Zorginstituut Nederland

Tolvaptan (Jinarc®)

Summary of recommendations by Zorginstituut Nederland dated 14 December 2015, based on an evaluation by the WAR (Scientific Advisory Committee).

The WAR has approved a pharmacotherapeutic report for the medicine tolvaptan (Jinarc®). They reached the following conclusion.
Based on the criteria of the Medicines Reimbursement System (GVS), tolvaptan is not mutually replaceable with any other drug included in the GVS. However, tolvaptan is not eligible for placing on list 1B of the GVS, as the methodological quality of the pharmacoeconomic analysis is not good enough to be able to make a reliable statement on its cost-effectiveness in the Netherlands. For this reason Zorginstituut Nederland advises negatively on including tolvaptan (Jinarc®) in the GVS.

Medicine. **Tolvaptan (Jinarc®)**, 15, 30, 45, 60 and 90 mg tablets.

Background

In a letter dated 10 August 2015, the Minister of Public Health, Welfare and Sport asked Zorginstituut Nederland to carry out a substantive assessment of whether tolvaptan (Jinarc®) is mutually replaceable with a drug that is already included in the Medicines Reimbursement System (GVS). If not, then the Minister asked for an assessment of the therapeutic value of the drug for the indication concerned and also for a pharmacoeconomic analysis.
Zorginstituut Nederland, advised by the Scientific Advisory Board (WAR), has now completed this assessment. Its considerations are specified in the pharmacotherapeutic report.

Tolvaptan is indicated for slowing the progression of cyst development and renal insufficiency of autosomal dominant polycystic kidney disease (ADPKD) in adults with chronic kidney disease (CKD) stage 1 to 3 at initiation of treatment when there are signs of rapidly progressing disease. The product is available in the form of 15, 30, 45, 60 and 90 mg tablets. The dose is twice daily in split dose regimens of 45 mg +15 mg, 60 mg + 30 mg or 90 mg + 30 mg. The total daily doses are 60, 90 or 120 mg.

Investigation of mutual replaceability

Based on current GVS criteria, tolvaptan is not mutually replaceable with any other drug included in the GVS.
In order to determine whether the drug is eligible for placing on List 1B of the GVS, its therapeutic value and cost-effectiveness have to be determined.

Therapeutic value

Weighing up effectiveness against unfavourable effects results in an added therapeutic value of tolvaptan compared to best supportive care for slowing the progression of cyst development and renal insufficiency of ADPKD in adults with CKD stage 1 to 3 at initiation of treatment when there are signs of rapidly progressing disease. The comment is made here that there is limited evidence in adults with stage 3b CKD (eGFR 30-40 ml/min/1.73m^2) at initiation of treatment.
If age alone is taken into account in the definition for signs of rapid progression, an upper age limit of 50 years should apply. According to the professional group, there is little chance of rapid progression above the age of 50 years.

Pharmacoeconomic analysis
The applicant claims that treatment with tolvaptan is a cost-effective intervention for the treatment of ADPKD for the above-mentioned indication. Zorginstituut Nederland concludes, however, that the methodological quality of the calculation of cost-effectiveness was insufficient.

The applicant estimated the deterministic cost-effectiveness ratio to be €80,079 per QALY. Furthermore, the applicant concludes that tolvaptan has a 50% chance of being a cost-effective treatment at a reference value of €80,000 per QALY. However, Zorginstituut Nederland expects that, due to the many uncertainties regarding the input data and assumptions in the model, the actual cost-effectiveness for the Dutch situation will be considerably less favourable than that indicated by the applicant.

Taking into account uncertainties about the number of patients showing signs of rapid disease progression, the percentage of patients in the various stages of CKD disease, and uncertainty surrounding market penetration, the inclusion of tolvaptan (Jinarc®) on List 1B of the GVS would involve additional costs to the pharmaceutical budget of between 8 and 13 million euro in 2018.

Zorginstituut Nederland's advice
Based on the criteria for mutual replaceability, tolvaptan is not eligible for placing on List 1A of the GVS.
Nor is tolvaptan eligible for placing on List 1B of the GVS. Though it is true that tolvaptan does have an added therapeutic value in slowing the progression of cyst development and renal insufficiency of ADPKD in adults with CKD stage 1 to 3, the methodological quality of the pharmacoeconomic analysis is insufficient to be able to make a reliable statement about its cost-effectiveness.
Zorginstituut Nederland therefore advises against including tolvaptan (Jinarc®) in the GVS.

After the Minister of Public Health, Welfare and Sport has made a decision, and the applicant is prepared to submit a new pharmacoeconomic file that complies with the criteria of Zorginstituut Nederland for an acceptable cost-effectiveness analysis, Zorginstituut Nederland will perform a reassessment and will subsequently advise the Minister of Public Health, Welfare and Sport.

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The original text of this advice of Zorginstituut Nederland was in Dutch. Although great care was taken in translating the text from Dutch to English, the translation may nevertheless have resulted in discrepancies. Rights may only be derived on the basis of the Dutch version of the advice of Zorginstituut Nederland.
Furthermore, Zorginstituut Nederland points out that only the summary of this report was translated. A proper understanding of all relevant considerations and facts would require familiarity with the Dutch version of this report, including all appendices.