HAUTE AUTORITÉ DE SANTÉ

DIABETOLOGY
New indication
September 2018

TRANSPARENCY COMMITTEE OPINION SUMMARY

BYDUREON (exenatide), antidiabetic

Insufficient clinical benefit to justify reimbursement for type 2 diabetes in combination with basal insulin with or without metformin

Main points

- BYDUREON now has MA in combination with a basal insulin for type 2 diabetes patients having failed to achieve adequate glycaemic control.
- Its efficacy on HbA1c variation has only been compared versus placebo, in combination with insulin glargine ± metformin, eventhough a comparison versus a clinically relevant comparator was feasible and all other GLP1 analogues have been compared to an active comparator.
- The effect size of BYDUREON versus placebo appears to be modest.
- There is no evidence of a reduction in insulin use with the addition of BYDUREON.

Pre-existing indications*

BYDUREON already has MA for adults with type 2 diabetes to improve glycaemic control in combination with other medicinal products intended to treat diabetes, where the current treatment, combined with diet and exercise, does not provide adequate glycaemic control.

Therapeutic strategy

- The implementation of effective lifestyle and dietary measures is part of the therapeutic arsenal for type 2 diabetes. In case of failing control of type 2 diabetes by a bitherapy combining basal insulin (NPH, detemir or glargine) and metformin, the available therapeutic possibilities are as follows:
  - addition of a GLP-1 agonist for patients with a BMI ≥30kg/m² or for whom weight gain would be a concern,
  - or intensification of insulin therapy.
- **Role of the medicinal product in the therapeutic strategy**
  The clinical data fail to demonstrate the clinical relevance of the efficacy of BYDUREON in patients not controlled by basal insulin-metformin bitherapy. Therefore, BYDUREON, in combination with basal insulin ± metformin, has no role in the therapeutic strategy for type 2 diabetes.

Clinical data

- 464 patients in total were randomised to receive exenatide once a week (n = 233) or placebo (n = 231), of whom 82.6% (n=381) were treated with metformin at the time of inclusion. BYDUREON demonstrated its superiority versus placebo in respect of HbA1c level variation at 28 weeks (primary endpoint), with a modest reduction of the HbA1c level of – 0.96% [CI 95%: - 1.11; -0.80] in the exenatide group versus – 0.23% [CI 95%: - 0.38; -0.07] in the placebo group; so a difference of – 0.73% (p <0.001) between the 2 treatment groups. After 28 weeks of treatment, no significant difference was demonstrated between the 2 groups regarding the variation of the daily insulin dose versus baseline. A small proportion of patients required an alternative treatment: 4 patients (1.7%) in each group.

* This summary does not cover this indication.

- The incidence of hypoglycaemia was comparable between the exenatide group and the placebo group. Events at the injection site were reported mostly in the exenatide group: 18 patients (7.8%) versus 7 patients (3.0%) for the placebo group. These adverse effects were all of low or moderate severity and the most frequent were the appearance of a nodule or erythema at the injection site. Gastrointestinal events were reported mostly in the exenatide group: 35 patients (15.1%) versus 25 patients (10.8%) for the placebo group. No evidence was found of an increase in cardiovascular events in the exenatide group compared to the placebo.

Benefit of the medicinal product

- The actual clinical benefit* of BYDUREON is insufficient to justify public funding cover in combination with a basal insulin ± metformin for adults having failed to achieve adequate glycaemic control with these medicinal products.
- Not approved for non-hospital pharmacy reimbursement or for hospital treatment.

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This document was drafted on the basis of the Transparency Committee opinion dated 19 September 2018 (CT-16841) 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.