

Chantix (varenicline) Tablets Review

October 2006

Approved by FDA May 10, 2006 (Pfizer)

CHANTIX (varenicline) is a prescription NON-NICOTINIC smoking cessation treatment. It is a selective nicotinic receptor agonist indicated to aid in smoking cessation treatment in adults. Compared to previously available smoking cessation products (nicotine replacement therapy and bupropion sustained-release) it has a unique mechanism of action. It is a partial agonist selective for alpha-4, beta-2 nicotinic acetylcholine receptor subtypes. It binds with high affinity to these receptors, and its agonist action is thought to reduce the craving to smoke as well as the withdrawal symptoms from nicotine. By occupying the receptor sites, varenicline prevents binding of nicotine if the individual smokes while receiving treatment, thereby reducing the satisfaction associated with smoking.

Recommendation

Varenicline provides another option when considering available smoking cessation therapies. Comparative studies with agents other than bupropion SR are not available. Efficacy and effectiveness beyond 12 weeks or in populations other than those included in studies remains to be determined. Varenicline, therefore, should be considered second line therapy in patients failing to quit using first line alternatives of nicotine-replacement therapy (NRT) or bupropion SR smoking cessation therapy or having a contraindication to those therapies. There are few contraindications or other restrictions and low potential for drug interactions. **Varenicline would not be added to hospital formularies at this time. In an outpatient setting it offers a second line option when used as outlined in clinical trials.**

Safety — (no long term data)

*Sound Alike/Look Alike:** Chenix (chenodiol)
Pediatric Use: CHANTIX has not been studied in patients younger than 18 years old.
Pregnancy Risk: **Category Factor C**

Chantix (varenicline) has not been studied in pregnant or nursing women and is therefore not recommended in these patients. No contraindications are included in the prescribing information. Varenicline is almost completely absorbed and minimally metabolized. Approximately 92% of a dose is excreted unchanged in the urine. Renal elimination is primarily through glomerular filtration along with active tubular secretion. Dosage adjustment in renal impairment is as follows: $Cl_{cr} \geq 30$ mL/minute: No adjustment required; $Cl_{cr} < 30$ mL/minute. No dosage adjustment is required in hepatic impairment. There are no clinically meaningful drug interactions observed for varenicline to date. It does not inhibit or induce any of the following cytochrome P-450 enzymes: 1A2, 2A5, 2B6, 2C8, 2C9, 2C19, 2D6, 2E1, and 3A4/5, or induce 1A2 or 3A4. Pharmacokinetic differences have not been noted due to age, race, gender or smoking status. Mean age of study participants in the studies ranged from 42 to 45.4 for the various randomized groupings. **Successful cessation of smoking may alter pharmacokinetic properties of other medications (eg, theophylline, warfarin, insulin).**

Tolerability =

Nausea was the most common side effect occurring in about 30% of patients in the studies. Generally it was mild to moderate and for most people, but not all, it went away. In studies, more than one in ten people who took varenicline had nausea, headache, trouble sleeping (18%), or changes in dreams (13%). About 3% of patients discontinued treatment because of the nausea.

Efficacy =?

Studies were conducted in generally healthy smokers in clinical trials sponsored by Pfizer which provided funding, study drug, placebo and monitoring. Two identically designed, 12 week studies with follow-up for 40 weeks were conducted (see below). The primary outcome was abstinence at weeks 9-12 and secondarily continuous abstinence during the follow-up period. An additional study assessed the effects of an additional 12 weeks of therapy. In all studies, patients received an educational booklet on smoking cessation and received up to 10 minutes of counseling at each **weekly** visit.

** Similarity of drug names involves confusion between look-alike and/or sound-alike brand names and/or trade names. This may be names may cause confusion when handwritten or communicated verbally.

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	<i>Gonzales D. et al. JAMA 2006 296:47-55</i>			<i>Jorenby DE et al. JAMA. 2006 296:56-63</i>		
	<i>Varenicline</i>	<i>Bupropion SR*</i>	<i>Placebo*</i>	<i>Varenicline</i>	<i>Bupropion SR*</i>	<i>Placebo*</i>
Carbon monoxide–confirmed abstinence weeks 9 through 12	44% n=352	29.5% n=329 p<0.001	17.7% n=344 p<0.001	43.9% n=344	29.8% n=342 p<0.001	17.6% n=341 p<0.001
Continuous abstinence weeks 9 through 24	29.5%	20.7% p=0.007	10.5% p<0.001	29.7%	20.2% P=0.003	13.2% p<0.001
Continuous abstinence weeks 9 through 52 *	21.9%	16.1% p=0.057	8.4% p<0.001	23%	14.6% p=0.004	10.3% p<0.001

* significance vs. varenicline

Exclusion criteria for studies included serious or unstable disease within 6 months, seizure risk, diabetes mellitus requiring insulin or oral hypoglycemics medications, hepatic or renal impairment, clinically significant cardiovascular disease within 6 months, uncontrolled hypertension, severe COPD, history of cancer (except skin), history of clinically significant allergic reactions, major depressive disorder within the past year requiring treatment, panic disorder, psychosis, bipolar disorder, eating disorders, alcohol or drug abuse dependency within last year, use of tobacco products other than cigarettes, use of NRT, clonidine, or nortriptyline with the month prior to enrollment, BMI <15 or >38, prior varenicline or bupropion exposure, pregnant or nursing, investigational drug within 30 days, intention to donate blood or blood products during the treatment phase, use of marijuana or other tobacco products, and clinically significant abnormalities in screening lab values. In the Gonzales trial abstinence at 52 weeks shows 28.1% of the varenicline group abstinent vs. 22.8 % of the bupropion SR group vs. placebo 14%. Comparative clinical trials between varenicline and other agents are not available, nor has the efficacy of it in combination with other smoking cessation therapies been studied.

Price –

Drug	Drug Store.com	AWP
Chantix 0.5mg and 1mg tablets #56	\$106.99/28 day supply (\$3.83/day)	\$112.00
Bupropion g.eq. sustained release 150mg po qdx3d, then 150mg BID	\$69.98 (generic)	\$0.99 MAC

All patients receiving varenicline will have the opportunity to enroll in a free behavioral support program designed to help them address critical behavioral components of addiction and relapse.

Monthly Pricing: Gum at 9/day =, Patches (for 21mg, 14, or 7mg)

Simplicity =

Dosing starts 1 week before target quit date. A course of treatment is 12 weeks.

Initial Dosing: Days 1-3: 0.5mg once daily, Days 4-7: 0.5mg twice daily

Packaging reflecting this dosing titration is available.

Maintenance Dosing (week 2-12): 1mg twice daily

Orally food has no effect on pharmacokinetics. Varenicline should be taken after eating and with a full glass of water to reduce nausea.

Patients who cannot tolerate adverse events may require temporary reduction in dose.

If patient successfully quits smoking during the 12 weeks, may continue for another 12 weeks to help maintain success. If not successful in first 12 weeks, then stop medication and reassess factors contributing to failure.

ADDITIONAL INFORMATION:

www.deathsfromsmoking.net. See this web site for information on the hazards of smoking and the benefits from stopping. One in five American adults, or nearly 45 million people smoke cigarettes, which kills nearly 512,000 American men and women a year. About 192,000 die in middle age from smoking. Tobacco use, particularly cigarette smoking, is the single most preventable cause of death in the U.S. and is responsible for a growing list of cancers, as well as chronic diseases, including those of the lung and heart. About one in three of all cancer deaths is due to smoking.