Semaglutide (Rybelsus®)

Prescribing Information Sheet, November 2020

This document provides general prescribing information on the use of Semaglutide. For the most up to date information, consult the summary of product characteristics

For information on Bedfordshire and Luton Joint Prescribing Committee (JPC) recommendations on place in therapy, prescribing and monitoring requirements and responsibilities, please consult the 'Overarching Shared Care Guideline for the use of Glucagon-like peptide 1 (GLP 1) agonists.' Document.

Licensed Indication	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.
Drug dose	**Adult patients 18 years and over:-** The starting dose of semaglutide is 3 mg once daily for one month. After one month, the dose should be increased to a maintenance dose of 7 mg once daily. After at least one month with a dose of 7 mg once daily, the dose can be increased to a maintenance dose of 14 mg once daily to further improve glycaemic control. **Switching between oral and subcutaneous (s.c.) administration:** The effect of switching between oral and s.c. semaglutide cannot easily be predicted because of the high pharmacokinetic variability of oral semaglutide. Exposure after oral semaglutide 14 mg once daily is comparable to s.c. semaglutide 0.5 mg once weekly. An oral dose equivalent to 1.0 mg of s.c. semaglutide has not been established.
Dose modifications in Special Populations	**Elderly** No dose adjustment is required based on age. Therapeutic experience in patients ≥75 years of age is limited. **Renal impairment** No dose adjustment is required for patients with mild, moderate or severe renal impairment. Experience with the use of semaglutide in patients with severe renal impairment is limited. Semaglutide is not recommended in patients with end-stage renal disease. **Hepatic impairment** No dose adjustment is required for patients with hepatic impairment. Experience with the use of semaglutide in patients with severe hepatic impairment is limited. Caution should be exercised when treating these patients with semaglutide.

	Added to other hypoglycaemic agents Patients treated with 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
Administration details	Rybelsus is a tablet for once-daily oral use. – This medicinal product should be taken on an empty stomach at any time of the day. – It should be swallowed whole with a sip of water (up to half a glass of water equivalent to 120 ml). Tablets should not be split, crushed or chewed, as it is not known whether this impacts absorption of semaglutide. – 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 semaglutide
Formulations	Rybelsus 3 mg tablets contains 3 mg semaglutide. Rybelsus 7 mg tablets contains 7 mg semaglutide Rybelsus 14 mg tablets contains 14 mg semaglutide.
Duration of Action	Orally administered semaglutide has a low absolute bioavailability and a variable absorption. Daily administration according to the recommended posology in combination with a long half-life reduces day-to-day fluctuation of the exposure. With an elimination half-life of approximately 1 week, semaglutide will be present in the circulation for about 5 weeks after the last dose.
Contra-indications / Cautions	Clinicians should refer to the Summary of Product Characteristics (SPC's) or the current electronic BNF for full details **Contra-indications** Semaglutide is contra-indicated in patients who have experienced hypersensitivity to the active substance or to any of the excipients; diabetic ketoacidosis. No therapeutic experience in patients with severe congestive heart failure. **Cautions** Semaglutide should not be used in patients with type 1 diabetes mellitus or for the treatment of diabetic ketoacidosis. There is no therapeutic experience in patients with congestive heart failure New York Heart Association (NYHA) class IV and semaglutide is therefore not recommended in these patients. There is no therapeutic experience with semaglutide in patients with bariatric surgery. 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 and 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 in patients with a history of pancreatitis. Caution should be exercised when using semaglutide orally in patients with diabetic retinopathy, as increased risk of diabetic retinopathy has been observed in patients treated with insulin and S/C semaglutide. 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. Long-term glycaemic control decreases the risk of diabetic retinopathy. This medicinal product contains 23 mg sodium per tablet, equivalent to 1% of the WHO recommended maximum daily intake of 2 g sodium for an adult.
Side effects	Clinicians should refer to the Summary of Product Characteristics (SPC) and current electronic BNF for full details Semaglutide is denoted as a black triangle (▼) drug. Report all side effects using the yellow card scheme A list of very common/common side effects include: • Hypoglycaemia when used with insulin or sulfonylurea • Nausea • Diarrhoea • Hypoglycaemia when used with other OADs • Diabetic retinopathy complications • Vomiting • Abdominal pain • Abdominal distension • Constipation • Dyspepsia • Gastritis • Gastro-oesophageal reflux disease • Flatulence • Fatigue • Increased lipase • Increased amylase • Decreased appetite **MHRA warning (June 2019)** – 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 Semaglutide was not subject to the EU review. At the time of publication of the MHRA warning, no UK reports of diabetic ketoacidosis in association with semaglutide has been received. However, the theoretical risk of ketoacidosis when changes are made to insulin dose cannot be excluded.
Drug Interactions	Semaglutide delays gastric emptying and has the potential to impact the rate of absorption of concomitantly administered oral medicinal products.

	Thyroxine 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 semaglutide at the same time as levothyroxine. Clinicians should check the Summary of Product Characteristics (SPC) and the current electronic BNF for a full list of potential drug interactions before starting any new medication or when stopping any existing medication.
Alcohol	There is no specific interaction between semaglutide and alcohol, however, for general health reasons it recommended that both men and women should drink no more than 14 units / week and they should also have at least two alcohol-free days during the week.
Pregnancy and Breastfeeding	Women of childbearing potential are recommended to use contraception when treated with semaglutide. Studies in animals have shown reproductive toxicity. There are limited data from the use of semaglutide in pregnant women. Therefore, semaglutide should not be used during pregnancy. If a patient wishes to become pregnant, or pregnancy occurs, semaglutide should be discontinued. Semaglutide should be discontinued at least 2 months before a planned pregnancy due to the long half-life. In lactating rats, semaglutide, salcaprozate sodium and/or its metabolites were excreted in milk. As a risk to a breast-fed child cannot be excluded, Rybelsus should not be used during breast-feeding. The effect of semaglutide on fertility in humans is unknown. Semaglutide did not affect male fertility in rats. In female rats, an increase in oestrous length and a small reduction in number of ovulations were observed at doses associated with maternal body weight loss.
Effects on ability to drive and use machines	Semaglutide 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
Storage Conditions	Store in the original blister package in order to protect from light and moisture. This medicinal product does not require any special temperature storage conditions.

References:-

1. Summary of Product Characteristics for Rybelsus® (Semaglutide), accessed 05/11/2020
2. eBNF, accessed 05/11/2020
3. Drug Safety Update, MHRA, June 2019