HAUTE AUTORITÉ DE SANTÉ

DIABETOLOGY
New medicinal product
July 2018

TRANSPARENCY COMMITTEE OPINION SUMMARY

SULIQUA (insulin glargine/ lixisenatide), antidiabetic

Insufficient clinical benefit to justify reimbursement for type 2 diabetes

Main points

- SULIQUA has been granted marketing authorisation for the treatment of type 2 diabetes, to improve glycaemic control, in combination with metformin, when metformin, alone or combined with another oral antidiabetic, or with basal insulin is unable to provide adequate glycaemic control.
- The available clinical data fail to demonstrate the clinical benefit of combining SULIQUA with metformin in terms of reduction in HbA1c, reduction in insulin consumption or in morbidity and mortality compared to an insulin multi-injection scheme.
- SULIQUA has no role in the therapeutic strategy for type 2 diabetes.

Therapeutic strategy

- 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: VICTOZA (liraglutide, one injection per day), BYETTA (exenatide, 2 injections per day), or TRULICITY (dulaglutide, one injection per week), for patients with a BMI ≥30 kg/m², or for whom weight gain would be of concern,
  - or intensification of insulin therapy in one of 3 ways:
    - progressive transition to a basal/bolus regimen, initially with a single injection of rapid-acting insulin analogue before the most hyperglycaemia-inducing meal,
    - transition from the outset to a basal/bolus regimen with 3 injections of rapid-acting insulin analogue (one before each meal),
    - transition to two premixed insulin injections.

- **Role of the medicinal product in the therapeutic strategy**

  The available clinical data fail to demonstrate the clinical relevance of SULIQUA efficacy in patients not controlled by basal insulin-metformin bitherapy. SULIQUA has no role in the therapeutic strategy for type 2 diabetes.

Clinical data

- One open-label study compared SULIQUA ± metformin (n=367) to insulin glargine ± metformin (n=369) in type 2 diabetic patients insufficiently controlled by basal insulin ± metformin (10.6% of patients included did not receive metformin). Upon inclusion, mean HbA1c value was of 8.08 ± 0.71%. SULIQUA ± metformin was superior to glargine ± metformin in terms of HbA1c variation at 30 weeks, with a difference of -0.52 ± 0.060% CI95% [-0.633; -0.397], p<0.0001, reflecting the efficacy of lixisenatide used for 68.8% of patients, at a dose of between 15 µg and 20 µg.
  After 30 weeks of treatment, there was no reduction in insulin consumption.
- Gastrointestinal disorders (diarrhoea, nausea, vomiting) were more frequent in the SULIQUA group than in the insulin glargine group (17.0% *versus* 7.9%). The incidence of documented hypoglycaemia episodes, that was comparable between the two groups (40.0% in the SULIQUA *versus* 42.5% in the comparator group), should be weighted by the fact that the insulin dose in the insulin glargine group could not exceed 60 IU.
- This study failed to demonstrate the contribution or benefit of administering the SULIQUA fixed-dose combination over an insulin multi-injection scheme in the context of intensification of basal insulin treatment. The comparison of SULIQUA to insulin glargine was not optimal as the insulin dose was limited to 60 IU in the insulin glargine

group and the patients in the SULIQUA group could receive up to 20 µg lixisenatide. Limiting the insulin dose to 60 IU in the insulin glargine group prevented demonstration of the insulin-sparing effect with SULIQUA.

Special prescription requirements

- Medicinal product subject to initial prescription reserved for endocrinology, diabetes and metabolic disease or internal medicine specialists. Unrestricted renewal.

Benefit of the medicinal product

- The actual clinical benefit* of SULIQUA is insufficient to justify public funding cover.
- 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 25 July 2018 (CT-16640) available at **www.has-sante.fr**

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