



CICLESONIDE AND VARENICLINE: WHAT IS THE ROLE FOR THESE NEW DRUGS IN CURRENT PHARMACOTHERAPY?

1. ALVESCO® (CICLESONIDE): a once-daily inhaled corticosteroid

Unique Features

Ciclesonide is a parent compound that is not pharmacologically active. Once inhaled, it is converted by esterases in the lungs to its active metabolite (des-ciclesonide). This active metabolite is a potent glucocorticoid that results in targeted anti-inflammatory activity.^{1,2} It is formulated as a solution delivered by a hydrofluoroalkane (HFA) inhaler that creates a small-particle aerosol, allowing greater lung deposition and less oral exposure.^{2,3} The combination of low oropharyngeal deposition of ciclesonide and minimal conversion of ciclesonide to the active metabolite in the oropharynx, may minimize the risk for local adverse events such as oral candidiasis and hoarseness.⁴ The high protein binding (99%) and rapid clearance of des-ciclesonide limit the amount of free drug available systemically, thereby reducing the potential for systemic effects.^{3,5} Ciclesonide forms reversible lipid conjugates in the lung, creating a reservoir of active drug that may prolong anti-inflammatory activity in the lungs to allow once daily dosing.⁵ Alvesco® does not need to be shaken before administration because it is a solution.¹

Indication¹

It is indicated for prophylactic management of steroid-responsive asthma in patients 18 years of age and older. It is not presently recommended for patients younger than eighteen years old.

Safety

There is little published safety information from long-term, controlled clinical trials of ciclesonide.³ Oropharyngeal adverse effects (sore throat, dry mouth, hoarseness or voice alteration, pharyngitis and candidiasis) occurred at low rates in clinical trials. Rates were similar for ciclesonide and placebo treated patients.³ Studies on cortisol secretion suggest that ciclesonide does not have a suppressive effect on the hypothalamic-pituitary-adrenal axis.³ Further, long-term studies are needed to determine whether ciclesonide reduces the incidence of systemic corticosteroid adverse effects, such as reduced bone density, cataracts, reduced growth velocity in children and adrenal suppression.

Efficacy

Relatively few clinical trials have been performed comparing ciclesonide to other inhaled corticosteroids. Most of these trials have been limited to 12 weeks duration and compared ciclesonide to a less than equivalent dose of comparator. Current trials suggest similar efficacy to existing inhaled corticosteroids, fluticasone and budesonide. These trials have not looked at outcomes such as asthma exacerbations and Emergency Room visits.

Availability/Cost

Alvesco® 100mcg MDI (120 doses) ~\$44.00; 200mcg MDI (120 doses) ~\$74.00 (wholesale prices). Not currently on the Saskatchewan formulary, or covered by EDS.

Place in Therapy

Alvesco® seems to work as well as Flovent® (fluticasone) and Pulmicort® (budesonide) for improving lung function and asthma symptoms. There is some evidence of reduced local (oropharyngeal) side effects, but more long-term data is needed before we can determine if Alvesco® reduces systemic adverse effects as well. **Given the available evidence, Alvesco® does not currently offer any significant advantages over other available inhaled steroids.**

Prepared by Amber Simmons, Hospital Pharmacy Resident

2. CHAMPIX® (VARENICLINE): A New Smoking Cessation Drug

Unique Features^{1,3}

Varenicline is the first partial nicotine agonist indicated for smoking cessation. It binds to the alpha-4 beta-2 nicotinic acetylcholine receptor but produces significantly less activity than nicotine. It also selectively blocks nicotine binding at the receptor preventing stimulation of the central nervous dopamine system and inhibiting the reinforcement and reward experience associated with smoking. Unlike bupropion, varenicline does not appear to lower the seizure threshold. Currently there are no contraindications to the use of varenicline.

Indication²

Health Canada has approved Champix® for smoking cessation treatment in adults in conjunction with smoking cessation counseling.

Safety^{1,3}

Varenicline is not recommended in patients under 18 years. The most commonly reported adverse events include nausea (30%); sleep disturbance (18%), headache (15%), abnormal dreams (13%), constipation (8%), flatulence (6-9%), vomiting (5%) and change in taste perception (5-8%). The incidence of nausea is dose-related and can be managed by dose reduction and slower titration to therapeutic dose. Further long-term studies are needed to determine whether the use of varenicline leads to weight gain.

Efficacy^{3,4}

Clinical trials suggest that varenicline produces a superior rate of smoking abstinence after 9 to 12 weeks of treatment when compared with placebo, number needed to treat (NNT) = 8, and when compared with bupropion SR, NNT = 7. After 52 weeks, however, the cessation rates for subjects treated with varenicline and bupropion SR were not significantly different.³ Varenicline has not been tested head-to-head with nicotine replacement therapies.

Availability/Cost

Champix® is expected to become available in pharmacies by late April, 2007.² At this time, it is not known how much Champix® will cost in Canada. In the United States, Chantix® (the American brand name for varenicline) retails for \$3.90 – \$4.80 per day.⁵

Place in Therapy^{3,4}

The rates of smoking abstinence reported in the trials were the combined effect of counseling and active treatment with varenicline. Studies are needed to assess the effect of varenicline on smoking cessation without the use of behavioral therapies. Trials comparing it with nicotine replacement therapy and further trials with bupropion are needed. Longer duration trials are needed to assess its effectiveness on relapse prevention. **Overall, current evidence suggests that varenicline is more effective than placebo and bupropion SR for smoking cessation, at least short-term. It also appears to cause fewer side effects than bupropion SR. Thus, varenicline can be considered an effective option for smoking cessation in combination with regular counseling/behavioral therapies.**

Prepared by Gurpreet Parmar, SPEG Student and Karen Jensen, Drug Information Consultant

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