

CEDAC FINAL RECOMMENDATION and REASONS for RECOMMENDATION

DARIFENACIN (Enablex[®] – Novartis Pharmaceuticals Canada Inc.)

Description:

Darifenacin is an anticholinergic agent that is approved for use in the treatment of overactive bladder.

Dosage Forms:

7.5 and 15 mg tablets

Recommendation:

The Canadian Expert Drug Advisory Committee (CEDAC) recommends that darifenacin not be listed.

Reasons for the Recommendation:

1. The Committee reviewed eight randomized controlled trials (RCTs) of one to 12 weeks in duration, five of which were placebo controlled, two in comparison with oxybutynin and one in comparison with tolterodine. Of the placebo controlled RCTs, four reported a statistically significant reduction in the median number of incontinence episodes with darifenacin (range of 1.4 to 4.3 fewer episodes per week) and three reported statistically significant reductions in the median frequency of micturition with darifenacin (range of 0.7 to 0.9 fewer micturitions per day). In the RCTs comparing darifenacin with oxybutynin and tolterodine, there were no differences in efficacy between the treatment groups.
2. Darifenacin causes typical anticholinergic side effects and the incidence of dry mouth and constipation were significantly higher in darifenacin versus placebo treated patients. In comparison with other anticholinergic agents, darifenacin was reported to cause a higher incidence of constipation compared with tolterodine and a lower incidence of dry mouth compared to oxybutynin.
3. Darifenacin offers the theoretical potential of a reduction in central nervous system side effects compared with oxybutynin (due to reduced penetration of the blood-brain barrier and selectivity for muscarinic M3 receptors), but this purported advantage has not yet been proven in clinical trials in elderly patients in whom this adverse effect is most important.
4. Darifenacin costs \$1.58 per day which is more expensive than immediate-release oxybutynin (\$0.50 – 0.75 per day) and trospium (\$1.50 per day, or less for patients with renal dysfunction). The Committee felt that there was insufficient evidence in support of an advantage of darifenacin over these agents.

Common Drug Review

Of Note:

1. Both published and unpublished data were reviewed and taken into consideration in making this recommendation.
2. The Committee had concerns about the increase in number of anticholinergic agents available to treat overactive bladder disorder, the increased use of these agents and their risk to benefit ratio, especially in elderly patients. The Committee recommends that drug plans consider a drug class review of the effectiveness, safety and cost-effectiveness of these agents.