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Indiana Medicaid Therapeutics Committee **Therapeutic Class Review Summary**

Therapeutic Class:

Smoking Deterrent Agents

Overview:

According to the American Cancer Society, cigarettes kill more Americans than alcohol, car accidents, suicide, AIDS, homicide, and illegal drugs. Smoking is the most preventable cause of premature death in the country. In 2002, a staggering 430,700 deaths were expected in the US from tobacco use. Yet, an estimated 46.2 million US adults were current smokers in 2001. Cigarette smoking is a major cause of cancers of the lung, larynx, oral cavity, pharynx and esophagus and is a contributing cause in the development of cancers of the bladder, pancreas, uterus, cervix, kidney, stomach, and some leukemias. Moreover, smoking is also a major cause of heart disease, bronchitis, emphysema, and stroke and contributes to the severity of colds and pneumonia. Smokers who quit before age 50 have half the risk of dying in the next 15 years compared with those who continue to smoke. Additionally, quitting smoking substantially decreases the risk of each of the cancers and major diseases previously mentioned.

The Department of Health and Human Services (DHHS) states in their 2008 guidelines that the seven first-line pharmacotherapies for smoking cessation include: bupropion SR, nicotine gum, nicotine inhaler, nicotine lozenge, nicotine nasal spray, nicotine patch, and varenicline. Recommended second-line agents are clonidine and nortriptyline. (clonidine and nortriptyline are not discussed in this review.) The guidelines also state that certain combinations of first-line medications have been shown to be effective smoking cessation treatments. Effective combination medications are long-term (> 14 weeks) nicotine patch + other NRT (gum and spray), the nicotine patch + the nicotine inhaler, and the nicotine patch + bupropion SR.

In 1988, the Surgeon General determined that nicotine is the addictive drug in tobacco. The repeated, compulsive seeking or use of a substance despite harmful consequences characterizes addiction. Addiction is often accompanied by adverse physical and psychological dependence on a substance. Nicotine is a potent ganglionic and CNS stimulant, the actions of which are mediated via nicotine-specific receptors. Biphasic actions are observed depending on the dose administered. The main effect of nicotine in small doses is stimulation of all autonomic ganglia; with larger doses, initial stimulation is followed by blockade of transmission. Nicotine products for smoking cessation that are currently on the market include a transdermal patch, an inhaler, a nasal spray, gum and a lozenge. These products are indicated to aid with nicotine withdrawal following cessation of smoking.

Bupropion and varenicline are alternative smoking cessation aids that may exert changes in affect, mood, and the motivation to use nicotine. The mechanism by which bupropion enhances the ability to abstain from tobacco smoking is unknown, but is probably related to inhibition of noradrenergic or dopaminergic neuronal uptake. The resultant increase in norepinephrine may attenuate nicotine withdrawal symptoms, while increased dopamine at neuronal sites may reduce nicotine cravings and the urge to smoke. Varenicline partially stimulates $\alpha 4\beta 2$ receptors to produce a modest level of mesolimbic dopamine thereby diminishing nicotine cravings and withdrawal symptoms. Varenicline also has the added benefit of blocking the effects of nicotine by occupying receptor sites. Smokers with a negative affect are less likely to be able to quit.

DHHS guidelines recommend behavior modification through counseling as well as pharmacotherapy for effective smoking cessation treatment outcomes. Comparative clinical data available for the smoking deterrent agent class is limited. A randomized, comparative trial suggests that there is no difference in abstinence rates in patients using gum, the transdermal patch, nasal spray or inhaler. However, patients using the nasal spray were the least compliant because of adverse effects, and patients using the patch were the most compliant. This is the only trial that evaluated available nicotine replacement agents (lozenge excluded) at the time of study completion. Bupropion is shown to increase smoking abstinence alone or in combination with a nicotine transdermal system. Varenicline may be more efficacious than bupropion in increasing smoking abstinence; however, its safety and efficacy in combination with other smoking cessation therapies has not been studied. Recently, the FDA issued a Public Health Advisory regarding the potential of varenicline to cause behavioral and psychiatric side effects including severe depression, mood changes, and suicidal thoughts, and recommended caution in patients with a known history of psychiatric illness. Of note, bupropion has a black box warning for the increased risk of suicidal thinking and behavior in children and adolescents.

| Generic Name | Trade Name | Dosage Form | Manufacturer | Rx | Generic Available |
|---------------------|-----------------------|-------------------------|---------------------|-----------|--------------------------|
| Bupropion | Zyban® | Tablet | GSK, various | Y | Y |
| Nicotine | Habitrol® | Patch | Novartis | N | N |
| Nicotine | Prostep® | Patch | Aveva | N | N |
| Nicotine | Nicotrol® | Patch | Pharmacia | N | N |
| Nicotine | Nicotine | Patch | Aveva | N | N |
| Nicotine | Nicoderm CQ® | Patch | GSK | N | N |
| Nicotine | Nicotrol® | Inhaler, Nasal spray | Pharmacia | Y | N |
| Nicotine | Nicorette® | Gum | GSK | N | Y |
| Nicotine | Thrive® | Gum | Novartis | N | Y |
| Nicotine | Commit® Nicorette® | Lozenge | GSK, Perrigo | N | Y |
| Varenicline | Chantix™ | Tablet | Pfizer | Y | N |



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Indiana Medicaid Therapeutics Committee
*Therapeutics Class Review Summary of
Smoking Deterrent Agents*

Summary:

Tobacco-related illnesses are associated with high rates of morbidity and mortality. Smoking cessation agents can be clinically effective and cost effective relative to other medical and disease prevention interventions. However, clinical literature suggests that successful permanent smoking cessation occurs with dual counseling and pharmacologic intervention treatment programs. Many of these agents are over-the-counter and generically available. Varenicline is a new prescription agent that may be more efficacious than bupropion in increasing smoking abstinence. Selection of a smoking deterrent agent for the preferred list should take into consideration ease of administration, probable patient compliance, and cost.