors, erythromycin, ketoconazole, itraconazole or ritonavir.

Almotriptans duration of action is similar to other triptans, about 3 hours. Its side effect profile is similar to other triptans, except that it had significantly less chest pain associated with its use.¹ Almotriptan is a good option for patients unable to tolerate other triptans because of chest pain, however, because of the potential of this class of compounds to cause coronary vasospasm, almotriptan should not be given to patients with documented ischemic or vasospastic coronary artery disease.² Adverse effects seen with the 12.5mg dose have been shown to be similar to placebo, 18% vs. 16%, respectively.³

A double-blind, randomized, parallel-group study of 1255 patients with migraine was done to compare almotriptan with sumatriptan.¹ Patients were randomized to almotriptan 12.5mg or sumatriptan 50mg. Headache relief, defined as a decrease in pain to mild or no pain at two hours, was similar between the two groups. Headache freedom, defined as a decrease in pain to no pain at two hours, was found to favor sumatriptan over almotriptan, 24.0% and 17.9%, respectively. No statistically significant differences were found in headache reoccurrence. There was a significant difference in treatment-related adverse events and chest pain, favoring almotriptan.

Table 1 - Cost Comparison

Drug	Almotriptan (Axert [®]) 12.5mg	Naratriptan (Amerge [®]) 2.5mg	Rizatriptan (Maxalt [®]) 10mg	Sumatriptan (Imitrex [®]) 50mg	Zolmitriptan (Zomig [®]) 2.5mg
Response Rate	60%	42-66%	48-77%	50-58%	62-65%
Cost per tablet	\$12.50	\$17.58	\$16.16	\$16.01	\$14.73

* Table adapted from *J Clin Pharmacol* 2000; 40:687-700.

* Response rate is based on reduction of pain from severe to moderate to mild or none 2 hours post dosing.

* Costs are based on AWP Drug Topics Red Book Update June 2001.

In conclusion, almotriptan is a competitively priced triptan, but is still an expensive treatment option when compared to other migraine therapies. Almotriptan is an effective treatment for migraine that is especially appropriate for patients unable to take other triptans because of chest pain.

ESOMEPRAZOLE (NEXIUM[®])

Esomeprazole is a proton pump inhibitor that was approved in February 2001. Esomeprazole is the S-isomer of omeprazole, which comes off patent later this year. It works like other proton pump inhibitors, by binding to the gastric acid pump and preventing acid release into the stomach.⁴ Esomeprazole has been proven to be an effective agent when treating erosive esophagitis and GERD, but does not offer any significant benefit over traditional proton pump inhibitor therapy.

Esomeprazole is similar to omeprazole except that it has increased bioavailability but this does not translate to superior clinical efficacy.⁴ It was evaluated for the treatment of erosive esophagitis and GERD, maintenance healing and H.pylori eradication.

Esomeprazole was evaluated in an 8-week, randomized, double-blind trial involving 2425 patients with erosive esophagitis.⁵ Healing rates were 93.7% in the esomeprazole 40mg group compared to 84.2% in the omeprazole 20mg group. These results were statistically significant but probably not clinically significant, because this was a large study and small clinical differences could translate into statically significant differences.

A second study compared esomeprazole 40mg, esomeprazole 20mg and omeprazole 20mg in 1960 patients with reflux esophagitis.⁶ At week 8; there was a statistically significant higher healing rate in the esomeprazole groups versus omeprazole 20mg.

Another study was done to evaluate esomeprazole in maintenance healing. 318 patients were randomized to esomeprazole 40mg, esomeprazole 20mg, esomeprazole 10mg or placebo.⁸ Healing was maintained in 93.6% in the esomeprazole 40mg group, 93.2% in the esomeprazole 20mg group, 57.1% in the esomeprazole 10mg group and 29.0% in the placebo group after 6 months.

Lastly, esomeprazole was used for the eradication of H.pylori. Patients received one of three treatment regimens for 10 days: 1) esomeprazole 40mg qd, amoxicillin 1g bid, and clarithromycin

500mg bid (EAC) 2) esomeprazole 40mg daily and clarithromycin 500mg bid (EC) or 3) esomeprazole 40mg alone (E).⁹ The highest eradication rate was seen in the EAC group, which was 77% effective. This is not as effective as other regimens for H.pylori, which demonstrate 80-90% eradication.

Cost Comparison

Drug	Esomeprazole (Nexium®)	Lansoprazole (Prevacid®)	Omeprazole (Prilosec®)	Pantoprazole (Protonix®)	Rabeprazole (Aciphex®)
Dose	20-40mg	30mg	20mg	40mg	20mg
Cost	\$115	\$110	\$108	\$85.50	\$105.69

* Costs based on AWP Drug Topics Red Book Update, June 2001 for 30 days supply.

Esomeprazole is an effective agent in the treatment and maintenance healing of GERD and erosive esophagitis. No studies have compared esomeprazole 40mg to omeprazole 40mg. Although esomeprazole has increased bioavailability and is metabolized more slowly than omeprazole, treatment with esomeprazole appears to offer minimal clinical advantages.

GALANTAMINE (REMINYL®)

Galantamine is a reversible and competitive inhibitor of acetylcholinesterase, approved in February 2001 for the treatment of mild to moderate Alzheimer's disease. In addition to inhibiting acetylcholinesterase, galantamine causes enhanced responsiveness of nicotinic receptors when exposed to acetylcholine.¹⁰ Studies have not shown that this translates into any clinical advantages. Galantamine has similar efficacy to other acetylcholinesterase inhibitors, producing moderate benefits and many adverse reactions.

It is recommended that patients be started on 4mg twice daily and titrated every 4 weeks, if tolerated, to a total dose of 16-24mg.¹⁰ Dose titration and taking galantamine with food minimizes gastrointestinal side effects that are often associated with discontinuation of therapy. If the dosage schedule is interrupted for several days then galantamine should be re-started at the lowest dose. Nausea, vomiting, diarrhea, dizziness and headache were the most common side effects. In clinical studies, adverse effects were seen in over 80% of patients. Galantamine is hepatically metabolized by the CYP3A4 and CYP2D6 enzyme systems. It is recommended that it not be given with erythromycin, ketoconazole or paroxetine.¹⁰

Three clinical studies have evaluated the efficacy of galantamine in patients with mild to moderate Alzheimer's disease.^{11, 12, 13} All three studies were able to demonstrate statistically significant improvements based on the 70 point ADAS-cog scale. However, these small improvements of 2-4 points rarely translate into improved patient functioning.

Galantamine is a modestly effective therapy for the treatment of Alzheimer's disease, which is associated with a high rate of adverse reactions. Extensive hepatic enzyme metabolism makes

galantamine susceptible to drug interactions, not seen with rivastigmine. However, galantamine is effective at lower doses, making galantamine a better choice for patients that are unable to tolerate high doses. Considering the high cost of therapy, minimal therapeutic gain and high rate of troublesome adverse effects, galantamine should be used sparingly.

Cost Comparison

Drug	Donepezil (Aricept®)	Galantamine (Reminyl®)	Rivastigmine (Exelon®)	Tacrine (Cognex®)
Dose	5-10mg	16-32mg	3-12mg	20mg qid
ADAS-Cog Change	~ 4	3.1-4.1	-1.24 – 4.97	~ 4
Cost	\$108	\$130-259	\$130	\$153

* Costs based on AWP Drug Topics Red Book Update for June 2001 for one months supply.

References

1. Spierings E., et al. Oral Almotriptan vs Oral Sumatriptan in the Abortive Treatment of Migraine. Arch Neurol 2001; 58: 944-950.
2. Axert package insert. Chicago, IL: Pharmacia Corporation; May 2001.
3. Deleu D. and Hanssens Y. Current and Emerging Second-Generation Triptans in Acute Migraine Therapy: A Comparative Review. J Clin Pharmacol 2000; 40: 687-700.
4. Nexium package insert. Wilmington, DE; AstraZeneca; February 2001.
5. Richter J., et al. Efficacy and Safety of Esomeprazole Compared With Omeprazole in GERD Patients With Erosive Esophagitis: A Randomized Controlled Trial. Am J of Gastroenterology 2001; 96: 656-665.
6. Kahrilas P., et al. Esomeprazole improves healing and symptom resolution as compared with omeprazole in reflux oesophagitis patients: a randomized controlled trial. Aliment Pharmacol Ther 2000; 14: 1249-1258.
7. Lind T., et al. Esomeprazole provides improved acid control vs. omeprazole in patients with symptoms of gastro-oesophageal reflux disease. Aliment Pharmacol Ther 2000; 14: 861-867.
8. Johnson D., et al. Esomeprazole Once Daily for 6 Months Is Effective Therapy for Maintaining Healed Erosive Esophagitis and for Controlling Gastroesophageal Reflux Disease Symptoms: A Randomized, Double-Blind, Placebo-Controlled Study of Efficacy and Safety. Am J of Gastroenterology 2001; 96: 27-34.
9. Laine L., et al. Esomeprazole-Based Helicobacter pylori Eradication Therapy and the Effect of Antibiotic Resistance: Results of Three US Multicenter, Double-Blind Trials. Am J of Gastroenterology 2000; 95: 3393-3398.
10. Reminyl package insert. Titusville, NJ; Janssen Pharmaceutica; March 2001.
11. Wilcock G., Lilienfeld S., and Gaens E. Efficacy and safety of galantamine in patients with mild to moderate Alzheimer's disease: multicentre randomized controlled trial. BMJ 2000; 321; 1-7.
12. Tariot P., et al. A 5-month, randomized, placebo-controlled trial of galantamine in AD. Neurology 2000; 54: 2269-2276.
13. Raskind M., et al. Galantamine in AD. Neurology 2000; 54: 2261-2268.

