



Therapeutic Class ReviewSM

Behavior Modification – varenicline (Chantix[®])

December 2006

New Product for Review:
varenicline (Chantix[®])

Dossier Provided by Manufacturer: Yes
Dossier Evaluation: 3

- 1- dossier w/missing components
- 2- all components present, except pharmaco-economic model
- 3- all components present (comprehensive)

Available Therapeutic Alternatives:

<i>Prescription Products</i>	
Preferred/Formulary	Non-Preferred/Non-Formulary
bupropion SR (Zyban [®]) – generic	varenicline (Chantix [®]) [Pfizer]
	nicotine inhaled (Nicotrol [®] Inhaler) [Pfizer]
	nicotine nasal (Nicotrol NS [®]) [Pfizer]

<i>Non-Prescription (OTC) Products</i>
nicotine gum (Nicorette) – generic
nicotine transdermal system (Nicoderm CQ, others) – generic
nicotine lozenge (Commit [®]) [GSK Consumer]

Executive Summary

Product Description

- Varenicline (Chantix, formally called Champix) is:
 - A non-nicotine-based medication that is used to help individuals quit smoking.
 - The first new prescription medication approved for smoking cessation in over a decade since bupropion (Zyban).
- Varenicline (Chantix) binds to nicotine receptors in the brain and provides some nicotine-like effects that:
 - ease withdrawal symptoms and block the effects of nicotine from cigarettes.
 - fool the brain into believing that the urge to smoke tobacco has been satisfied.

- One treatment course for varenicline (Chantix) = 12 weeks.
Recommended dosing is 1 mg orally twice daily after a 1-week titration schedule:
 - Days 1-3: 0.5 mg once daily.
 - Days 4-7: 0.5 mg twice daily.
 - Days 8 – End of treatment: 1mg twice daily.
- Smoking cessation therapies (including varenicline [Chantix]) are more likely to succeed for patients who are motivated to stop smoking and who are provided additional advice and support. Patients should be provided with appropriate educational materials and counseling to support the quit attempt.
- Varenicline (Chantix) is marketed as:
 - Having better efficacy than bupropion (Zyban) in smoking cessation.
 - Easing withdrawal from nicotine.
- Under most benefit plans, coverage for smoking cessation products are prescription riders.
 - All medications for smoking cessation, including varenicline (Chantix), require support and counseling programs to be successful.
 - Smoking cessation treatment is an investment in both the products and services that are necessary to be effective.

Evidence

- All of the clinical trials evaluating varenicline (Chantix) for smoking prevention were fatally flawed.
 - Drop-out rates ranged from 24% to 37%. These high rates erode randomization and confound the results.
 - Differences in drop-out rates between groups were as high as 11%. The studies made the assumption that any patient who dropped out was a failure; this may have biased the results in the favor of varenicline (Chantix).
 - Extending the duration of treatment with varenicline (Chantix) may reduce the relapse rate, but this study did not have an active comparator.
- There is no useful data indicating that varenicline (Chantix) is more effective than existing formulary products as an aid to smoking cessation treatment.
 - The head-to-head trials suffered the same flaws discussed above.
 - Drop out rates were 5% to 6% higher in the bupropion group, potentially confounding and biasing the results.
 - For the endpoint of continuous abstinence rate, weeks 9-52 (judged to be the most clinically significant), varenicline (Chantix) was statistically superior to bupropion in only one of the two head-to-head trials.
- There is no useful data indicating that varenicline (Chantix) is safer than existing formulary products as an aid to smoking cessation treatment.
 - Overall rates of adverse events were comparable between varenicline (Chantix) and bupropion.
 - Patients receiving varenicline (Chantix) reported nearly a 30% incidence of nausea.

- Considerations in Subpopulations:
 - **Pediatrics** - Because the safety and effectiveness of varenicline (Chantix) in pediatric patients have not been established, use in patients under 18 years of age is not recommended.
 - **Geriatrics**: A combined single and multiple-dose pharmacokinetic study demonstrated that the pharmacokinetics of 1 mg varenicline given QD or BID to 16 healthy elderly male and female smokers (aged 65-75 yrs) for 7 consecutive days was similar to that of younger subjects.
 - **Gender**: No specific recommendations.
 - **Race, ethnicity**: No specific recommendations.

Conclusion

- Varenicline (Chantix) is non-preferred/non-formulary because there is:
 - No useful evidence for improved efficacy over existing formulary agents.
 - No useful evidence for improved safety over existing formulary agents.
 - Higher cost relative to other formulary agents.

Products^{1,2,18}

Drug Products	FDA approval ^a	FDA approved indications	Usual Dose/Route	Cost ^b	Potential Off-label Uses ^c
bupropion SR - generic (Zyban) -	05/1997	- smoking cessation treatment - depression	150 mg twice daily	\$75 (MAC)	- neuropathic pain - weight loss
nicotine inhalation system (Nicotrol Inhaler)	05/1997	smoking cessation treatment	Individualized, usually 6 to 16 cartridges per day	\$141 - \$423	
nicotine nasal spray (Nicotrol NS)	03/1996	smoking cessation treatment	1-2 mg (2-4 sprays) per hour increasing to 40 mg (~ ½ bottle) per day as needed	\$141	- Blepharospasm
nicotine polacrilex (Nicorette, generic)	01/1984	smoking cessation treatment	2- 4 mg as needed. Recommend a minimum of 9 pieces of gum per day for 1 st 6 weeks	\$34 - \$41	- Gilles de la Tourette's syndrome; Adjunct
nicotine transdermal system (Nicoderm CQ, Nicotrol, generic)	07/1996	smoking cessation treatment	1- 21 mg patch daily X 6 weeks, then 14mg patch daily X 2 weeks, then 7 mg patch daily X 2 weeks	\$58	- Down syndrome - Malignant atrophic papulosis - Ulcerative colitis
varenicline (Chantix)	05/2006	smoking cessation treatment	0.5mg daily x 3 days, then 0.5mg twice daily x 4 days, then 1mg twice daily for 12 weeks total, with an option 12 week extension.	\$112	

^a Date applies to approval date for the original brand name medication where there are now generics available.

^b Cost estimate based on AWP (average wholesale price) listed in First Data Bank or MAC (maximum allowable cost) as of August 2006 for 1 month of therapy.

^c As listed in © 1974 - 2006 Thomson MICROMEDEX database or as referenced.

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