Healthcare Improvement Scotland | SMC Advice on new medicines

Advice document
SMC2754

cabozantinib film-coated tablets (Cabozantinib Ipsen)

Ipsen Ltd

07 February 2025

The Scottish Medicines Consortium (SMC) has completed its assessment of the above product and, following review by the SMC executive, advises NHS Boards and Area Drug and Therapeutics Committees (ADTCs) on its use in NHSScotland. The advice is summarised as follows:

ADVICE: following an abbreviated submission

cabozantinib (Cabozantinib Ipsen) is accepted for use within NHSScotland.

Indication under review: as monotherapy for the treatment of hepatocellular carcinoma (HCC) in adults who have previously been treated with sorafenib.

Cabozantinib offers an additional treatment choice in the therapeutic class of protein kinase inhibitors.

Another protein kinase inhibitor was accepted for use under the end of life process.

This advice applies only in the context of an approved NHSScotland Patient Access Scheme (PAS) arrangement delivering the cost-effectiveness results upon which the decision was based, or a PAS/ list price that is equivalent or lower.

Chair
Scottish Medicines Consortium

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1. Clinical Context

1.1. Medicine background

Cabozantinib is a protein kinase inhibitor that blocks mesenchymal epithelial transition factor (MET), vascular endothelial growth factor (VEGF) receptors and other tyrosine kinases including the GAS6 receptor (AXL).[1]

The recommended dose of cabozantinib for hepatocellular carcinoma (HCC) is 60 mg orally once daily. Treatment should continue until the patient is no longer clinically benefiting from therapy or until unacceptable toxicity occurs. For further details including dose modifications, please refer to the Summary of Product Characteristics (SPC).[1]

1.2. Relevant comparator(s)

Regorafenib is another protein kinase inhibitor that has previously been accepted for use by SMC as monotherapy for the treatment of adult patients with HCC who have been previously treated with sorafenib (SMC 1316/18). Regorafenib blocks multiple protein kinases, including kinases involved in tumour angiogenesis (VEGFR1-, -2, -3, TIE2), oncogenesis (KIT, RET, RAF-1, BRAF, BRAF V600E), metastasis (VEGFR3, PDGFR, FGFR) and tumour immunity (CSF1R).[2]

2. Summary of Clinical Evidence

2.1. Evidence to support comparable efficacy with relevant comparators

Evidence to support the efficacy and safety of cabozantinib in adults with HCC previously treated with sorafenib comes from CELESTIAL, a phase III, randomised, double-blind, placebo-controlled study. Eligible patients had previously been treated with sorafenib, had disease progression after at least one systemic treatment for HCC, and may have received up to two previous systemic regimens for advanced HCC. Patients were randomised 2:1 to receive cabozantinib 60 mg orally once daily (n=470) or placebo (n=237). The study demonstrated a statistically significant overall survival (OS) benefit with cabozantinib compared with placebo, with a median OS of 10.2 months versus 8.0 months (hazard ratio 0.76, 95% confidence interval: 0.63 to 0.92, p=0.005).[1, 3]

In the absence of direct evidence comparing cabozantinib and regorafenib, the submitting company presented a matching adjusted indirect comparison (MAIC) and a Bucher indirect treatment comparison (ITC). Both ITCs used data from the CELESTIAL[3] study (for cabozantinib) and RESORCE[4] study (for regorafenib), using placebo as the common comparator. The results suggested that cabozantinib is likely to have comparable efficacy to regorafenib.

3. Company Estimate of Eligible Population, Uptake and Budget Impact

3.1. Company's number of patients assumed to be eligible for treatment

The company estimated that there would be 2 patients eligible for treatment with cabozantinib in year 1, increasing to 5 patients in year 5.

3.2. Budget Impact assumption

Medicines reviewed under the abbreviated submissions process are estimated to have a limited net budget impact and resource allocation across NHS Scotland.

References

1. Ipsen Ltd. Cabozantinib film-coated tablets (Cabozantinib Ipsen) Summary of product characteristics. Electronic Medicines Compendium www.medicines.org.uk Last updated 01 August 2024.
2. Bayer plc. Regorafenib (Stivarga®) Summary of product characteristics. Electronic Medicines Compendium www.medicines.org.uk Last updated 18 May 2023.
3. Abou-Alfa GK, Meyer T, Cheng A-L, El-Khoueiry AB, Rimassa L, Ryoo B-Y*, et al.* Cabozantinib in Patients with Advanced and Progressing Hepatocellular Carcinoma. New England Journal of Medicine. 2018;379(1):54-63. 10.1056/NEJMoa1717002
4. Bruix J, Qin S, Merle P, Granito A, Huang Y-H, Bodoky G*, et al.* Regorafenib for patients with hepatocellular carcinoma who progressed on sorafenib treatment (RESORCE): a randomised, double-blind, placebo-controlled, phase 3 trial. The Lancet. 2017;389(10064):56-66. 10.1016/S0140-6736(16)32453-9

This assessment is based on data submitted by the applicant company up to and including 29 January 2025.

Medicine prices are those available at the time the papers were issued to SMC for consideration. SMC is aware that for some hospital-only products national or local contracts may be in place for comparator products that can significantly reduce the acquisition cost to Health Boards. These contract prices are commercial in confidence and cannot be put in the public domain, including via the SMC Detailed Advice Document. Area Drug and Therapeutics Committees and NHS Boards are therefore asked to consider contract pricing when reviewing advice on medicines accepted by SMC.

Patient access schemes: A patient access scheme is a scheme proposed by a pharmaceutical company in order to improve the cost-effectiveness of a medicine and enable patients to receive access to cost-effective innovative medicines. A Patient Access Scheme Assessment Group (PASAG), established under the auspices of NHS National Services Scotland reviews and advises NHSScotland on the feasibility of proposed schemes for implementation. The PASAG operates separately from SMC in order to maintain the integrity and independence of the assessment process of the SMC. When SMC accepts a medicine for use in NHSScotland on the basis of a patient access scheme that has been considered feasible by PASAG, a set of guidance notes on the operation of the scheme will be circulated to Area Drug and Therapeutics Committees and NHS Boards prior to publication of SMC advice.

Advice context:

No part of this advice may be used without the whole of the advice being quoted in full.

This advice is based on the estimation of at least similar comparative efficacy and limited net budget impact compared with other medicinal products, within the same therapeutic class, that are in routine use within NHSScotland.

This advice represents the view of the Scottish Medicines Consortium and was arrived at after evaluation of the evidence submitted by the company. It is provided to inform the considerations of Area Drug & Therapeutics Committees and NHS Boards in Scotland in determining medicines for local use or local formulary inclusion. This advice does not override the individual responsibility of health professionals to make decisions in the exercise of their clinical judgement in the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.