HAUTE AUTORITÉ DE SANTÉ

NEPHROLOGY – PAEDIATRICS
New indication
July 2018

TRANSPARENCY COMMITTEE OPINION SUMMARY

MIMPARA (cinacalcet), anti-parathyroid agent

Insufficient clinical benefit to justify its reimbursement in the treatment of secondary hyperparathyroidism (HPT) not properly managed with conventional treatments in paediatric dialysis patients ≥ 3 years, with end-stage renal disease

Main points

- MIMPARA has MA in the treatment of secondary hyperparathyroidism (HPT) not properly managed with conventional treatments in paediatric dialysis patients ≥ 3 years, with end-stage renal disease.
- There is no significant difference between the combination of cinacalcet with standard treatments and standard treatments alone on the reduction in iPTH.
- There are uncertainties as to the safety of cinacalcet in children, in particular in terms of hypocalcaemia.

Pre-existing indications*

MIMPARA already has MA in adults, in the treatment of secondary hyperparathyroidism, parathyroid cancer and primary hyperparathyroidism (see MA for further details).

Therapeutic strategy

- Mineral and bone metabolism is highly impaired in chronic kidney disease. In paediatrics, it is closely monitored due to its considerable effects on children's growth and adult height. Mineral and bone anomalies are defined by the combination of one or several of the following: calcium, phosphorus, parathormone (PTH) or vitamin D anomalies, bone or growth anomalies, vascular or soft tissue calcifications.
- Hyperphosphataemia treatment must make it possible to maintain phosphataemia within the physiological ranges of the child's age (higher in infants). This treatment includes restricted phosphorus intake adapted to age and renal function, calcium-based chelating agents to be taken during meals and secondly, non-calcium chelating agents (without aluminium).
- Treatment for hypocalcaemia is based on sufficient dietary intake, calcium salt (outside meals) and active vitamin D derivative supplementation.
- In the event of hypercalcaemia, the active vitamin D derivatives should be discontinued and the calcium-based chelating agents should be discontinued (or reduced).
- Hyperparathyroidism is treated indirectly by correcting hypocalcaemia, hyperphosphataemia and vitamin D deficiency. It can be treated directly with calcimimetics.
- **Role of the medicinal product in the therapeutic strategy**

  Pending further results, MIMPARA does not currently have a role in the treatment of secondary HPT in children aged 3 years and over, on dialysis, with ESRD, where secondary HPT is not properly managed by conventional treatments.

Clinical data

- A placebo-controlled study having included dialysis patients aged 6 to <18 years-old, was terminated early further to the death of a patient in the cinacalcet group for which the causal role of hypocalcaemia could not be ruled out.

* This summary does not concern these indications.

21 patients in total were included in the placebo group and 22 in the cinacalcet group, corresponding to around half the expected inclusions. Eight patients from the placebo group and 4 from the cinacalcet group completed the treatment. In the analysis only taking the data collected before early treatment termination into account, the proportion of patients having achieved a ≥ 30% reduction in mean iPTH level (primary endpoint) was 54.5% (12/22) in the cinacalcet group and 19.0% (4/21) in the placebo group (p=0.017).

- A randomised, open-label study compared the efficacy of cinacalcet combined with standard treatment for secondary HPT to standard treatment alone in dialysis patients aged 6 to <18 years-old. In total, 19 patients out of 28 included from the standard treatment alone group and 16 out of 27 included from the cinalcalcet group completed the study. No difference was demonstrated between the treatment groups: the proportion of patients achieving a reduction of ≥ 30% in mean iPTH level (primary endpoint) was 22.2% in the cinacalcet + standard treatment group (6/27) and 32.1% in the standard treatment alone group (9/28).
- The most common adverse events were hypocalcaemia, nausea, vomiting and muscle spasms.

Benefit of the medicinal product

- The actual clinical benefit* of MIMPARA is insufficient in this indication extension to justify its reimbursement by public funding.
- Not approved for non-hospital pharmacy reimbursement and for hospital treatment for this indication extension.

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This document was drafted on the basis of the Transparency Committee opinion dated 11 July 2018 (CT-16723) available at **www.has-sante.fr**

* The actual clinical benefit of a medicinal product (ACB) consists of its benefit particularly on the basis of its clinical performances and the severity of the disease treated. The HAS Transparency Committee assesses the ACB, which may be high, moderate, low, or insufficient for the medicinal product to be covered by public funding.