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2023016749

National Health Care Institute
Care
Medicinal Products

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Contact
Ms M. de Vries
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Our reference
2023016749

Date 28 July 2023
Re: Package advice lock procedure medicinal product darolutamide (Nubeqa®)

Dear Mr Kuipers,

The National Health Care Institute advises you on the assessment of darolutamide (Nubeqa®) for the treatment of adult men with metastatic hormone-sensitive prostate cancer (mHSPC) in combination with docetaxel and androgen deprivation therapy (ADT), hereinafter called darolutamide + docetaxel + ADT. The reason for this advice was that darolutamide was being placed in what is known as the 'lock procedure' for expensive medicinal products.

The National Health Care Institute advises you to include darolutamide (Nubeqa®) in the basic health insurance package for the above mentioned indication, provided that the price negotiations successfully deliver a net price that does not exceed that of the existing treatment with abiraterone.

General

At your request, the National Health Care Institute assesses whether new care should be part of the standard health insurance package from the perspective of the basic healthcare package paid from joint premiums. In this decision, we weigh the matter, both in a scientific sense and from a social basis, and we weigh the aspects of efficiency and transparency. The National Health Care Institute assessed darolutamide on the basis of the four package criteria[1]: effectiveness[2], cost-effectiveness[3], necessity and feasibility. The National Health Care Institute is advised in this matter by the Scientific Advisory Board (WAR) for advice on established medical science and medical practice and on budget impact. We also consulted stakeholders during the assessment process.

Scientific weighting

At the time this assessment was started, patients in the Netherlands are being treated predominantly with docetaxel + ADT or abiraterone + ADT. Docetaxel has been the standard treatment for a long time, but after the patent for abiraterone ended (autumn 2022), a marked shift occurred in the treatment landscape.

[1] Real-world package management 4 (2023). National Health Care Institute, Diemen. Via www.zorginstituutnederland.nl
[2] Assessment of the established medical science and medical practice 2023. National Health Care Institute, Diemen. Via: www.zorginstituutnederland.nl
[3] Cost-effectiveness report (2015). National Health Care Institute, Diemen. Via www.zorginstituutnederland.nl

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Therefore, the National Health Care Institute considers both treatments as the comparative treatment in this assessment.

The beneficial and undesirable effects of darolutamide in men with mHSPC are studied in the ARASENS study. This was a randomized controlled phase III in which darolutamide + docetaxel + ADT was evaluated for effectiveness and safety compared to docetaxel + ADT. The addition of darolutamide to the treatment with docetaxel + ADT resulted in clinically relevant gains in OS (HR: 0.68 [95% CI: 0.57 – 0.80]). Because the median has not yet been reached in the darolutamide arm, it is not possible to determine the absolute survival gain. The estimated 48-month (4 years) survival was 62.7% and 50.4% in the darolutamide + docetaxel + ADT arm and the docetaxel + ADT arm, respectively. The quality of life seems to be preserved in both treatment arms. The safety profile of darolutamide + docetaxel + ADT is similar to that of docetaxel + ADT.

A recently published network meta-analysis (NMA) has been used for the comparison with abiraterone + ADT. This analysis uses the latest data from the individual darolutamide (ARASENS) and abiraterone (LATITUDE and STAMPEDE) studies. Based on the NMA, the treatment effect between darolutamide and abiraterone is estimated to be an HR of 0.80 (95% CI 0.64 – 1.00). This point estimation does not indicate a clinically relevant difference in survival. Due to the uncertainties associated with this analysis, it is unclear whether darolutamide + docetaxel + ADT results in a clinically relevant improvement in overall survival, compared to abiraterone + ADT. The rate of intervention-related Grade 3 or more undesirable effects did not differ between darolutamide + docetaxel + ADT and abiraterone + ADT. Quality of life has not been indirectly compared between darolutamide in combination with docetaxel + ADT and abiraterone + ADT. Based on the individual studies, the quality of life is likely to be maintained after the addition of the various interventions.

The National Health Care Institute concludes that darolutamide + docetaxel + ADT in metastatic hormone-sensitive prostate carcinoma complies with the established medical science and medical practice. Because an added value compared to abiraterone + ADT has not been demonstrated, the National Health Care Institute concludes that there is an equal value with abiraterone + ADT.

Other considerations
In view of the very recent cieBOM recommendation (March 2023), it is likely that in the near future, in patients deemed to be in need of treatment intensification, a shift will occur towards the triplet combination of abiraterone + docetaxel + ADT. The triplet combination with abiraterone + docetaxel + ADT was also included in the NMA described above, based on the PEACE-1 study. Based on this NMA, this therapy can probably be considered equivalent to darolutamide + docetaxel + ADT.

During the review, the occupational group indicated that for cost reasons, they will be treating patients with the triplet combination abiraterone + docetaxel + ADT and, based on this, they see the biggest role for darolutamide + docetaxel + ADT in particular for patients who cannot be treated with abiraterone. Reasons for this are intolerance of abiraterone (contraindicated) or prednisone/prednisolone with which this treatment is associated. This narrowed status determination of darolutamide (only for patients who cannot be treated with abiraterone) based on

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cost considerations is not a reason to change the approach of the current assessment.

Budget impact analysis
The National Health Care Institute estimates that 3,250 patients will be treated with darolutamide in the third year after market introduction. Treatment with the combination therapy darolutamide + docetaxel + ADT costs €23,922 per patient every six months and €41,074 per year for year 2 and beyond, based on the list price. This results in costs of €93.1 million in the third year, taking into account the substitution of docetaxel + ADT and abiraterone + ADT based on the current list prices.

There is uncertainty about the use and price of abiraterone. The patent for abiraterone expired in September 2022. Clinicians expect that abiraterone will be increasingly prescribed instead of docetaxel. However, it is uncertain exactly how much the number of users will increase. In addition, it is likely that hospital purchasing arrangements will further reduce expenditure on abiraterone in the future, but it is uncertain exactly how much this reduction will be. There are indications that this reduction will be between 70% and 90%. In that case, the budget impact of darolutamide will increase.

Other considerations
This budget impact analysis did not take into account the recent changes in the treatment landscape regarding the availability of the triplet treatment of abiraterone + docetaxel + ADT. Based on the recent cieBOM advice and the positioning for darolutamide + docetaxel + ADT by the occupational group, it is likely that patient numbers will be lower in practice.

Cost-effectiveness
Given that based on the current available data, a clinically relevant added value compared to the current standard treatment with the already reimbursed product abiraterone has not been demonstrated, a cost-effectiveness analysis is not warranted.

Package advice
The National Health Care Institute advises you to include darolutamide in the package for the treatment of adult men with metastatic hormone-sensitive prostate cancer (mHSPC) in combination with docetaxel and androgen deprivation therapy (ADT), provided that the net price of darolutamide after successful price negotiations does not exceed the net price of abiraterone. We advise you to take into account the recent patent expiration of abiraterone. We would like to point out that the Insured Package Advisory Committee (ACP) has advised the National Health Care Institute in general terms that the price for a treatment should be reduced when several medicinal products are available for the same indication.

Yours sincerely,

Sjaak Wijma
Chairperson of the Executive Board