HAUTE AUTORITÉ DE SANTÉ

TRANSPARENCY COMMITTEE

SUMMARY

2 DECEMBER 2020

The legally binding text is the original French opinion version

dulaglutide

TRULICITY 0.75 mg, 1.5 mg, 3 mg, 4.5 mg solution for injection in pre-filled pen

Reevaluation (0.75 mg and 1.5 mg strengths)
Inclusion of range extensions (3 mg and 4.5 mg strengths)

Key points

Favourable opinion for reimbursement only in the treatment of adults with insufficiently controlled type 2 diabetes mellitus as an adjunct to diet and exercise in addition to other medicinal products for the treatment of diabetes, including insulin, only:

- as dual therapy with metformin,
- as triple therapy with metformin and insulin or with metformin and a sulfonylurea.

Unfavourable opinion for reimbursement as monotherapy and as dual therapy with insulin.

What therapeutic improvement?

Therapeutic improvement with TRULICITY 0.75 mg and 1.5 mg (dulaglutide) in the same way as liraglutide (VICTOZA), in the treatment of adults with type 2 diabetes mellitus to improve glycaemic control, in addition to other medicinal products for the treatment of diabetes, including insulin, when the current treatment, combined with diet and exercise, does not provide adequate glycaemic control, only:

- as dual therapy with metformin,
- as triple therapy with metformin and insulin or with metformin and a sulfonylurea.

No clinical added value of TRULICITY 3 mg and 4.5 mg (dulaglutide) compared with the existing forms.

Role in the care pathway?

The objective of treatment of type 2 diabetes is to prevent the numerous serious and disabling complications, such as microangiopathy (affecting the retina, nerves, heart and kidneys) and sudden complications of macroangiopathy, such as myocardial infarction, stroke, etc. Diabetes promotes the development of heart failure. The Committee also highlights the importance of ensuring patients are well informed and the importance of their compliance with treatment for successful management of the disease. The initial management of type 2 diabetes is based on non-medicinal interventions and, in particular, the implementation of lifestyle and dietary measures. In the event of failure to meet the blood glucose target, medicinal treatment with metformin or, in the event of contraindications, a sulfonylurea is recommended as first-line therapy, in addition to these measures. Drug combinations are envisaged following the failure of monotherapy.

Role of the medicinal product in the care pathway

Following the failure of monotherapy with metformin or a sulfonylurea, a new treatment line with an antidiabetic drug from a different therapeutic class will be added to the first-line treatment. The choice between the different drug families that can be used as second or third-line treatment (gliflozins, gliptins, alphaglucosidase inhibitors, GLP1 analogues and insulins) will notably be determined on the basis of the safety profile of the medicinal products, the availability of conclusive cardiovascular or renal morbidity and mortality study results and the preferences of patients after they have been given appropriate information.

If the decision is to prescribe a GLP-1 analogue, given the results observed in terms of reduction of the 3P-MACE endpoint with dulaglutide at a dosage of 1.5 mg/week compared to placebo in the REWIND study, TRULICITY (dulaglutide) may be chosen as first-line treatment, in the same way as liraglutide (VICTOZA), for which the results in the LEADER study provide a similar demonstration in terms of reduction of the 3P-MACE endpoint.
In the absence of usable clinical data concerning monotherapy and the combination of dulaglutide with basal insulin alone, TRULICITY (dulaglutide) has no role in the therapeutic strategy for type 2 diabetes as monotherapy and as dual therapy with basal insulin.

COMMITTEE'S CONCLUSIONS

Clinical benefit

◗ Diabetes is a chronic disease with potentially serious complications, particularly cardiovascular. The objective of treatment of type 2 diabetes is to prevent its numerous, serious and often disabling complications, that are often insidious, such as microangiopathy (affecting the retina, nerves, heart and kidneys) and sudden complications of macroangiopathy, such as myocardial infarction, stroke, etc. Diabetes promotes the development of heart failure.

◗ TRULICITY (dulaglutide) proprietary medicinal products are preventive treatments for cardiovascular complications of diabetes.

◗ There are medicinal alternatives to these proprietary medicinal products.

◗ The efficacy/adverse effects ratio of TRULICITY (dulaglutide) proprietary medicinal products cannot be qualified as monotherapy or dual therapy with insulin, due to the absence of conclusive clinical data.
It is high as dual therapy with metformin, as triple therapy with metformin and a sulfonylurea or as triple therapy with metformin and insulin.

◗ If the decision is to prescribe a GLP-1 analogue, given the results observed in terms of reduction of the 3P-MACE endpoint with dulaglutide at a dosage of 1.5 mg/week compared to placebo in the REWIND study, TRULICITY (dulaglutide) may be chosen as first-line treatment, in the same way as liraglutide (VICTOZA), for which the results in the LEADER study provide a similar demonstration in terms of reduction of the 3P-MACE endpoint.

Public health impact

Considering:

- the seriousness of the disease and, in particular, the microvascular and macrovascular complications associated with this disease,
- the high and constantly increasing prevalence of type 2 diabetes,
- the medical need currently met by medicinal products having all demonstrated an efficacy on an intermediate laboratory endpoint (and not a surrogate endpoint), change in HbA1c, as well as by medicinal products, gliflozins or SGLT2 inhibitors having shown evidence of a reduction in cardiovascular and renal morbidity and mortality, only in combination and following the failure of monotherapy with metformin or a sulfonylurea; and of the unmet need to have access to an antidiabetic drug having shown evidence of a reduction in cardiovascular and renal morbidity and mortality, which improves patients' compliance and adhesion to treatment, with a satisfactory safety profile,
- efficacy data provided with dulaglutide in the REWIND study in terms of reduction of cardiovascular events in the 3P-MACE composite endpoint, and the new safety data available with dulaglutide, an additional impact of TRULICITY (dulaglutide) on morbidity and mortality is expected,
- the lack of data on a potential impact on the organisation of care, and the absence of data on a potential impact on quality of life of TRULICITY (dulaglutide), however, considering the results of the study for the cardiovascular endpoints, an impact on the organisation of care and quality of life is expected with TRULICITY (dulaglutide),
- the response provided by TRULICITY (dulaglutide) to the identified medical need,

TRULICITY (dulaglutide) is likely to have an additional impact on public health.

Considering all these elements, the Committee deems that the clinical benefit of TRULICITY (dulaglutide) is:

- **substantial in the indication in addition to other medicinal products for the treatment of diabetes, including insulin, when the current treatment, combined with diet and exercise, does not provide adequate glycaemic control, only:**
  - **as dual therapy with metformin,**
  - **as triple therapy with metformin and insulin or with metformin and a sulfonylurea.**
- **insufficient to justify public funding coverage:**
  - **as monotherapy, for the treatment of adults with insufficiently controlled type 2 diabetes mellitus as an adjunct to diet and exercise when metformin is considered inappropriate due to intolerance or contraindications,**
  - **as dual therapy with insulin.**

The Committee issues a favourable opinion for inclusion of TRULICITY (dulaglutide) 3 mg and 4.5 mg in both the hospital formulary list and the retail formulary list of reimbursed proprietary medicinal products approved for use in the indication in addition to other medicinal products for the treatment of diabetes, including insulin, where the current treatment, combined with diet and exercise, does not provide adequate glycaemic control, only:
- **as dual therapy with metformin,**
- **as triple therapy with metformin and insulin or with metformin and a sulfonylurea.**

and at the MA dosages,
and an unfavourable opinion in the indications:
- **as monotherapy, for the treatment of adults with insufficiently controlled type 2 diabetes mellitus as an adjunct to diet and exercise when metformin is considered inappropriate due to intolerance or contraindications,**
- **as dual therapy with insulin.**

◗ **Recommended reimbursement rate: 65%**

Clinical Added Value

TRULICITY 0.75 and 1.5 mg

Considering,
- **initial data having demonstrated the efficacy of dulaglutide, a GLP1 analogue, in combination with other treatments, versus clinically relevant comparators, on reduction of the intermediate laboratory outcome measure, HbA1c, in combination with other medicinal products as dual or triple therapy,**
- **demonstration of the superiority of dulaglutide at a dosage of 1.5 mg per week compared to placebo in the REWIND study for a clinically relevant cardiovascular endpoint, i.e. the reduction in events in the 3P-MACE composite endpoint with 3 components (cardiovascular death, non-fatal myocardial infarction, non-fatal stroke), in type 2 diabetic patients, mainly in primary prevention (62.8%),**
- **the similar demonstration previously provided by liraglutide (VICTOZA) in the LEADER study in terms of non-inferiority and then superiority compared to placebo on the 3P-MACE composite endpoint,**
- **new safety data for dulaglutide that has not revealed any new signals,**
- **the medical need to have access to antidiabetic drugs providing evidence of cardiovascular protection, for efficient and optimal management of patients with type 2 diabetes,**

and despite:
- **the reduction in absolute cardiovascular risk judged to be low in the REWIND study,**
- **the absence of demonstration of a reduction in the occurrence of cardiovascular events with other drugs belonging to the GLP-1 analogue class, in particular exenatide, lixisenatide, semaglutide,**

the Committee considers that TRULICITY (dulaglutide) 0.75 mg and 1.5 mg provides a minor clinical added value (CAV IV), in the same way as liraglutide (VICTOZA), in the treatment of adults with type 2 diabetes mellitus to improve glycaemic control, in addition to other medicinal products for the treatment of diabetes, including insulin, when the current treatment, combined with diet and exercise, does not provide adequate glycaemic control, only:
- **as dual therapy with metformin,**
- **as triple therapy with metformin and insulin or with metformin and a sulfonylurea.**

TRULICITY (dulaglutide) 3 mg and 4.5 mg

The TRULICITY (dulaglutide) 3 mg and 4.5 mg medicinal products are a range supplement that provide no clinical added value (CAV V) compared to the TRULICITY (dulaglutide) forms already approved.