HAUTE AUTORITÉ DE SANTÉ

NEPHROLOGY-ENDOCRINOLOGY
New medicinal product
April 2017

BRIEF SUMMARY OF THE TRANSPARENCY COMMITTEE OPINION

PARSABIV (etelcalcetide), anti-parathyroid agent

No clinical benefit demonstrated in the treatment of secondary hyperparathyroidism in adult patients on haemodialysis compared to MIMPARA.

Main points

- PARSABIV has Marketing Authorisation for the treatment of secondary hyperparathyroidism (SHPT) in adults with chronic kidney disease (CKD) on haemodialysis therapy.
- In one randomised comparative study versus MIMPARA, the percentage of patients who had a decrease of >50% of the mean parathormone (PTH) level compared to baseline and those having a decrease >30% was greater in the arm treated with PARSABIV.
- Hypocalcaemia and cardiac disorders were more frequently observed in the arm treated with PARSABIV.

Therapeutic use

- In patients at CKD stage 5D, serum PTH level should be maintained between approximately 2 and 9 times the normal upper limit of the assay kit used. Furthermore, they suggest that significant variations of serum PTH level even within this range lead to a treatment or treatment change to prevent the progression of the PTH level beyond this interval.
- In patients at CKD stage 5D, whose serum PTH is high or progressively increasing, calcitriol or vitamin D derivatives/analogues or calcimimetics, or combinations thereof, are used to reduce PTH levels.
- In patients at CKD stages 3-5D with severe hyperparathyroidism, who do not respond to medical/pharmacological treatment, parathyroidectomy is suggested.
- **Role of the proprietary medicinal product in the therapeutic strategy**
  PARSABIV is a second-line treatment, in case of failure of conventional treatments already available (phosphate chelators, vitamin D analogues), in patients needing control of serum PTH (maintenance of PTH between 2 and 9 times the upper limit of the assay kit used or significant variation within this interval).

Clinical data

- In one randomised, comparative study that included a total of 683 patients, the non-inferiority of PARSABIV versus MIMPARA was demonstrated for the primary endpoint: percentage of patients who had a decrease >30% of the mean serum PTH level during the assessment phase (week 20 to 27 of treatment) compared to baseline. For two of the secondary endpoints of the same study: the percentage of patients who had a decrease of >50% of the mean PTH level compared to baseline and those having a decrease of >30%, the difference between arms was statistically significant, in favor of the PARSABIV arm, since the analyses were hierarchised. There was no difference between arms for the mean number of days with vomiting or nausea per week during the first 8 weeks of treatment.
- Two randomised, placebo-controlled studies that included a total of 1023 patients had reduction of the mean serum PTH for a primary endpoint. In each of these two studies, the percentage of patients who had a decrease of >30% of the mean parathormone (PTH) level during the assessment phase compared to baseline was significantly higher in the PARSABIV arm than in the placebo arm.
- In the study that compared MIMPARA to PARSABIV, for a median treatment duration of 181 days in each arm, the most common adverse events were asymptomatic reduction of calcaemia, nausea, vomiting, headaches, hypotension, hypertension, diarrhoea. Asymptomatic reduction of calcaemia and hypotension were more common in the PARSABIV arm; nausea and diarrhoea were more common in the MIMPARA arm. Serious adverse events

concerned, respectively 27.3% and 25.1% of patients. The most common ones were infections. The adverse events “of particular interest” more common in the PARSABIV arm than the MIMPARA arm were: hypocalcaemia, injection reaction and heart failure. Deaths concerned, respectively, 1.8% and 2.7% of patients, the most common causes of death were cardiac disorders: 0.9% in the MIMPARA arm versus 1.8% in the PARSABIV arm.

- In one followup study for a median treatment duration of 362 days, around 90% of patients had at least one adverse event, 40% a serious adverse event, 4.6% stopped treatment due to an adverse event and 5.7% died. The most common adverse events were: reduction of calcaemia, diarrhoea, vomiting, nausea and muscle spasms. The most common serious adverse events were: hyperkalaemia, cardiovascular events (congestive heart failure, atrial fibrillation, cardiac arrest, myocardial infarction, chest pain, syncope, coronary arterial disease, hypotension, hypertension).
- The significant risks identified for PARSABIV are hypocalcaemia, worsening of heart failure, long QT secondary to hypocalcaemia and potential major risks of ventricular arrhythmia, injection reactions and hypersensitivity, convulsions, fractures and co-administration of etelcalcetide and cinacalcet.

Benefit of the medicinal product

- The actual clinical benefit* of PARSABIV is substantial.
- Taking into account:
  - the statistically-significant difference in favour of PARSABIV compared to MIMPARA on a biological endpoint: the proportion of patients having a reduction of more than 50% and more than 30% of the mean serum PTH level on treatment, before dialysis, relative to study baseline,
  - the absence of efficacy data concerning the effect of PARSABIV on morbidity and mortality consecutive to secondary hyperparathyroidism in adult patients with chronic kidney disease on haemodialysis therapy,
  - the greater frequency of hypocalcaemia and cardiac disorders in the PARSABIV arm compared to the MIMPARA arm.

  PARSABIV does not provide clinical added value (CAV V) compared to MIMPARA in the indication of the Marketing Authorisation.
- Recommends inclusion on the list of reimbursable products for hospital use.

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This document was created on the basis of the Transparency Committee Opinion of 19 April 2017 (CT-15893) and is available at **www.has-sante.fr**

* The actual clinical benefit (ACB) of a medicinal product describes its benefit primarily in terms of its clinical efficacy and the seriousness of the condition being treated. The HAS Transparency Committee assesses the ACB, which can be substantial, moderate, low or insufficient for reimbursement for hospital use.

** The clinical added value (CAV) describes the improvement in treatment provided by a medicinal product compared with existing treatments. The HAS Transparency Committee assesses the degree of CAV on a scale from I (major) to IV (minor). A level V CAV means “no clinical added value”.