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ENDOCRINOLOGY
New indication
September 2018

TRANSPARENCY COMMITTEE OPINION SUMMARY

TRESIBA (insulin degludec), long-acting insulin analogue

High clinical benefit in the treatment of type 1 diabetes in children (1 – 17 years) but no demonstrated clinical improvement compared to LEVEMIR (insulin detemir).

Main points

- TRESIBA has MA for the treatment of diabetes in adolescents and children from 1 year of age.
- Its non-inferiority has been demonstrated compared to insulin detemir in terms of HbA1c variation over 26 weeks, in combination with insulin aspart.
- No benefit in respect of safety, quality of life or convenience of use has been demonstrated.

Pre-existing indication*

TRESIBA already has MA for the treatment of diabetes in adults.

Therapeutic strategy

There are a number of possible insulin therapy regimens for children and adolescents with type 1 diabetes. The choice of insulin therapy regimen is dependent on the glycaemic targets for each child and adolescent, their preferences, lifestyle and those of their family. Basal-bolus or pump administration regimens are the closest replications of normal physiology. Pump administration is the closest approximation of normal insulin secretion physiology, in exchange for regular and repeated self-monitoring of blood glucose and insulin adjustments. Treatment acceptability (particularly the number of daily injections required) is an important factor to take into account, particularly for very young children.
In cases of poor metabolic control, a change of insulin regimen is discussed after taking into account the other factors of blood sugar control: diet, exercise and compliance.

Role of the medicinal product in the therapeutic strategy

TRESIBA is a first-line treatment for type 1 diabetes in adolescents and children from 1 year of age, in combination with a fast-acting insulin or a fast-acting analogue, in the context of a basal-bolus regimen. No clinical feedback is available in respect of the flexibility of the time of administration of the dose with TRESIBA for children and adolescents, unlike for adults.

Clinical data

- A randomised open-label study with 2 parallel groups, including 350 children with type 1 diabetes aged between 1 year and 17 years of age compared TRESIBA to insulin detemir in combination with a fast-acting insulin aspart based on a "basal-bolus" regimen over 26 weeks. After 26 weeks of treatment, the sensitivity analysis on the per protocol population demonstrated a difference in estimated HbA1c variation between the 2 groups of 0.19 (CI95% [0.01; 0.37]) and on the intention-to-treat population, a difference in HbA1c variation of 0.15 (CI95% [-0.03; -0.32], p = 0.003), confirming that TRESIBA treatment is non-inferior to insulin detemir treatment.
- After 26 weeks of treatment, the percentage of patients having had an adverse event was 92.5% in the TRESIBA group and 89.7% in the insulin detemir group. The main adverse events were: rhinopharyngitis, headaches, increased blood ketone levels, respiratory tract infections, fever and hypoglycaemia. A 26-week extension phase assessed the long-term safety. After 52 weeks of treatment, 98% of the patients of the TRESIBA group and 96%

* This summary does not cover this indication.

of the patients of the insulin detemir group had hypoglycaemic episodes, with no difference between the 2 groups in terms of rates of confirmed hypoglycaemia, severe hypoglycaemia or nocturnal hypoglycaemia.

Benefit of the medicinal product

- The actual clinical benefit* of TRESIBA is high.
- TRESIBA does not provide an improvement in actual clinical benefit** (IACB V) compared to insulin detemir in the management of type 1 diabetes in children over 1 year of age and adolescents.
- Approved for non-hospital pharmacy reimbursement and for hospital treatment.

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This document was drafted on the basis of the Transparency Committee opinion dated 5 September 2018 (CT-16983) available at **www.has-sante.fr**

* The actual clinical benefit (ACB) of a medicinal product 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.

** The improvement in actual clinical benefit (IACB) consists of the clinical improvement offered by a medicinal product compared to existing treatments. The HAS Transparency Committee assesses the IACB rating from I, major, to IV, minor. An IACB rating of V (equivalent to "no IACB") denotes a "lack of clinical improvement"