

Valsartan

Product:

VALSARTAN (Diovan®), 40mg tablet

Class of drugs:

Angiotensin II receptor blocker (ARB)

Indication:

Treatment of mild to moderate high blood pressure

Manufacturer:

Novartis Pharmaceuticals Canada Inc.

CED Recommendation

The CED recommended that valsartan (Diovan) 40mg not be listed on the Ontario Drug Benefit (ODB) Formulary on the basis that it has not proven more effective, but is proportionately more expensive than available alternatives.

Executive Officer Decision

Based on the CED's recommendation, the Executive Officer decided not to list valsartan (Diovan) 40mg tablets.

Status

No funding through the Ontario Public Drug Programs.

Highlights of Recommendation:

- ◆ Valsartan (Diovan) is used to treat mild to moderate high blood pressure (hypertension). It may also be used in patients after they have experienced a heart attack.
- ◆ Diovan 40mg is a new strength of valsartan. Diovan 80mg and 160mg tablets are currently listed on the Ontario Drug Benefit (ODB) Formulary
- ◆ Two classes of drugs can be used to treat patients after a heart attack: angiotensin converting enzyme (ACE) inhibitors, or angiotensin II receptor blockers (ARBs). Currently, ACE inhibitors, such as captopril, are the standard of treatment following a heart attack. There are many different drugs from both classes currently available on the Ontario Drug Benefit (ODB) Formulary.
- ◆ Valsartan (Diovan) may be used in patients where an ACE inhibitor is not appropriate.
- ◆ Based on the available evidence, valsartan (Diovan) has been shown to be as effective but not better than captopril.
- ◆ The recommended dose of valsartan (Diovan) following a heart attack has not been studied. It is unclear from the available study what the appropriate dose is for valsartan (Diovan) following a heart attack.
- ◆ Valsartan (Diovan) 40mg, at \$1.05 per tablet, is priced the same as the 80mg and 160mg tablets.
- ◆ **Overall, the Committee noted that valsartan (Diovan) has not been proven to work better than standard treatment, such as captopril, after a heart attack. Valsartan (Diovan) 40mg is not proportionately priced compared to the 80mg and 160mg strengths.** Therefore, the Committee recommended that valsartan (Diovan) 40mg not be listed on the Ontario Drug Benefit (ODB) Formulary.

Background:

Valsartan (Diovan) is an angiotensin II receptor blockers (ARB), approved for use in the treatment of mild to moderate hypertension (high blood pressure) in once daily dosages of 80mg and 160mg.

Valsartan (Diovan) 40mg is indicated as a starting dose for certain patients who may be at risk of serious cardiac complications that may result in death and who are not able to start treatment with an ACE inhibitor. The manufacturer's recommended starting dose for this indication is 20mg twice daily, with gradual dose increases to a target dose of 160 mg twice daily.

Heart attack remains one of the world's leading causes of death. While progress has been made in treating heart attacks in the emergency room, people who survive the acute phase of a heart attack have permanently damaged hearts and are at increased risk for repeat attacks, heart failure, or other serious complications, including death.

Treatment with ACE inhibitors may reduce these risks and may reduce death in patients with damaged hearts after an acute heart attack. ACE inhibitors are the standard treatment for patients with heart failure or damage to the left valve of the heart muscle (left ventricular dysfunction). Trials with ACE inhibitors have demonstrated benefits in the left ventricle, improvement in symptoms of congestive heart failure and reduction in repeat heart attacks as well as death. Recent clinical trials have also established that ARBs, such as valsartan (Diovan), are an acceptable alternative to ACE inhibitors, especially in patients who cannot tolerate ACE inhibitors.

There are approximately 10 different ACE inhibitors and 5 ARBs, including valsartan (Diovan), listed on the ODB Formulary.

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Detailed Discussion:

- ◆ The manufacturer, Novartis Pharmaceuticals Canada Inc., asked the Ministry of Health and Long-Term Care to consider listing valsartan (Diovan) 40mg on the ODB Formulary.
- ◆ The CED has reviewed valsartan (Diovan) 40mg tablet twice between March and October 2006.
- ◆ The VALIANT study (Pfeffer et al. *NEJM* 2003;349:1893-1906) is a multicentre, double-blind randomized controlled trial comparing captopril monotherapy, valsartan (Diovan) monotherapy and the combination of valsartan (Diovan) and captopril in myocardial infarction complicated by heart failure, left ventricular dysfunction or both. The results from this non-inferiority study demonstrated that valsartan (Diovan) is as effective as captopril in reducing mortality in patients who are at high risk of cardiovascular events after a myocardial infarction. Mortality from any cause and cause-specific mortality were similar in the three treatment arms.
- ◆ Dose selection in the VALIANT study was based on protocols used in valsartan (Diovan) trials for the treatment of heart failure. The noted titration schedule in the VALIANT trial was made to accommodate hemodynamically unstable post-MI patients. These adjustments included a lower starting dose of 20mg twice daily, and potentially a more protracted titration regimen to achieve the maximum dose of 160mg twice daily. The Committee commented that the more aggressive titration schedule would more likely be seen in a hospital, and not in a community setting.
- ◆ The Committee raised concerns regarding the potential use of this lower strength in the treatment of hypertension where there is no evidence of its effectiveness.
- ◆ The most common side effects with valsartan (Diovan) are headache and dizziness.
- ◆ Valsartan (Diovan) 40mg is priced the same as the 80mg and 160mg tablets at \$1.05 per tablet.

- ◆ Given the availability of the 80mg and 160mg tablets on the Formulary, the Committee recommended that the lower strength 40mg tablet should be priced proportionately lower than both of these higher strength tablets.
- ◆ Overall, the Committee noted that the available evidence does not demonstrate clinical superiority of valsartan (Diovan) versus captopril. Mortality rates were similar in the three treatment arms in the VALIANT study. Furthermore, it is unlikely that an aggressive titration schedule for valsartan (Diovan) would be used in the community setting and would be more limited to the hospital setting. There is also a risk of off-label use of the valsartan (Diovan) 40mg tablet that is below the recommended daily dose for the treatment of hypertension.

CEDAC Recommendation:

(<http://www.cadth.ca/index.php/en/cdr/recommendations>)

Valsartan (Diovan) 40mg was not reviewed by the Canadian Expert Drug Advisory Committee (CEDAC).



Ministry of
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