



Medical Assistance Division Medicaid Drug Utilization Review Newsletter

Volume 2 Issue 4

4th Quarter 2008



DUR Board Members

Manuel C. Archuleta, MD

Amy Bachyrycz, RPh,
PharmD

Greg D'Armour, RPh, PhC,
CGP

Martin Jagers, RPh, PharmD

John Lauriello, MD

Dennis Raisch, PhD, MS,
RPh

John Seibel, MD

Linda Stogner, MD

Gregory Toney, RPh,
PharmD, BCPP

Dale Whittleton, RPh

Inside This Issue

- Smoking Cessation:
Update in
Pharmacologic Therapy

Smoking Cessation: Update in Pharmacologic Therapy Deborah K. Brokaw, Pharm.D.

Tobacco use is one of the leading causes of illness and preventable death in the United States, accounting for more than 435,000 deaths each year.¹ These deaths are not only the result of active smoking, but also take into account the effects of secondhand smoke on non-smokers. Smoking has been known to cause many chronic diseases, but the majority of the mortality is due to lung cancer, ischemic heart disease, and chronic obstructive pulmonary disease (COPD).²

Despite an overall decline in smoking rates, approximately 21% of the adult US population (45 million) and 1/3 of the Medicaid population continue to smoke.^{1,3} Aside from the morbidity and mortality associated with tobacco use, it is responsible for approximately \$193 billion dollars in health-related costs and lost productivity each year.¹

Updated Guidelines

In May 2008, the United States Department of Health and Human Services published an update to their clinical practice guidelines for treating tobacco use and dependence. This update incorporated new treatment options and data that had become available since the 2000 guidelines were published. The underlying goal of the guidelines is for clinicians to strongly recommend the use of effective tobacco dependence counseling and medication treatments to patients who use tobacco. This is especially important since 70% of smokers report wanting to quit, and most cite a physician's advice to quit as an important motivator for attempting to quit smoking. Studies have also shown that advice delivered by any type of healthcare provider increases abstinence rates.¹

Healthcare providers should continue to use both counseling and pharmacologic strategies for their patients since both are effective methods for smoking cessation. However, when they are used in combination, they are more effective together than when used by themselves.¹

Recommended therapy

Who should receive medication for smoking cessation? All smokers who are trying to quit, unless contraindications exist. Unlike other sets of clinical practice guidelines, there was not one therapy identified as first line, rather seven first-line therapies that reliably increase long-term smoking abstinence rates. These include: Zyban® (bupropion sustained-release), Nicotine replacement therapies (lozenge, patch,

inhaler, nasal spray, gum) and Chantix[®] (varenicline). Equal weight was given to the different therapies since the authors thought it was important not to limit choices, but to identify effective treatments so they could choose the most appropriate therapy given patient specific variables (cost, comorbid conditions, patient preference, prior experience etc.). Second-line therapies include nortriptyline and clonidine. These drugs are currently not FDA approved for smoking cessation, and typically have more adverse effects associated with their use.¹

Combination therapy

Combination therapy is also recommended in the recent guidelines as being effective, since studies have shown lower nicotine withdrawal symptoms may occur in patients compared to monotherapy. Effective combinations include:

- Nicotine patch + Bupropion sustained release (SR)*
- Nicotine patch + Nicotine inhaler
- Nicotine patch (>14 weeks) + Nicotine replacement products (gum, nasal spray)

* FDA approved combination

Because of its nicotine antagonist effects, varenicline is not recommended to be used in combination with any form of nicotine replacement therapy. Patients who have used this combination have reported increased adverse effects.¹

Therapies not recommended

Various medications have been studied in clinical trials to assess their effectiveness for smoking cessation. The following medications have either been found ineffective or there is no evidence for their use in smoking cessation and are not recommended: selective serotonin re-uptake inhibitors, anxiolytics, benzodiazepines, beta-blockers, or meclizine.¹

Varenicline

Chantix[®] (varenicline) is the newest smoking cessation product that was approved by the Food and Drug Administration (FDA) on May 11, 2006. Unlike nicotine replacement products and bupropion, varenicline is a partial agonist selective for the $\alpha_4\beta_2$ nicotinic acetylcholine receptor. Efficacy in smoking cessation is hypothesized to be the result of its binding having partial agonist activity, which can diminish withdrawal symptoms by promoting a low level release of dopamine, while at the same time preventing the binding of nicotine to the $\alpha_4\beta_2$ nicotinic acetylcholine receptor.⁴ Therefore, varenicline is believed to not only stop the reward from smoking, but also reduce nicotine withdrawal symptoms.⁵

Compared to both placebo and bupropion SR, varenicline 1mg twice daily given for 12 weeks was more efficacious than either treatment.^{6,7} When varenicline was administered for an additional 12 weeks to smokers who previously were abstinent after 12 weeks of therapy, long-term abstinent rates were increased compared to placebo (43.6% vs. 36.9%, $p=0.02$).⁸ It is important to note that patients less than 18 years of age and those with a history of serious psychiatric illness were excluded from the trials. Nausea, which occurred in 30% of patients, was the most commonly reported adverse effect in clinical trials. The incidence was greater with the higher dose (1mg twice

daily), but was lessened with a slower titration period. Other reported adverse effects included insomnia (18%), headache (15%), and abnormal dreams (13%).^{4,5}

Within the past year, the FDA started to receive reports of serious neuropsychiatric events including changes in behavior, agitation, depressed mood, suicidal ideation, and suicide in patients currently on varenicline or who had discontinued therapy. Some of these patients had quit smoking, while others continued to smoke. As a result, a warning section and a patient medication guide were added to the package insert to reflect the information gathered from this ongoing research conducted by the FDA. It is recommended that all patients receiving varenicline be observed for these neuropsychiatric symptoms and/or exacerbation of pre-existing psychiatric illness (specifically schizophrenia, bipolar disorder, and major depressive disorder). If patients do experience any of these symptoms or any behavior out of the ordinary, they should stop taking the drug immediately and contact their healthcare provider.^{4,9}

Unanswered Questions

Despite all of the research that has been done on smoking cessation and the various therapies used, there are still many unanswered questions. There has yet to be one treatment that has been identified as the most efficacious, and since there are many reasons that people smoke, not one treatment will work for everyone. There is a lack of data regarding treatment strategies in populations such as young adults, minorities, and in patients with substance abuse and psychiatric conditions. More research is needed to clearly define the role and benefits of combination and extended duration therapy. One thing, however is certain, tobacco dependence is a chronic condition that requires ongoing assessment and repeated interventions. Healthcare providers should continue to encourage smoking cessation to all smokers and recommend effective smoking cessation therapies, both pharmacologic and non-pharmacologic, if they are willing to attempt quitting.

For more details regarding smoking cessation and for patient education materials please visit the following websites:

Centers for Disease Control and Prevention www.cdc.gov/tobacco

American Academy of Family Physicians www.familydoctor.org

American Heart Association www.americanheart.org

U.S. Department of Health and Human Services www.surgeongeneral.gov/tobacco

References:

1. Fiore MC, Jaén CR, Baker TB, et al. Treating Tobacco Use and Dependence: 2008 Update. Clinical Practice Guideline. Rockville, MD: U.S. Department of Health and Human Services. Public Health Service. May 2008.
2. CDC. Annual Smoking-Attributable Mortality, Years of Potential Life Lost, and Productivity Losses---United States, 1997--2001. *MMWR* 2005;54:625-8.
3. State Medicaid Coverage for Tobacco-Dependence Treatments---United States, 2006. *MMWR* 2008;57:117-122.
4. Pfizer Labs. Chantix[®] (varenicline) package insert. New York, NY; May 2008.
5. Zierler-Brown SL and Kyle JA. Oral varenicline for smoking cessation. *Ann Pharmacother* 2007;41:95-9.
6. Jorenby DE, Hays JT, Rigotti NA, et al. Efficacy of varenicline, an alpha4beta2 nicotinic acetylcholine receptor partial agonist, vs placebo or sustained-release bupropion for smoking cessation. *JAMA* 2006;56-63.
7. Gonzales D, Rennard SI, Nides M, et al. Varenicline, an alpha4beta2 nicotinic acetylcholine receptor partial agonist, vs sustained-release bupropion and placebo for smoking cessation: a randomized controlled clinical trial. *JAMA* 2006;296:47-55.
8. Tonstad S, Tonnesen P, Hajek P, et al. Effect of maintenance with varenicline on smoking cessation: a randomized controlled trial. *JAMA* 2006;296:64-71.
9. Information for Healthcare Professionals. Varenicline (marketed as Chantix) Information. U.S. Food and Drug Administration. Center for Drug Evaluation and Research. Available at: <http://www.fda.gov/cder/drug/InfoSheets/HCP/vareniclineHCP.htm>. Accessed on July, 30, 2008.