DAR DRUG ASSESSMENT REPORT **01 / 2022**

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▼ RYBELSUS®
ORAL SEMAGLUTIDE FOR TYPE 2 DM

An oral route that does not worth it

Hard to find its place in therapeutic because there are GLP-1 agonists with predictable absorption

REPORT [IN SPANISH]

IMPORTANT THERAPEUTIC INNOVATION

MODEST THERAPEUTIC INNOVATION

SOME ADDED VALUE IN SPECIFIC SITUATIONS

NO THERAPEUTIC INNOVATION

INSUFFICIENT EVIDENCE

DATA SHEET

WHAT IS IT?
Glucagon-Like Peptide-1 (GLP-1) analogue antidiabetic agent.

INDICATION
Treatment of adults with insufficiently controlled type 2 DM as an adjunct to diet and exercise. In Spain, it is only financed as a combination therapy with other antidiabetic drugs in patients with a BMI ≥ 30 kg/m^2.

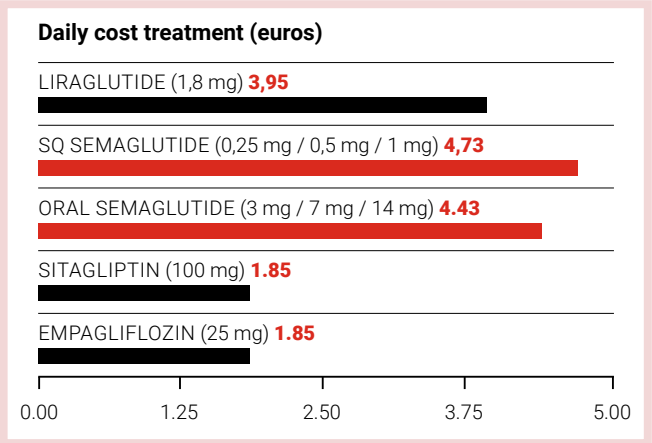
POSOLOGY AND METHOD OF ADMINISTRATION
Low absolute bioavailability (~1%) and variable absorption (2-4% of patients will have no exposure to treatment). Oral administration on an empty stomach (6 hours fast), with a sip of water and at least 30 minutes before eating or drinking or taking other oral medicinal products. Tablets should not be split, crushed or chewed. **Initial dose:** 3 mg/day; after 4 weeks increase to 7 mg/day and after another 4 weeks, it can be increased to 14 mg/day (maximum dose). When it is used in combination with a sulfonylurea or with insulin, dose reduction of the later should be considered due to the risk of hypoglycaemia. **Special populations:** Not recommended in end-stage renal disease or in children and adolescents under 18.

EFFECTIVENESS
Studies show a dose-dependent reduction in HbA1c values. **Compared to placebo:** in monotherapy and in combination with other antidiabetic drugs has shown to be effective in reducing HbA1c at week 26 (between 0.8% and 1.2% with the maximum dose). **Weight reduction:** it was only significant with semaglutide 14 mg (-2.3 kg). **Compared to active comparators:** its efficacy has been demonstrated compared to empagliflozin, sitagliptin and liraglutide in combination with other antidiabetics, with a difference in HbA1c decrease of 0.4%, 0.5% and 0.1%, respectively. All differences were statistically significant, but not clinically relevant. A significant weight reduction was observed when comparing semaglutide vs. sitagliptin (between 1.6 kg and 2.5 kg) and semaglutide vs. liraglutide (1.2 kg). No differences were found when it was compared to empagliflozin.

RISKS
Its safety profile is similar to SQ semaglutide. The most frequently reported adverse effects were nausea, diarrhoea and vomiting. They were generally mild or moderate and most of them were dose-dependent. There was an increased risk of diabetic retinopathy (between 0.5% and 1%) and a higher proportion of malignant and non-malignant neoplasms (6.4% and 5.7% respectively), so they were included as potential risks of special interest in the EMA Risk Management Plan. The results of cardiovascular safety studies do not indicate that oral semaglutide has a beneficial or detrimental effect. **Convenience:** administration on an empty stomach can make it difficult to take other concomitant drugs. The change between oral and SQ semaglutide cannot be predicted due to its high pharmacokinetic variability.

PLACE IN THERAPEUTICS
It is hard to find a place for it because there are SQ GLP-1 agonists with predictable absorption and other oral antidiabetics with greater experience of use.

PRESENTATIONS
Rybelsus® 3 mg; Rybelsus® 7 mg; Rybelsus® 14 mg 30 tablets (132.77€).



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