

Ozempic and Wegovy

A CLINICAL UNDERSTANDING OF SEMAGLUTIDE

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Diabetes is a worldwide epidemic. By 2050, it is projected that the number of people living with diabetes will more than double, reaching 1.3 billion globally.¹ Type 2 Diabetes Mellitus (T2DM) is a complex metabolic disorder that significantly reduces quality of life and leads to serious health complications.² Due to the increasing prevalence and associated complications of the disease, the need for effective treatment strategies is critical.

One recent therapeutic addition in the management of T2DM is Ozempic, an antidiabetic medicine containing semaglutide, approved by the Therapeutic Goods Administration (TGA) for lowering blood sugar in adults with insufficiently controlled T2DM, as an adjunct to diet and exercise.³ While its primary purpose is to support blood glucose regulation, a side effect of Ozempic is weight loss. In fact, not yet available in Australia, Wegovy is a new brand of semaglutide indicated specifically for the management of obesity, due to the significant impact this active ingredient can have on weight loss.⁴

The demand for weight loss products is high, with the prescription weight-loss drug market now a \$2.3 billion industry.⁵ Viral videos on TikTok and across other media that showcased the rapid weight loss achieved with Ozempic, led to a rapid increase in demand due to 'off-label' prescribing.⁴ This has resulted in global shortages, posing challenges for individuals who rely on this medication for management of T2DM.⁴

What is 'off-label' prescribing?

Off-label prescribing involves prescriptions to treat conditions other than those approved by the TGA. It is a regular occurrence in the Australian healthcare system, particularly for uncommon diseases and conditions or underrepresented patient groups.⁴



KEY HIGHLIGHTS

- Diabetes is expected to affect 1.3 billion people by 2050.
- Semaglutide (Ozempic) is approved for T2DM, however it is also used off-label for weight loss.
- Semaglutide enhances insulin sensitivity, reduces appetite, and delays gastric emptying.
- Semaglutide may lower cardiovascular risks, including heart attacks and strokes.
- Use of semaglutide may promote muscle loss and nutrient deficiencies; monitoring protein, vitamins (B12), and minerals (zinc) is essential.

MECHANISM OF ACTION OF SEMAGLUTIDE

As a glucagon-like-peptide-1 (GLP-1) agonist,⁶ semaglutide improves the efficiency of incretin function.⁷ Incretin acts to suppress gluconeogenesis, inhibit glucagon secretion, and increase insulin sensitivity.⁷ It also delays gastric emptying, therefore reducing appetite and decreasing caloric intake, which can lead to drastic weight reduction.⁸

Semaglutide is available in both oral tablets and subcutaneous injection pens. As a once-daily oral tablet (Rybelsus), it is available in 3 mg, 7 mg, and 14 mg doses.¹⁰ As a pre-filled syringe pen (Ozempic and Wegovy), various dose options are available which are injected subcutaneously once weekly.⁵ It is recommended to start with a lower dose and gradually increase to the target dose.⁵

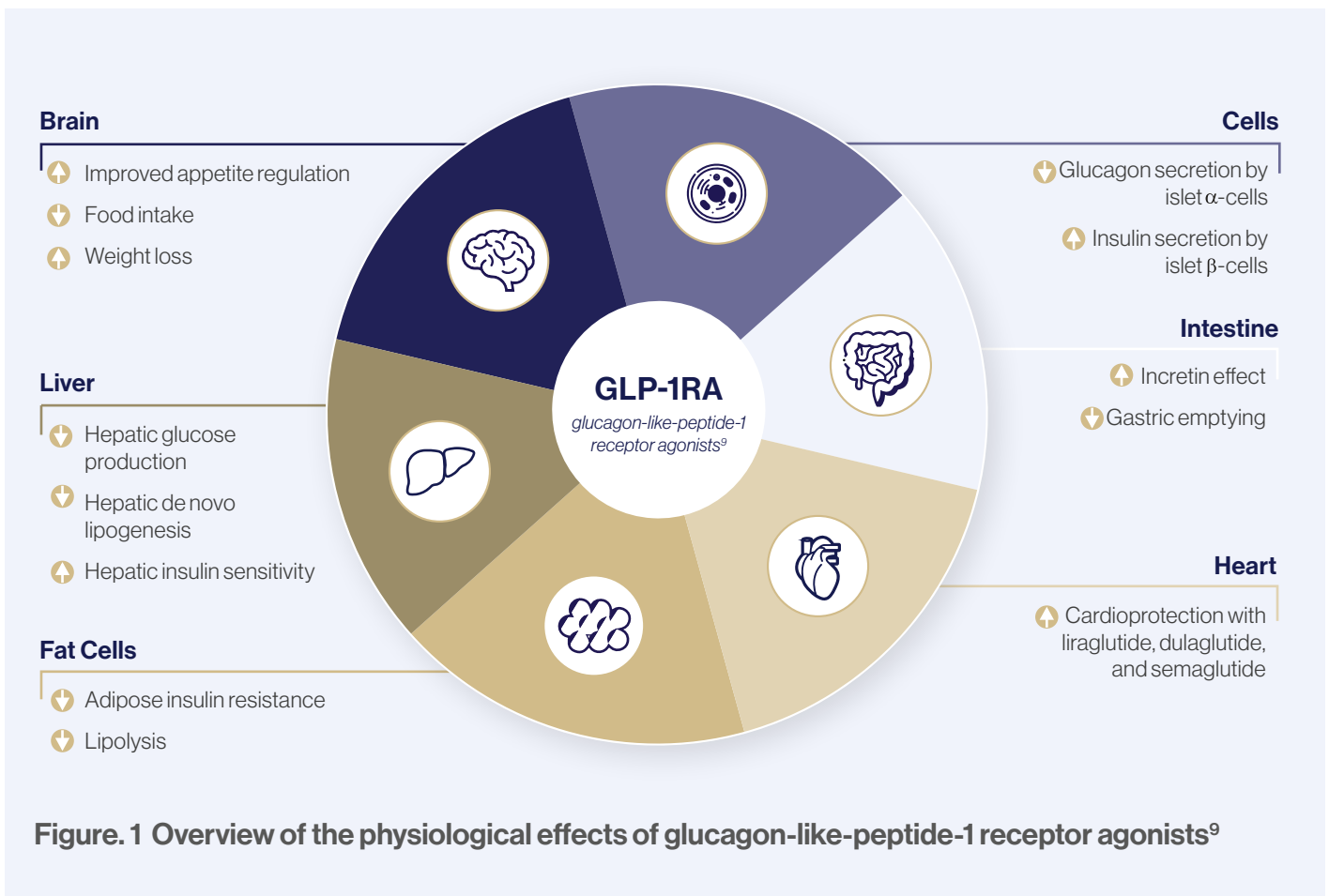


Figure. 1 Overview of the physiological effects of glucagon-like-peptide-1 receptor agonists⁹

CONDITIONS

Type 2 Diabetes Mellitus

Semaglutide supports the management of T2DM by reducing HbA1c levels,^{11,12} in addition to decreasing fasting and post-prandial glucose secretion.¹³ Studies have also shown that usage can lead to positive influences on hepatic beta cell function.¹³

As modifiable lifestyle factors such as obesity, poor diet, physical inactivity, and smoking can contribute to T2DM,¹⁴ dietary and lifestyle factors are recommended as first line treatment.¹⁵

If blood sugar levels remain unregulated, insulin therapy is typically used to further support the treatment of T2DM. The most common side effect for treatment with insulin is hypoglycaemia, with a global study reporting the occurrence of severe hypoglycaemia at 2.5 events per patient with T2DM each year.¹⁶ As semaglutide primarily lowers blood glucose by stimulating glucose-dependent insulin secretion, the risk of hypoglycaemia is low.⁶ A study comparing the use of insulin glargine with semaglutide as an add-on to metformin in patients with T2DM found that semaglutide resulted in fewer hypoglycaemic episodes and greater reductions in HbA1c and weight.¹⁷

Cardiovascular effects

A lack of glycaemic control increases adverse cardiovascular event risk in those with T2DM. Insulin resistance can cause alterations in signalling pathways, specifically in myocardial cells, which increases risk of heart failure, stroke, and myocardial infarction.¹⁸

Studies have demonstrated that semaglutide can reduce the risk of adverse cardiovascular events in patients both with and without diabetes.¹⁸ Semaglutide has also been shown to reduce atherosclerosis by impacting inflammatory pathways and reducing apoptosis in cardiac cells.⁷

Side effects and cautions

The main symptoms of semaglutide toxicity or misuse include gastrointestinal symptoms of nausea, vomiting, diarrhoea, and stomach pain.²⁰ When administered in high doses, semaglutide can cause acute kidney injury, detected through decreased or bloody urine, muscle twitching, and seizures.²¹ Whilst semaglutide can be used alongside insulin and metformin treatment, dosages of these medications should be reduced to decrease risk of hypoglycaemia.²² Acute pancreatitis has been observed with the use of GLP-1 agonists, so caution should be exercised in patients with a history of pancreatitis and symptoms monitored carefully.²³ Patients with a history of diabetic retinopathy should be monitored carefully when treated with semaglutide and insulin, as an increased risk of developing complications has been observed.²³ Semaglutide should not be used during pregnancy or lactation.²³

Clinical implications

Semaglutide is recommended as treatment for diabetics or for extreme weight-related comorbidities. As a health professional, it is important to acknowledge semaglutide usage in patients, and to understand individual intentions behind its usage, being mindful of potential signs of a compromised relationship with food.

When used specifically for weight loss, weight gain is typically seen in a matter of weeks to months once administration is ceased.²⁴ For those who are expected to finish their semaglutide treatment, plans need to be put in place for long-term weight management alongside the natural increase in calories that will occur when the medication is ceased.

It is also important to note that weight reduction is not solely attributed to body fat, it often also involves skeletal muscle. Decreased skeletal muscle mass can have a variety of consequences, such as increased risk for poor glycaemic control, reduced basal metabolic rate and sarcopenia. Therefore, consumption of adequate protein and regular exercise is a crucial focus to support muscle mass and minimise muscle wastage.²⁵

Due to the impact of semaglutide on hunger cues, patients need to be assessed as to whether they are meeting nutritional requirements with a reduced caloric intake.²⁶ In addition to assessing protein intake to prevent muscle wastage, a full dietary review should be made to ensure sufficient intake of vitamins and minerals,²¹ particularly albumin, vitamin B12, and zinc, which have been shown to be impacted following semaglutide administration.²⁵

As side effects of semaglutide can include gastrointestinal symptoms such as vomiting and diarrhoea, ensuring adequate hydration and electrolyte balance is crucial if these symptoms are present.²⁷

Finally, medication reviews are vital for patient welfare and to ensure optimal health. It is important to work with a medical doctor to regularly check HbA1c, fasting glucose, pancreatic enzyme, and kidney function biomarkers to ensure the patient is receiving the appropriate treatment.



SUMMARY

Ozempic and other novel treatment strategies are important to support the medical management of T2DM.

While protecting supply for their primary use will mitigate the health consequences of T2DM and reduce the consequences of off-label prescribing, understanding the broader use and nutritional implications of this medication is crucial.

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