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Our reference
2022027813

Date 29 July 2022
Subject Package advice for sacituzumab govitecan (Trodelvy®)

This is a corrected version of a letter previously sent on 15 July 2022, in which an inadvertently incorrectly specified medicinal product has been corrected under the 'General' heading.

Dear Mr Kuipers,

The National Health Care Institute is hereby making recommendations about sacituzumab govitecan (Trodelvy®) for the treatment of adult patients with inoperable or metastasized triple-negative breast cancer (mTNBC) who have previously received systemic therapies two or more times, including at least one for advanced disease. The reason for this advisory report was the placing of the above-mentioned medicinal product in the 'lock procedure' for expensive medicinal products.

Sacituzumab govitecan complies with the established medical science and medical practice for the treatment of adult patients with inoperable or metastasized triple-negative breast cancer who have previously received systemic therapies two or more times, including one line of therapy containing a taxane and at least one for advanced disease. The medicinal product has therapeutic added value compared to chemotherapy, in terms of both overall survival and progression-free survival. The National Health Care Institute advises you to include sacituzumab govitecan in the health insurance package for the specified indication. Based on the conservative estimate of cost-effectiveness, the National Health Care Institute believes that a discount of at least 75% should be appropriate. During the negotiations, we advise you to take into account the fact that expansions of the indications for sacituzumab govitecan are to be expected and also that new treatments for this group of patients may become available. The National Health Care Institute hopes that all parties, given the poor prognosis for this group of patients, are committed to ensuring that this medicinal product becomes available to Dutch patients quickly.

In this letter, I explain our findings and final conclusion.

General
At your request, the National Health Care Institute assesses whether new care should be part of the health insurance package. To be able to make a recommendation, the National Health Care Institute has assessed sacituzumab

govitecan on the basis of the four package criteria[1]: effectiveness[2], cost-effectiveness[3], necessity and feasibility. We consider these criteria from a scientific perspective and in terms of public support. We also review the aspects of efficiency and transparency. The National Health Care Institute is advised in its package reviews by two independent committees:

- the Scientific Advisory Board (WAR) for the review of evidence according to established medical science and medical practice, and to determine the cost-effectiveness; and
- the Package Advisory Committee for the social deliberations.

We also consulted stakeholders during the assessment process.

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Comprehensive weighting of package criteria

Established medical science and medical practice

Sacituzumab govitecan was investigated in one direct comparative, phase III, multicentre, open-label, randomised study (ASCENT). The results of this study show a clinically relevant effect of sacituzumab govitecan on overall survival. The increase was 5.4 months under treatment with sacituzumab govitecan compared to chemotherapy of the practitioner's choice. The associated hazard ratio (HR) was 0.48 (95% CI: 0.38– 0.59). A clinically relevant effect of sacituzumab govitecan was also observed on progression-free survival (median PFS increase 3.9 months, HR: 0.4%; 95% CI: 0.32– 0.52). Both the relative effect and the absolute effect on both overall survival and progression-free survival meet the PASKWIL criteria (palliative, adjuvant, specific side effects, quality of life, impact of treatment and level of evidence). The study did not indicate a deterioration in quality of life as a result of treatment with sacituzumab govitecan (based on a non-inferiority analysis).
Severe intervention-related undesirable effects occur more often during treatment with sacituzumab govitecan than with chemotherapy (64.0% versus 46.4%), but due to the low quality of the evidence, it is uncertain whether this difference is clinically relevant. Given the desirable effects, the National Health Care Institute therefore considers the undesirable effects to be acceptable.

The National Health Care Institute came to the final conclusion that sacituzumab govitecan in treatment of adult patients with inoperable or metastasized triple-negative breast cancer, who have previously received systemic therapies two or more times, including one line therapy containing taxane and at least one for advanced disease, has added value compared to chemotherapy. Sacituzumab govitecan is therefore in line with established medical science and medical practice.

Budget impact

The average total treatment costs per patient are €68,707. In the third year after inclusion in the health insurance package, about 277 patients are eligible for treatment with sacituzumab govitecan, which equates to a budgetary impact of €8.7 million (taking account of the substitution costs of chemotherapy).

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[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.

Cost-effectiveness
The pharmacoeconomic analysis is of sufficiently high methodological quality. The marketing authorisation holder reports an ICER of €196,929 per QALY gained for sacituzumab govitecan in comparison with chemotherapy. The National Health Care Institute has opted to use an ICER range, which is €196,929 to €241,231 per QALY gained. This range was calculated by the National Health Care Institute due to the great uncertainty around the correct distribution for the survival curve extrapolation. The ranges of the number of life-years for sacituzumab govitecan and chemotherapy are 1.26-1.53 (SG) and 0.77-0.87 (chemo) respectively. The National Health Care Institute suspects that the actual estimate of survival is between these two estimates. The gain in QALYs is 0.36-0.45.
Due to the high burden of disease, the National Health Care Institute has used a threshold of €80,000 per QALY gained in this pharmacoeconomic analysis. The probability that sacituzumab govitecan is cost-effective compared to chemotherapy at a threshold of €80,000 per QALY, is 0%. Based on the lower limit of the ICER range, the price reduction should be 65% to get the ICER under the threshold of €80,000. Based on the upper limit of the ICER range, the price reduction should be 75%.

Final conclusion
Sacituzumab govitecan complies with the established medical science and medical practice for the treatment of adult patients with inoperable or metastasized triple-negative breast cancer who have previously received systemic therapies two or more times, including one line therapy containing taxane and at least one for advanced disease. The medicinal product has therapeutic added value compared to chemotherapy, in terms of both overall survival and progression-free survival. The National Health Care Institute advises you to include sacituzumab govitecan in the health insurance package for the specified indication. Based on the conservative estimate of cost-effectiveness, the National Health Care Institute believes that a discount of at least 75% should be appropriate. During the negotiations, we advise you to take into account the fact that expansions of the indications for sacituzumab govitecan are to be expected and that new treatments for this group of patients may become available. The National Health Care Institute hopes that all parties, given the poor prognosis for this group of patients, are committed to ensure that this medicinal product becomes available to Dutch patients quickly.

Yours sincerely,

Peter Siebers
Acting Chair of the Executive Board

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