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2024009556

National Health Care Institute
Care
Medicinal Products

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Our reference
2024009556

Date 27 March 2024
RE: Package advice deucravacitinib (Sotyktu®)

Dear Mrs Dijkstra,

We are hereby sending you the package advice for deucravacitinib (Sotyktu®) for moderate-to-severe plaque psoriasis in adults who are candidates for systemic treatment. The reason for this advice was the placement of deucravacitinib in the lock procedure for expensive medicinal products.

Registered indication
Deucravacitinib is indicated for the treatment of moderate-to-severe plaque psoriasis in adults who are candidates for systemic treatment.

Claim by the marketing authorisation holder
Deucravacitinib has a added value over apremilast for the treatment of moderate-to-severe plaque psoriasis in adults who are candidates for systemic treatment based on statistically significant and clinically relevant improved efficacy and quality of life.

Package advice
The National Health Care Institute advises you to include deucravacitinib in the health insurance package for the treatment of moderate-to-severe plaque psoriasis in adults who are candidates for systemic treatment, where oral systemic treatment with conventional first-line label products is contraindicated. Based on a conservative estimate of cost-effectiveness, the National Health Care Institute believes that a discount of 10 to 15% is appropriate. The development of this package advice is explained below.

General
At your request, the National Health Care Institute assesses whether care should be part of the standard health insurance package from the perspective of the health insurance package paid from joint premiums. To this end, the National Health Care Institute carries out an assessment based on the four package criteria[1], effectiveness[2],

[1] Real-world package management 4 (2023). National Health Care Institute, Diemen. Via www.zorginstituutnederland.nl.

[2] Beoordeling Stand van de Wetenschap en Praktijk (2023). National Health Care Institute. Via:

cost-effectiveness[3], necessity[4] and feasibility[5].
The Scientific Advisory Board (WAR) advises the National Health Care Institute about the justification and conclusion of the assessment.

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Comprehensive weighting of package criteria

Established medical science and medical practice

The efficacy and safety of deucravacitinib were evaluated in 2 multicentre, randomised, double-blind, placebo- and apremilast-controlled Phase 3 studies in patients aged ≥18 years with moderate-to-severe plaque psoriasis who were candidates for systemic treatment or phototherapy. In total, 1686 patients were included. In determining the relative effectiveness of deucravacitinib compared to apremilast on the critical 'severity of disease' outcome, a 90% reduction in PASI score (PASI 90) and an sPGA score of 0 or 1 (sPGA 0/1) were assumed.[6] The relative effect in both studies is similar. The effect of deucravacitinib was sustained for up to 52 weeks. In both studies, clinically relevant, more patients achieved this crucial outcome parameter when treated with deucravacitinib compared to apremilast. Compared to apremilast, the treatment with deucravacitinib also resulted in a clinically relevant effect on quality of life in nearly twice as many patients.

Treatment with deucravacitinib leads to a potential reduction in the incidence of serious intervention-related adverse effects, compared to apremilast. However, this difference is not statistically significant. The number of events in both treatment arms is also very low. The percentage of patients discontinuing treatment due to adverse effects is lower in the treatment with deucravacitinib than in the treatment with apremilast. The most common side effect of deucravacitinib was infections.

Deucravacitinib complies with established medical science and medical practice for moderate-to-severe plaque psoriasis in adults who are candidates for systemic treatment where oral systemic therapy is desirable and treatment with conventional first-line label products is contraindicated. Deucravacitinib has added value compared to apremilast.

The Dutch Society for Dermatology and Venereology (NVDV) 'Psoriasis' guideline has not yet determined the place of deucravacitinib. In the context of this assessment, the NVDV has therefore drawn up a preliminary 'Viewpoint' for this

www.zorginstituutnederland.nl.

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

[4] Necessity deals with both the medical necessity and the result of the severity

[5] The package criterion of feasibility deals with whether it is feasible or sustainable to include a specific form of care in the basic health care package. It is therefore mainly a test of a number of implementation aspects such as health care organisation, support, ethical and legal aspects, budget impact and so on. See Real-world package management 4 (2023).

[6] The effect on the critical outcome parameter 'severity of disease' was determined by achieving a 90% decrease in the Psoriasis Area and Severity Index (PASI 90) and a static Physician Global Assessment score of 0 or 1 (SPGA 0/1), respectively. The PASI score is a composite, weighted measure to objectify the severity of psoriasis and the body surface area affected by the disease. The CHMP guideline sees an improvement of >90% on PASI as the best evidence of effectiveness. A PGA score is used in daily practice to determine the severity of the disease and to evaluate the effect of treatment. The CHMP guideline does not provide a clinical relevance limit for this. However, sPGA 0/1 is defined as treatment success in both clinical trials and daily practice (Dutch professional group).

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matter.[7] Because deucravacitinib in direct comparison appears to be more effective than apremilast in two randomised clinical trials, but *head-to-head* studies with biologicals are lacking so far, it is recommended that the placement of deucravacitinib be determined based on the same conditions as for prescribing apremilast. This determination is more stringent than the first line label of deucravacitinib, as approved by EMA. The NVDV recommends that deucravacitinib be prescribed for the treatment of moderate-to-severe plaque psoriasis in adults when oral systemic therapy is desirable and treatment with conventional first-line labels (acitretin, cyclosporin, dimethyl fumarate or methotrexate) is contraindicated. The latter is the case with an inadequate response, failure to achieve treatment success, a new contraindication, intolerance and/or adverse reactions.

Budget impact
The National Health Care Institute estimates that a market penetration of 97% will have occurred in the third year after market introduction, and that 652 patients will be treated with deucravacitinib when taking the placement of apremilast as a starting point. The costs per patient per year are €9,736. The total costs of deucravacitinib reach €6.2 million in the third year after market introduction. Taking into account substitution of apremilast, the use of deucravacitinib in these patients in the third year will likely come with additional costs, estimated at €1.2 million. This is based on apremilast's pharmacy purchase price (AIP). However, according to the National Health Care Institute, the actual net price is lower due to price reductions.
In addition, there is uncertainty about the number of patients who will be ultimately treated with deucravacitinib. It cannot be ruled out that, due to fewer (toxic) adverse reactions and higher efficacy than apremilast, (significantly) more than 75% of patients will be treated with deucravacitinib as early as year 2. In the longer term, a possible expiration of the apremilast patent in 2028 should be taken into account.

Cost-effectiveness
The pharmaco-economic analysis is of sufficient methodological quality and the outcomes can be used in decision-making. The marketing authorisation holder reports an ICER of €31,665 per QALY gained for deucravacitinib compared to apremilast. However, there is great uncertainty about the reliability and consistency of the quality of life outcomes that form the basis for this. This also applies to the representativeness of specific health care costs that are not based on prices current in the Netherlands but on prices in the United Kingdom that are, according to the National Health Care Institute, overestimated. For these reasons in particular, the National Health Care Institute thinks a more conservative calculation might be more realistic. This results in an ICER range of €40,789 - €71,381 per QALY gained. In this calculation, the costs of best supportive care (BOZ) are reduced by 50%. Regarding quality of life outcomes, the data from the base case analysis of the market authorisation holder was used to calculate the ICER lower limit; for the upper limit, the original data from the two studies was used. Based on the ICER range, the price of deucravacitinib should decrease by 10–15% to stay below the reference value of €20,000/QALY, which correlates with the burden of disease calculated by the National Health Care Institute for moderate-to-severe plaque psoriasis.

[7] The Viewpoint report *'Prescribing deucravacitinib in adults with moderate-to-severe psoriasis'*. This viewpoint report has not yet been published but will be included in the NVDV 'Psoriasis' guideline in 2024.

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Final conclusion
Deucravacitinib complies with established medical science and medical practice and has added value compared to apremilast. The National Health Care Institute supports the positioning of the NVDV regarding deucravacitinib and subsequently advises you to include deucravacitinib in the health insurance package for the treatment of moderate-to-severe plaque psoriasis in adults who are candidates for systemic treatment and for whom treatment with conventional first-line label products (acitretin, ciclosporin, simethyl fumarate and methotrexate) is contraindicated. Based on a conservative estimate of cost-effectiveness, the National Health Care Institute believes that a discount of 10 to 15% is desirable. The price negotiations should take into account that the budget impact was calculated on the basis of the pharmacy purchase price of apremilast, whereas the actual (net) price is lower due to price reductions, and also that the patent on apremilast is likely to expire in 2028.

Yours sincerely,

Sjaak Wijma
Chairperson of the Executive Board