RYBELSUS® semaglutide tablets

An aide memoire for healthcare professionals only

RYBELSUS® is indicated for the treatment of adults with insufficiently controlled type 2 diabetes mellitus to improve glycaemic control as an adjunct to diet and exercise[1]

- as monotherapy when metformin is considered inappropriate due to intolerance or contraindications
- in combination with other medicinal products for the treatment of diabetes

Please refer to the RYBELSUS® Summary of Product Characteristics prior to prescribing

Prescribing information and adverse event reporting information can be found on page 4

T-TWO-DM

These letters stand for...
Timing-Technique-Wise-Observations-Driving-Managing hypoglycaemia
Which can be used to guide you through the review process

Timing & Technique

STARTING DOSE[1]

3 mg Start with 3 mg once daily for 1 month

MAINTENANCE DOSE[1]

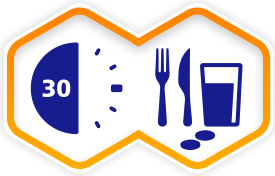
7 mg Increase dose to 7 mg once daily for at least 1 month

14 mg Based on individual needs, you may increase dose to 14 mg

Take on an empty stomach, upon waking*[1]

Take with a sip of water (up to 120 mL)*[1]

Tablets should not be split, crushed or chewed[1]



Patients need to wait at least 30 minutes before eating, drinking or taking other oral medications*[1]

Missed dose: If a patient misses a dose, they must skip the missed dose and take their normal dose the following day[1]

To maximise benefit of treatment it is important to take RYBELSUS® as instructed[1]

Wise about their medicine

RYBELSUS®[1]:

- Contains the active substance semaglutide. It is a medicine that is used to lower blood sugar levels. It is a glucagon-like peptide-1 (GLP-1) receptor agonist that selectively binds to and activates the GLP-1 receptor
- Reduces blood glucose in a glucose-dependent manner by stimulating insulin secretion and lowering glucagon secretion when blood glucose is high
- Has the additional benefits of reducing body weight gain and body fat mass by reducing appetite and lowering energy intake, and of reducing the preference for high-fat foods
- When used in combination with sulfonylurea and/or insulin, patients may have an increased risk of hypoglycaemia
- Has precautions for use -
  - patients should be informed of the characteristic symptom of acute pancreatitis (persistent, severe abdominal pain)
  - patients with diabetic retinopathy should be monitored closely and treated according to clinical guidelines

Observations & checks

Is the patient receiving all annual checks?† If not, refer patient to GP for clinical checks to be arranged, make the GP aware of any feedback provided.

Driving

RYBELSUS® has no or negligible influence on the ability to drive or use machines. When it is used in combination with a sulfonylurea or insulin, patients should be advised to take precautions to avoid hypoglycaemia while driving and using machines.[1]

Managing hypoglycaemia

The chance of hypoglycaemia occurring may be increased by:

- Taking too much of a diabetes medicine - such as insulin, sulfonylureas or glinides[2]
- Interaction with other medicines[1] (refer to the BNF or individual SPCs)

*See additional considerations.

†HbA_{1c}, blood pressure, serum cholesterol, serum creatinine, urine/albumin creatinine ratio, foot risk surveillance, Body Mass Index, smoking history, digital retinal screening.

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driving change FOR diabetes through COVID-19 and beyond

Using RYBELSUS® with other diabetes medications

When RYBELSUS® is used in combination with sulphonylurea and/or insulin, a reduction in the dose of sulphonylurea or insulin should be considered to reduce the risk of hypoglycaemia. Blood glucose self-monitoring is necessary to adjust the dose of sulphonylurea and insulin, particularly when RYBELSUS® is started and insulin is reduced. A stepwise approach to insulin reduction is recommended.[1]

Gastrointestinal events

Gastrointestinal disorders were the most frequently reported adverse reactions in clinical trials, including nausea, diarrhoea and vomiting, of mild to moderate severity, and of short duration.[1]

Patients treated with RYBELSUS® should be advised of the potential risk of dehydration in relation to gastrointestinal side effects and take precautions to avoid fluid depletion.[1]

RYBELSUS® delays gastric emptying which may influence the absorption of other oral medicinal products.[1]

There is no therapeutic experience with RYBELSUS® in patients with bariatric surgery.[1]

Practical tips for patients with gastrointestinal side effects:

Encourage patients to try and:

- ✓ Eat smaller portions
- ✓ Eat slowly
- ✓ Stay hydrated
- ✓ Stop eating at first sign of fullness

Encourage patients to avoid:

- ✗ Large portions
- ✗ Fried or fatty foods
- ✗ Overly sweet or spicy foods
- ✗ Drinking alcohol and smoking cigarettes

Select precautions and adverse events

Please refer to the RYBELSUS® Summary of Product Characteristics for full details

Diabetic ketoacidosis

RYBELSUS® should not be used in patients with type 1 diabetes mellitus or for the treatment of diabetic ketoacidosis.[1]

Diabetic ketoacidosis has been reported in insulin-dependent patients who had rapid discontinuation or dose reduction of insulin when treatment with a GLP-1 receptor agonist is started. A stepwise approach to insulin reduction is recommended.[1]

Diabetic retinopathy

In patients with diabetic retinopathy treated with insulin and sub-cutaneous semaglutide, an increased risk of developing diabetic retinopathy complications has been observed, a risk that cannot be excluded for RYBELSUS®.[1]

Caution should be exercised when using RYBELSUS® in patients with diabetic retinopathy. These patients should be monitored closely and treated according to clinical guidelines.[1]

Rapid improvement in glucose control has been associated with a temporary worsening of diabetic retinopathy, but other mechanisms cannot be excluded. Long-term glycaemic control decreases the risk of diabetic retinopathy.[1]

Hypoglycaemia

Patients treated with RYBELSUS® in combination with a sulfonylurea and/or insulin may have an increased risk of hypoglycaemia. Blood glucose self-monitoring is necessary to adjust the dose of sulfonylurea and insulin, particularly when RYBELSUS® is started and insulin is reduced. A stepwise approach to insulin reduction is recommended.[1]

Interactions and monitoring when using RYBELSUS®

Please refer to the RYBELSUS® Summary of Product Characteristics for the complete list

Thyroxine[1]

Total exposure (AUC) of thyroxine (adjusted for endogenous levels) was increased by 33% following administration of a single dose of levothyroxine. Maximum exposure (C_{max}) was unchanged. Monitoring of thyroid parameters should be considered when treating patients with RYBELSUS® at the same time as levothyroxine.

Warfarin[1]

RYBELSUS® did not change the AUC or C_{max} of R- and S-warfarin following a single dose of warfarin, and the pharmacodynamic effects of warfarin as measured by the international normalised ratio (INR) were not affected in a clinically relevant manner. However, upon initiation of RYBELSUS® treatment in patients on warfarin or other coumarin derivatives, frequent monitoring of INR is recommended.

Rosuvastatin[1]

AUC of rosuvastatin was increased by 41% [90% CI: 24; 60] when co-administered with RYBELSUS®. Based on the wide therapeutic index of rosuvastatin the magnitude of changes in the exposure is not considered clinically relevant.

Digoxin, oral contraceptives, metformin, furosemide[1]

No clinically relevant change in AUC or C_{max} of digoxin, oral contraceptives (containing ethinylestradiol and levonorgestrel), metformin or furosemide was observed when concurrently administered with RYBELSUS®.

Interactions with medicinal products with very low bioavailability (F: 1%) have not been evaluated.[1]

Additional considerations

For optimal effect RYBELSUS® should be taken on an empty stomach (at any time of the day, but ideally upon waking e.g. first thing in the morning). Tablets should not be split, crushed or chewed, as it is not known whether this impacts absorption.[1]

RYBELSUS® has a low absolute bioavailability and variable absorption. Absorption is decreased if taken with food or large volumes of water.[1]

120 ml is approximately equivalent to:

1/3 of a can of drink

2/3 of a small juice carton

Patients should wait at least 30 minutes before eating or drinking or taking other oral medicinal products. Waiting less than 30 minutes decreases the absorption of RYBELSUS®. A longer post-dose fasting period results in higher absorption of RYBELSUS®.[1]

For more information on RYBELSUS®, visit: rybelsus.info

You can contact the Novo Nordisk Customer Care Centre on 0800 0232573 (8.30am to 5.30pm weekdays and Bank Holidays*)

naomi

Novo Nordisk Automated On demand Medical Information

Scan the QR code to connect to NAOMI, our automated, on-demand, medical information chat service. NAOMI can provide information in response to questions from UK healthcare professionals and patients. NAOMI is accessible 24/7. Please note, this does not provide a live link to UK Novo Nordisk Medical Information.

References

1. RYBELSUS® Summary of Product Characteristics, Novo Nordisk Ltd.
2. NHS Choices. Low blood sugar (hypoglycaemia). Available at: https://www.nhs.uk/conditions/low-blood-sugar-hypoglycaemia/. Access date: November 2021

*Calls may be monitored for training purposes.

Prescribing Information

Rybelsus® ▼
tablets
semaglutide

Rybelsus® 3 mg tablets
Rybelsus® 7 mg tablets
Rybelsus® 14 mg tablets

Indications: Rybelsus® is indicated for the treatment of adults with insufficiently controlled type 2 diabetes mellitus to improve glycaemic control as an adjunct to diet and exercise

- as monotherapy when metformin is considered inappropriate due to intolerance or contraindications
- in combination with other medicinal products for the treatment of diabetes.

For study results with respect to combinations, effects on glycaemic control and cardiovascular events, and the populations studied, see sections 4.4, 4.5 and 5.1 of the SmPC.

Posology and administration: Administered once daily for oral use, should be taken on an empty stomach at any time of the day. The tablet should be swallowed whole with a sip of water (up to 120 ml). Tablets should not be split, crushed or chewed. The patient should wait at least 30 minutes before eating, drinking or taking other oral medicine. The starting dose of semaglutide is 3 mg once daily for 1 month. After 1 month the dose should be increased to a maintenance dose of 7 mg once daily. After at least 1 month with 7 mg the dose can be increased to a maintenance dose of 14 mg once daily to further improve glycaemic control. The maximum recommended single daily dose is 14 mg. Taking two 7 mg tablets to achieve the effect of a 14 mg dose has not been studied and is not recommended. If a dose is missed, the missed dose should be skipped and the next dose taken the following day. When semaglutide is used in combination with metformin and/or a sodium-glucose co-transporter-2 inhibitor (SGLT2i) or thiazolidinedione the current dose of metformin and/or SGLT2i or thiazolidinedione can be continued. Children & adolescents below 18 years: No data are available. Elderly: No dose adjustment, therapeutic experience in patients ≥75 is limited. Renal Impairment: No dose adjustment is required for patients with mild, moderate or severe renal impairment. Experience in patients with severe renal impairment is limited. Not recommended for use in patients with end-stage renal disease. Hepatic impairment: No dose adjustment is required for patients with hepatic impairment. Experience with severe hepatic impairment is limited. Caution should be exercised when treating these patients with semaglutide.

Contraindications: Hypersensitivity to the active substance or to any of the excipients.

Special warnings and precautions for use: In order to improve traceability of biological medicinal products, the name and batch number of the administered product should be clearly recorded. Semaglutide should not be used in patients with type 1 diabetes mellitus or for the treatment of diabetic ketoacidosis. Diabetic ketoacidosis has been reported in insulin-dependent patients whom had rapid discontinuation or dose reduction of insulin when treatment with a GLP-1 receptor agonist is started. Use of semaglutide in combination with a sulfonylurea or insulin may have an increased risk of hypoglycaemia. The risk of hypoglycaemia can be lowered by reducing the dose of sulfonylurea or insulin when initiating treatment with semaglutide. Blood glucose self-monitoring is necessary to adjust the dose of sulfonylurea and insulin, particularly when semaglutide is started and insulin is reduced. A stepwise approach to insulin reduction is recommended. Patients should be advised to take precautions to avoid hypoglycaemia while driving and using machines. There is no experience in patients with congestive heart failure NYHA class IV and is therefore not recommended in these patients. Use of GLP-1 receptor agonists may be associated with gastrointestinal adverse reactions that can cause dehydration, which in rare cases can lead to a deterioration of renal function. Patients treated with semaglutide should be advised of the potential risk of dehydration in relation to gastrointestinal side effects/take precautions to avoid fluid depletion. Acute pancreatitis has been observed with the use of GLP-1 receptor agonists. Patients should be informed of the characteristic symptoms of acute pancreatitis. If pancreatitis is suspected, semaglutide should be discontinued; if confirmed, semaglutide should not be restarted. Caution should be exercised when using semaglutide in patients with a history of pancreatitis. In patients with diabetic retinopathy treated with insulin and s.c. semaglutide, an increased risk of developing diabetic retinopathy complications has been observed, a risk that cannot be excluded for oral semaglutide. Caution should be exercised when using oral semaglutide in patients with diabetic retinopathy. These patients should be monitored closely and treated according to clinical guidelines. Rapid improvement in glucose control has been associated with a temporary worsening of diabetic retinopathy, but other mechanisms cannot be excluded. Compliance with the dosing regimen is recommended for optimal effect. If the treatment response is lower than expected, the physician should be aware that the absorption of semaglutide is highly variable and may be minimal and the absolute bioavailability is low. Oral semaglutide contains 23 mg sodium per tablet, equivalent to 1% of the WHO recommended maximum daily intake of 2 g sodium for an adult.

Fertility, pregnancy and lactation: Women of childbearing potential are recommended to use contraception when treated with semaglutide. Should not be used during pregnancy or breast-feeding. Discontinue at least 2 months before a planned pregnancy. Effect on fertility unknown.

Undesirable effects: Adverse events in clinical trials which could be considered **serious** include:
(≥1/10)**:** Hypoglycaemia when used with insulin or sulfonylurea
(≥1/100 to <1/10): Diabetic retinopathy complications
(≥1/1,000 to <1/100): Cholelithiasis
(≥1/10,000 to <1/1,000): Anaphylactic reaction, acute pancreatitis
(<1/10,000): N/A
Other **Very common** (≥1/10: Nausea, diarrhoea
Other **Common** (≥1/100 to <1/10): Hypoglycaemia when used with other OADs, decreased appetite, vomiting, abdominal pain, abdominal distension, constipation, dyspepsia, gastritis, gastro-oesophageal reflux disease, flatulence, fatigue, increased lipase, increased amylase.
Of medical interest: Increased heart rate

MA numbers and Basic NHS Price:
Rybelsus® 3 mg x 30 tablets, EU/1/20/1430/2, £78.48
Rybelsus® 7 mg x 30 tablets, EU/1/20/1430/5, £78.48
Rybelsus® 14 mg x 30 tablets, EU/1/20/1430/8, £78.48
Legal category: POM.

For full prescribing information please refer to the **SmPC** which can be obtained from: Novo Nordisk Limited, 3 City Place, Beehive Ring Road, Gatwick, W. Sussex, RH6 0PA.
Marketing Authorisation Holder: Novo Nordisk A/S, Novo Allé, DK-2880 Bagsværd, Denmark.

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Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store. Adverse events should also be reported to Novo Nordisk Limited (Telephone Novo Nordisk Customer Care Centre 0800 0232573). Calls may be monitored for training purposes.