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National Health Care Institute
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Our reference
2021047762

Date 17 January 2022
Subject Package advice acalabrutinib (Calquence®)

Dear Mr Kuipers,

The National Health Care Institute advises you on acalabrutinib (Calquence®) for the treatment in primary and secondary healthcare of adult patients with chronic lymphatic leukaemia (CLL). The reason for this advice was the placing of acalabrutinib (for this indication) in the lock procedure for expensive medicinal products.

The National Health Care Institute has concluded that acalabrutinib meets the statutory criterion of 'established medical science and medical practice' for the indication mentioned. The National Health Care Institute has determined that the therapeutic value of this medicinal product is comparable to that of the already reimbursed ibrutinib. Both treatment options have a clinically relevant effect on the progression free survival (PFS) rate. However, the use of acalabrutinib is associated with additional costs. The National Health Care Institute is unable to determine the amount of these additional costs because the actual price of ibrutinib is not known. We advise you to include acalabrutinib in the package, provided the price negotiations with the marketing authorisation holder (MAH) successfully deliver a net price that does not exceed that of ibrutinib. We would like to point out that the Insured Package Advisory Committee has recommended that the price for a treatment should be reduced if more resources for the same indication were available.

General

At your request, the National Health Care Institute assesses whether new care should be part of the health insurance package, and makes a decision based on the health insurance package paid from joint premiums. We take into consideration the degree of certainty that this will be achieved, both in the scientific sense, as well as in terms of public support, and we consider the efficiency and transparency aspects. The National Health Care Institute has assessed acalabrutinib on the basis of the four package criteria[1]: effectiveness[2],

[1] Real-world package management 3 (2013). National Health Care Institute, Diemen. Via www.zorginstituutnederland.nl

[2] Established medical science and medical practice assessment: updated version (2015). National Health Care Institute,
Diemen. Via www.zorginstituutnederland.nl

cost-effectiveness[3], necessity and feasibility. The National Health Care Institute is advised by the Scientific Advisory Board (WAR) for advice on established medical science and medical practice and on cost-effectiveness, and the Insured Package Advisory Committee for the social assessment. We also consulted stakeholders during the assessment process.

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Integral weighting of package criteria

Established medical science and medical practice
Reimbursement is requested for:

- adult patients with previously untreated CLL with chromosome 17p (del17p) deletion or a tumour suppressor gene TP53 mutation and non-fit patients not eligible for anti-CD20 treatment;
- adult patients with CLL who have had at least one prior treatment for CLL.

The effectiveness of acalabrutinib compared to obinutuzumab + chlorambucil in patients with previously untreated CLL has been investigated in the ELEVATE-TN study. The results show that acalabrutinib is clinically relevant, effective and safe. Based on the results of a network meta-analysis (NMA) on PFS, acalabrutinib in patients with not previously treated CLL may be non-inferior to ibrutinib (hazard ratio [HR] 0.35; 95% credible interval [CrI] 0.18-0.66).

Based on the results of a direct comparison between acalabrutinib and ibrutinib, acalabrutinib may be non-inferior to ibrutinib in patients who have had at least one other treatment for CLL on three outcome measures: PFS (HR 1.00; 95% confidence interval [CI] 0.79-1.27), time to next treatment, and overall survival (HR 0.82; 95% CI 0.59-1.15). Only patients with del(17p) and/or del(11q) are included in this direct comparison. Since the results of the direct comparative study for this group of patients are likely to be similar to the results for the whole group of patients who have already had one previous treatment, the results of the direct comparative study can be extrapolated to the entire population.

Based on the reported intervention-related grade ≥3 undesirable effects and the number of people who have stopped the treatment due to undesirable effects, no preference can be determined for ibrutinib or acalabrutinib. In both treatments, the undesirable effects appear acceptable in relation to the effect achieved with the treatment. Acalabrutinib may offer an advantage in patients with (a history of) cardiovascular disease or patients who have discontinued treatment with ibrutinib because of cardiovascular side effects.

The National Health Care Institute concludes that acalabrutinib meets the established medical science and medical practice for the treatment of the groups of patients with CCL that were mentioned above.

Budget impact
The National Health Care Institute estimates that after 3 years approximately 121 patients will be treated with acalabrutinib in primary healthcare, and 146 patients in secondary healthcare. The costs for a full year's treatment with acalabrutinib are €62,761 per patient. It is assumed that the treatment takes longer than 3 years.

[3] Cost-effectiveness report (2015). National Health Care Institute, Diemen. Via www.zorginstituutnederland.nl

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The total costs of treatment with acalabrutinib in primary healthcare is estimated at €6.2 million and for treatment of refractory or recurring patients in secondary healthcare at €7.4 million in the third year after market introduction. The additional costs are nil when the substitution of the current standard treatment (ibrutinib) is taken into account, calculated with the gross price.

Cost-effectiveness
Because of the similarities in effectiveness (equal therapeutic value) of acalabrutinib and ibrutinib, the National Health Care Institute has not carried out any cost-effectiveness analysis.

Final conclusion
The National Health Care Institute advises you to include Calquence® in the health insurance package, provided the price negotiations with the marketing authorisation holder (MAH) successfully deliver a net price that does not exceed that of ibrutinib. Since there is an equal value compared to ibrutinib, which is already being reimbursed, and there are no indications that one product is preferable to another, we advise you to take the net price of ibrutinib into account during the price negotiations. We would like to point out that the Insured Package Advisory Committee has recommended that the price for a treatment should be reduced when more resources are available.

Yours sincerely,

Sjaak Wijma
Chair of the Executive Board