

## CEDAC FINAL RECOMMENDATION on RECONSIDERATION and REASONS for RECOMMENDATION

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### PEGVISOMANT (Somavert™ – Pfizer Canada Inc.)

#### **Description:**

Pegvisomant is a growth hormone receptor antagonist that is approved for the treatment of acromegaly in patients who have had an inadequate response to surgery, and/or radiation therapy, and other medical therapies, or for whom these therapies are not appropriate. Acromegaly is a clinical syndrome due to the overproduction of growth hormone by a pituitary tumor. Excessive growth hormone increases the level of serum insulin-like growth factor I (IGF-I) resulting in tissue and organ overgrowth.

#### **Dosage Forms:**

10 mg, 15 mg and 20 mg vial for subcutaneous injection

#### **Recommendation:**

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

#### **Reasons for the Recommendation:**

1. The Committee considered the results of two randomized controlled trials (RCTs) of six and 12 weeks duration that compared pegvisomant with placebo in adults with acromegaly and elevated IGF-I who were not receiving other pharmacologic therapies for acromegaly (dopamine agonists and somatostatin analogues). In the 12 week RCT, pegvisomant 20 mg daily resulted in a greater proportion of patients with normalization of serum IGF-I levels (82% versus 10%). While statistically significant improvements in mean symptom scores for soft tissue swelling, excessive perspiration and fatigue were noted, there were no differences in the changes in quality of life between the study groups using the Short Form 36 questionnaire.
2. While pegvisomant has been shown to reduce IGF-I levels, it is uncertain whether a reduction in IGF-I levels is a valid surrogate endpoint for improvement in clinical outcomes, including survival.
3. The Committee was concerned that the efficacy of pegvisomant has only been assessed in a 12 week RCT, though acromegaly is a chronic condition. As such, the long-term benefits and risks of pegvisomant for patients with acromegaly are unknown.
4. Pegvisomant therapy costs approximately \$60,000 to \$80,000 per year for doses of 15 and 20 mg per day, respectively. The economic analysis submitted by the manufacturer estimated the cost per quality-adjusted life year (QALY) to be \$137,000. However, this may be a significant underestimate since this analysis rested on several assumptions that are uncertain and not supported by the present clinical data, namely that pegvisomant would significantly increase survival, that quality of life would be significantly improved, and that pegvisomant would be used without concomitant use of somatostatin analogs.

**Of Note:**

1. Both published and unpublished information were reviewed and taken into consideration in making this recommendation.
2. Safety issues include elevation of hepatic enzymes in 10% of patients who received pegvisomant in extension studies.
3. In keeping with its mandate, Committee recommendations are based on cost-effectiveness relative to current accepted therapy and using conventional criteria, pegvisomant has not been shown to be cost-effective. However, this by itself is only one of the factors that is considered when drug plans make a decision about funding. Pegvisomant has demonstrated a biological effect in a disease in which patients do not always respond to dopamine agonists and somatostatin analogues. It has been argued that the costs of drugs to treat rare diseases are often high because of the relatively small number of patients for whom the drug is indicated. On the other hand, reimbursement of pegvisomant would raise questions about equity, since drugs that have not been shown to be cost-effective for other diseases are not generally reimbursed.

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**Common Drug Review**