

Latest news: Tirzepatide prefilled pen; remission and cardiorenal benefits; and low-energy diets in primary care

Stay abreast of the latest news that could impact diabetes nursing.

Tirzepatide to be available in prefilled injection pen

Eli Lilly has announced that the Medicines and Healthcare products Regulatory Agency (MHRA) has become the first major regulator to issue marketing authorisation for tirzepatide solution for injection in an alternative KwikPen presentation. It will be available through prescription in Great Britain for two indications:

1. For the treatment of adults with insufficiently controlled type 2 diabetes as an adjunct to diet and exercise:
 - As monotherapy when metformin is considered inappropriate due to intolerance or contraindications.
 - In addition to other medicinal products for the treatment of diabetes.
2. For weight management, including weight loss and weight maintenance, as an adjunct to a reduced-calorie diet and increased physical activity in adults with an initial BMI of:
 - $\geq 30 \text{ kg/m}^2$ (obesity), or
 - $\geq 27 \text{ kg/m}^2$ to $< 30 \text{ kg/m}^2$ (overweight) in the presence of at least one weight-related comorbidity (e.g. hypertension, dyslipidaemia, obstructive sleep apnoea, cardiovascular disease, prediabetes or type 2 diabetes).

Tirzepatide (sold as Mounjaro) is a once-weekly GIP analogue combined with a GLP-1 analogue. It works by activating both GIP and GLP-1 receptors to promote the secretion of incretin hormones that increase the production of insulin and decrease the glucose produced by the liver, lowering blood glucose.

It has previously received marketing authorisation for these indications in different presentations. The Mounjaro KwikPen will, however, deliver four doses, rather than the one dose from the previously approved Mounjaro pen. It is hoped that presenting a month's treatment in one pen will allow for convenient use.

The most common side effects are nausea, diarrhoea, vomiting and constipation. Hypoglycaemia is very common in people with diabetes when used with a sulfonylurea or insulin. Women with obesity or overweight using oral contraceptives should consider also using a barrier method of contraception or switching to a non-oral contraceptive method.

With nearly one in three adults being obese, demand for the drug is expected to be high. When supplies become available in the coming weeks, healthcare professionals are being asked to ensure that all prescribing is within the authorised indications.

Diabetes remission provides lasting cardiorenal benefits

New findings from the landmark Look AHEAD study have revealed that achieving remission from type 2 diabetes through weight loss is associated with large reductions in rates of both chronic kidney disease (CKD) and cardiovascular disease (CVD).

Increasingly, remission from type 2 diabetes is being seen as a goal that many people can attain. While previously associated with bariatric surgery, the Look AHEAD and DiRECT studies

demonstrated that lifestyle interventions can also be effective in achieving remission from diabetes and prediabetes. The impact of remission through such interventions on long-term health outcomes, however, has not been examined.

Look AHEAD was a 12-year, multicentre, randomised control trial that compared the effects of an intensive lifestyle intervention with that of diabetes support and education. Researchers conducted observational *post hoc* analyses of the study data to establish whether achieving remission resulted in a reduction in the incidence of diabetes-related CKD and CVD.

The analytical sample size was 4488 (58% female; mean age, 59 years; mean diabetes duration, 6 years; and mean BMI, 35.8 kg/m^2). Diabetes remission (defined as taking no diabetes medication and an $\text{HbA}_{1c} < 48 \text{ mmol/mol}$) was recorded during at least one follow-up visit in 12.7% of participants. Most remissions were relatively short-lived, with the percentage of participants with remission decreasing to 4% by the eighth year of the study.

Those with any evidence of remission had a 33% lower rate of CKD (HR, 0.67 [95% CI, 0.52–0.87]) and a 40% lower rate of CVD (HR, 0.60 [95% CI, 0.47–0.79]) in adjusted analyses, compared to those without remission. The magnitude of the risk reduction was greatest for those with evidence of longer-term remission.

The authors conclude that these associations may be affected by post-baseline improvements in weight, fitness, HbA_{1c} and LDL-cholesterol. While

this study demonstrates the promise of lifestyle-based remission, they caution that the long-term sustainability of such intensive interventions is unclear and emphasise the need for continued follow-up in remission studies.

The full study findings can be read [here](#).

Type 2 diabetes remission with low-energy diet

A study has added to the growing body of evidence that remission of type 2 diabetes may be achieved with aggressive lifestyle changes. DiRECT-Aus set out to determine if a 12-month intervention, incorporating low-energy total diet replacement (TDR), could induce remission in adults with recently diagnosed type 2 diabetes in an Australian primary care setting.

The open-label, single-arm intervention trial recruited adults aged 20–65 years with type 2 diabetes duration of ≤ 6 years, with HbA_{1c} at entry $\geq 6.5\%$ (≥ 48 mmol/mol), BMI >27.0 kg/m² and who were not treated with insulin. At baseline, there

were equal numbers of males and females, with mean age of 52.5 years, weight of 106.9 kg, BMI of 37.7 kg/m², HbA_{1c} of 7.1% (54 mmol/mol) and type 2 diabetes duration of 2.8 years. Glucose-lowering medications were used by 88%.

Participants ($n=155$) underwent a 13-week TDR (800–950 kcal, depending on BMI), with fortnightly dietitian visits. This was followed by an 8-week structured food reintroduction and 31 weeks of supported weight management. An increase in daily physical activity was also encouraged, with a target of 15 000 steps.

At 12 months, 86 (56%) of participants had achieved type 2 remission (defined as HbA_{1c} $<6.5\%$ [<48 mmol/mol] and off glucose-lowering medications for ≥ 2 months ± 7 days). The number was highest at the end of the TDR phase at 102 (66%), with 99 (64%) and 92 (90%) at 6 and 9 months, respectively.

Across all of the participants, the mean adjusted weight loss after the TDR was 11.2% (95% CI, 10.3–12.1). At 12 months, it was 8.1% (7.2–9.1). The likelihood of

remission was proportional to weight loss, with remission being achieved by 87% of participants who reduced their weight by $>15\%$. The TDR was well tolerated, with only a few serious adverse events that were largely related to hypotension.

Following an intensive lifestyle intervention delivered in primary care, the rate of remission of type 2 diabetes of around one in two participants was similar to the findings of both the DiRECT and DIADEM-I trials, despite being conducted in different countries and across different ethnicities. The investigators conclude that a low-energy TDR is a robust intervention for type 2 diabetes remission, particularly if adopted within 6 years of diagnosis.

The full study findings can be read [here](#). ■

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