

## GLP-1 RAs (Glucagon-like peptide-1 receptor agonists) - Prescribing in Chronic Kidney Disease (CKD) and supporting kidney patient access

The UK Renal Pharmacy Group recommends timely access of GLP-1 RAs to people with CKD (including kidney transplants):

- Reduced kidney function does not appear to affect tolerability or safety of GLP-1 RAs.
- GLP-1 RAs can be prescribed to kidney patients (including kidney transplant) for weight loss, cardiovascular risk reduction and/or type 2 diabetes with minimal risk. Level of risk is likely similar to the general population because GLP-1 RAs are not metabolised by the kidney.
- Standard starting doses of GLP-1 RAs can be used in kidney patients at all levels of kidney function, including end stage kidney disease (ESKD) receiving dialysis and kidney transplant patients. Normal titration schedules can usually be followed.
- There is no evidence that GLP-1 RAs affect tacrolimus or other commonly used immunosuppressants.
- Kidney patients should be considered a priority group for GLP-1 RAs because:
  - Large, randomised control trials demonstrate kidney protection in chronic kidney disease (CKD) patients with diabetes.
  - Obesity accelerates kidney function decline in patients with CKD, irrespective of diabetes status.
  - Advanced CKD and ESKD is associated with high rates of morbidity and mortality and is very expensive to treat.

### Background and rationale

GLP-1 RAs (e.g. semaglutide [Ozempic®, Wegovy®], tirzepatide [Mounjaro, Zepbound®]) are medications used to treat type 2 diabetes and/or obesity, which should be used in combination with diet and increased physical activity. They work by helping to control blood sugars, increasing the feeling of satiety (fullness) and delaying gastric emptying

(how quickly food moves through the stomach). They are similar in action to natural GLP-1 RA, which is produced by the body.

Evidence from large clinical trials (including patients with CKD stage 1-4) indicate GLP-1 RAs have cardiovascular benefit and are kidney protective.<sup>1-5</sup> Despite these benefits, GLP-1 RAs are not commonly prescribed to patients with CKD, and this may, in part, be due to a lack of understanding of their safety in this group.

[Kidney Disease Improving Global Outcomes \(KDIGO\) Clinical Practice Guideline for Diabetes Management in CKD](#) has prioritised the use of GLP-1 RAs in CKD patients with type 2 diabetes since 2022. Following this publication, trials have reported kidney and cardiovascular protective effects of GLP-1 RAs.<sup>5-7</sup>

GLP-1 RA trials in CKD patients without diabetes are awaited – however, pharmacokinetic data support that both Semaglutide and Tirzepatide are effective and can be used with minimal risk in all stages of CKD (including kidney transplants), ESRD and dialysis. There is no evidence that GLP-1 RAs interact with tacrolimus or other immunosuppression.<sup>1-5,7</sup>

In the general population the National Institute of Clinical Excellence (NICE) has approved semaglutide (Wegovy®) and Tirzepatide (Mounjaro/Zepbound®) for weight loss alongside diet and exercise.

The UK Renal Pharmacy Group therefore recommends timely access of GLP-1 RAs to CKD patients with and without diabetes. Further, given the high rates of morbidity and mortality with advanced CKD (and the potential for GLP-1 RAs to delay progression of CKD) the UK Renal Pharmacy Groups recommends that kidney patients are a priority treatment group.

### **Frequently asked questions and practical advice for patients/caregivers:**

#### **Are GLP-1 RAs only for people with diabetes?**

*No, while originally used for people with diabetes they are now also licensed for weight loss and cardiovascular risk reduction. They work in the same way for diabetes and weight loss, but they are usually marketed under different names depending on the indication, and doses for weight loss tend to be slightly higher. Ozempic® is the version of semaglutide used for diabetes whereas Wegovy® is the version used for weight loss. Tirzepatide comes as Mounjaro® and Zepbound®.*

#### **Are GLP-1 RAs safe in chronic kidney disease?**

*Although not currently licenced for use in renal patients in the UK, there is growing evidence to suggest that GLP-1s can improve kidney health and safeguard against cardiovascular complications and are therefore beneficial to renal patients.<sup>2-7</sup> GLP-1 RAs are similar to the*

*natural GLP that the body produces, and they are metabolised in the same way, so people with CKD are not expected to react differently to the general population or have more severe side effects.*

### **Is there a renal function cut off for GLP-1 RAs?**

*No, they can be used at all stages of renal function, including dialysis. They can be dosed and up-titrated as normal. Some of the common side effects may be more problematic in renal patients so it's important that patients discuss with GPs/renal teams before starting treatment so any risks can be mitigated.<sup>3-7</sup>*

### **What are the common side effects?**

*As with all medications there are risks associated with using GLP-1 RAs. Common side effects include nausea, vomiting, diarrhoea and constipation. Some patients find that the side effects are dose specific and experience more/worse side effects at the higher doses. This is particularly important for some patient groups. For example, constipation may affect how well peritoneal dialysis patients are able to dialyse. Constipation can also cause an increase in potassium levels, so it is very important to treat as soon as possible.*

*Patients experiencing vomiting and/or diarrhoea can be at risk of dehydration and for CKD patients this may worsen any residual renal function.*

*There is also a rare but serious side effect of pancreatitis which requires urgent medical treatment. Symptoms of pancreatitis include a sudden severe pain in the abdomen which can radiate to the back.*

*GLP-1 RAs can increase the risk of hypoglycaemia in patients with diabetes so more frequent monitoring of blood glucose is essential.*

*It is very important that patients and carers are aware to inform their GP / medical team if they experience any side effects so they can be treated promptly.*

### **Are there any contra-indications or patients who can't have GLP-1 RAs?**

*Patients with a family or personal history of thyroid cancer should avoid as the clinical trials have shown there is a small increased risk of developing thyroid cancer.*

*Patients with a history of pancreatitis or gallbladder conditions should avoid as pancreatitis is a rare but serious side effect.*

*Patients with proliferative diabetic retinopathy should avoid as a sudden increase in glucose control can worsen retinopathy.*

*Patients with known delayed gastric emptying or gastroparesis should use with caution as GLP-1 RAs will further slow gastric motility. Consider that patients taking these medicines who are undergoing surgeries or procedures with general anaesthesia or deep sedation may have residual gastric contents despite preoperative fasting<sup>9</sup>*

*Pregnant women, those trying to get pregnant or breastfeeding women should avoid.*

### **Will GPs be able to initiate GLP-1 RAs for weight loss in renal patients?**

*While the NHS has recently approved the use of semaglutide and tirzepatide for weight loss the criteria for eligibility is very specific and most renal patients are unlikely to fit the criteria, so currently only eligible people have access weight management medicines under the NHS.*

### **Will patients be able to get semaglutide/tirzepatide from renal clinics?**

*Most renal units will not be able to supply these drugs as they also need to follow the NICE eligibility criteria and most hospital formularies do not currently include these drugs for weight loss in renal patients.*

### **What to do if patients want to obtain from a private weight loss clinic**

*It is very important that patients are aware to let their renal team and GP know if they decide to buy semaglutide/tirzepatide so medical records can be updated, and healthcare providers are aware patients have started on therapy. It is also very important that patients know to contact their GP or renal team if they experience any side effects so they can be signposted towards the appropriate care.*

### **Other things to consider:**

For dialysis patients, rapid weight loss will mean dry weight needs to be reassessed frequently to ensure patients are appropriately dialysed.

A reduction in weight may also mean improvement of blood pressure or diabetes, and may warrant a review of their regular medication.

While patients lose weight in the form of fat, they can also lose lean muscle, so it is very important that treatment is combined with weight-bearing exercises, depending on patients' physical ability to avoid losing muscle mass.

GLP-1 RAs will cause a decrease in appetite, so patients will eat less. It is very important that patients follow a well-balanced diet high in protein to avoid becoming malnourished. Patients should be booked to see a renal dietician if possible, or

signposted towards healthy eating renal specific resources, such as:

<https://www.kidney.org/nutrition>

## **References:**

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