Pharmacotherapeutic report, summary

Vandetanib (Caprelsa®) for the indication
'metastatic medullary thyroid cancer'

Approved on 24 September 2012 by the Medicinal Products Reimbursement Committee (CFH)

Medicine. Vandetanib (Caprelsa®) tablets, 100 mg and 300 mg.

Registered indication. "Caprelsa is indicated for the treatment of aggressive and symptomatic medullary thyroid cancer (MTC) in patients with unresectable locally advanced or metastatic disease. For patients who do not have a mutation in a gene called the 're-arranged during transfection' (RET) gene, or if this is not known, a possible lower benefit should be taken into account before individual treatment decision ('Conditional registration').

Posology. 300 mg once daily.

Mechanism of action. Vandetanib is a powerful inhibitor of the vascular endothelial growth factor receptor-2 (VEGRF-2), the epidermal growth factor receptor (EGFR) and RET-tyrosine kinases. Vandetanib inhibits tumour growth and angiogenesis in both *in vitro* and *in vivo* models.

Summary of the therapeutic value

Intended effects. Based on a very limited and provisional analysis of the disease progression and tumour response, without definitive survival data, the biological efficacy of vandetanib on metastatic medullary thyroid cancer has been plausibly demonstrated, particularly for the sub-group of patients with a positive RET-mutation status. It has also been plausibly demonstrated that vandetanib has an effect on delaying the progression of pain.

Unintended effects. Serious adverse drug reactions of vandetanib are not rare. These include severe cardiac arrhythmias (*torsade de pointes* and ventricular tachycardia are uncommon (≥ 1/1,000 to < 1/100), QTc-extension common (≥ 1/100 to < 1/10)), the severe posterior reversible encephalopathy syndrome (PRES/RPLS), erythema multiforme and interstitial lung disease (sometimes fatal).

Experience. There is limited clinical experience with vandetanib.

Applicability. The risk of cardiac side effects, particular *torsade de pointes*, may be increased in patients with electrolyte imbalance.

Ease of use. Vandetanib is administered per os.

Final conclusion. Vandetanib has a therapeutic added value in comparison with placebo for the treatment of aggressive and symptomatic medullary thyroid cancer (MTC) in patients with unresectable locally advanced or metastatic disease, provided that treatment is limited to patients in whom the disease follows a symptomatic and aggressive course.

*The original text of this **CFH Report** of CVZ was in Dutch. Although great care was taken in translating the text from Dutch to English, the translation may nevertheless have resulted in discrepancies. Rights may only be derived on the basis of the Dutch version of CVZ's CFH-report.*

Furthermore, CVZ points out that only the summary of this report was translated. A proper understanding of all relevant considerations and facts would require familiarity with the Dutch version of this report, including all appendices.