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Clinical Expert Summary

Sitagliptin (Januvia®▼) 25 mg and 50 mg for the improvement of glycaemic control in type 2 diabetes mellitus patients with moderate renal impairment (creatinine clearance [CrCl] ≥ 30 to < 50 ml/min), severe renal impairment (CrCl < 30 ml/min) or with end-stage renal disease (ESRD) requiring haemodialysis or peritoneal dialysis (licence extension).

1. Existing guidelines

The clinical experts highlighted the following guideline:

- National Institute for Health and Clinical Excellence (NICE). Type 2 diabetes: the management of type 2 diabetes. Clinical guideline 87 (2009)[1].

2. Disease prevalence/incidence

It is estimated that approximately 30% of patients with type 2 diabetes mellitus (T2DM) have chronic kidney disease stage 3 (CKD) or worse, i.e. an estimated glomerular filtration rate (eGFR) less than 60 mls per minute.

3. Current treatment options

The clinical experts reported that metformin is the default first line oral hypoglycaemic therapy for patients with T2DM, but that metformin has restrictions in CKD: metformin should not be used in patients with CKD stage 4 (eGFR < 30 ml/min). The clinical experts stated that after meformin, the options are sulphonylurea drugs (but with caution in patients with CKD due to risk of hypoglycaemia, plus weight gain as a side-effect), pioglitazone (recognised side effects include fluid retention, weight gain, congestive cardiac failure and bone fracture, which are all relevant in the elderly CKD population), acarbose (not used to any extent in the UK due to bowel side effects) and insulin (side effects of weight gain and hypoglycaemia, along with issues of patient education, increased self-monitoring etc.). In addition, they noted that GLP-1 injectables currently have limitations according to CKD.

4. Unmet needs

The clinical experts state that until recently, no DPP4 inhibitors were licensed for use in patients with CKD stage 3. They report that the formula used to calculate eGFR (the MDRD equation) is inaccurate in patients with a normal creatinine, and is heavily influenced by age, which meant that many elderly people with T2DM were excluded for treatment with DPP4 inhibitors. This was viewed by experts as an inappropriate restriction, given that this group of patients are at a high risk of hypoglycaemia on sulphonylurea drugs and insulin. The new licence, with a dose restriction of sitagliptin (from 100 mg once daily to 25 mg and 50 mg once daily) means that patients with CKD stage 3 can now be treated with this agent.

5. Knowledge of product in given indication

The clinical experts noted that the use of DPP4 inhibitors in the management of people with T2DM is to be welcomed and will limit the numbers being treated with insulin (with all of its attendant staff and monitoring costs, as well as the increased risk of weight gain and, most importantly, hypoglycaemia). The clinical experts added that sitagliptin was particularly attractive as it has the most extensive safety data and the broadest licensed indication, including all triple oral therapy combinations and use with insulin.

One expert involved in compiling this response declared a personal specific interest in relation to sitagliptin for the indication under consideration.

1 National Institute of Health and Clinical Excellence. Clinical guideline 87. Type 2 diabetes: the management of type 2 diabetes. May 2009. Available at: http://www.nice.org.uk/nicemedia/live/12165/44320/44320.pdf. Accessed Apr 2012.