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National Health Care Institute
Care
Medicinal Products

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Our reference
2021041794

Date 10 November 2021
Subject Package advice venetoclax (Venclyxto®)

Dear Mr Blokhuis,

The National Health Care Institute advises you about venetoclax (Venclyxto®) in combination with a hypomethylating agent (HMA) for the treatment of adult patients with newly diagnosed acute myeloid leukaemia (AML) who are not eligible for intensive chemotherapy. The reason for this advice was the placing of the said medicinal product (for this indication) in the lock procedure for expensive medicinal products.

The National Health Care Institute has concluded that venetoclax meets the statutory criterion of 'established medical science and medical practice' for the indication mentioned. The National Health Care Institute has found that the addition of venetoclax to a hypomethylating agent has a clinically relevant effect on survival. This is a cost-effective medicinal product for the indication mentioned, but there are arguments to advise you to negotiate the price. We therefore advise you to include venetoclax in the health insurance package for the above indication, provided that the price negotiations with the marketing authorisation holder result in a lower price that is at least in line with the current price arrangement, and even lower.
We would like to explain our findings and final conclusion below.

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 care 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 assessed venetoclax on the basis of the four package criteria[1]: effectiveness[2], cost-effectiveness[3], necessity and feasibility.

[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

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

The National Health Care Institute is advised by two independent committees: the Scientific Advisory Board (WAR) for advice on established medical science and medical practice and on cost-effectiveness, and the Insured Package Advisory Committee (ACP) 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
Overall survival results are based on a planned interim analysis (75% maturity). The median follow-up was 20.7 months in the venetoclax + azacitidine arm and 20.2 months with azacitidine (HMA monotherapy). Median overall survival was 14.7 months in the venetoclax + azacitidine arm and 9.6 months with HMA monotherapy, which results in a hazard ratio (HR) of 0.66 (95% confidence interval (95% BI): 0.52-0.85). This effect is clinically relevant.
Median time to a significant and clinically relevant decrease in the EORT CLC-C30 score (≥10 points) was numerically longer in the venetoclax + azacitidine arm than with HMA monotherapy (16.5 vs 9.3 months), but this was not statistically significant (HR 0.81; 95% BI: 0.55-1.18).
The VIALE-A study shows that the addition of venetoclax to azacitidine treatment results in a clinically relevant increase in the incidence of severe adverse intervention-related effects compared to azacitidine monotherapy. 24.4% of the patients in the venetoclax + azacitidine arm stopped the study due to adverse intervention-related effects, compared to 20.1% of the patients in the control arm. This gives an RR of 1.21 (95% BI: 0.82-1.78).
The National Health Care Institute concludes that venetoclax, combined with a hypomethylating agent, in patients with newly diagnosed acute myeloid leukaemia who are not eligible for intensive chemotherapy, meets the established medical science and medical practice.

Budget impact
Treatment with venetoclax in the VIALE-A study lasted on average 9.9 months (301 days) and cost €37,672 (based on the pharmacy purchase price). This price is equal to the price used for calculations in the advice for venetoclax in combination with obinutuzumab (in case of previously treated CLL) in October 2020.
The macro costs are €11 million in the third year after inclusion in the package. This is related to 196 patients in the third year.

Cost-effectiveness
The cost-effectiveness analysis provided is of sufficient methodological quality. The ICER of venetoclax + HMA is €74,031 per QALY compared to HMA monotherapy and is cost effective at a reference value of €80,000 per QALY.

Other considerations
Venetoclax is already reimbursed for various applications in chronic lymphatic leukaemia (CLL). For the combination treatments with rituximab and obinutuzumab, financial arrangements were made that will be in effect until 2027.

Package advice

The National Health Care Institute advises you to include venetoclax in the health insurance package, provided that the price negotiations with the marketing authorisation holder result in a lower price that is at least in line with the current price arrangement. The results are based on an interim analysis and there are uncertainties about the quality of life. These uncertainties have been taken into account in the assessment of the established medical science and medical practice; this is an effective and cost-effective tool. These uncertainties are also part of our advice to negotiate the price. Venetoclax is already being reimbursed for several indications. This supports the argument that at least the price negotiated for previous indications should be matched, or even lower. Lower because a substantial price reduction is fair as it is expected that the reimbursement of previous indications has already largely recouped the investments made.

Finally, the National Health Care Institute urges the physicians' association to investigate the appropriateness of the substance, such as the possibility of shorter treatment and the effectiveness of venetoclax in specific molecular subtypes.

Yours sincerely,

Sjaak Wijma
Chair of the Executive Board

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