NHS
Kent and Medway

Position Statement: DPP-4 inhibitors (gliptins) in the management of Type 2 Diabetes

DPP-4 Inhibitors (Gliptins)

Dipeptidyl peptidase-4 inhibitors, DPP-4 inhibitors, (also known as "gliptins") are a class of oral diabetic medications used in the management of type 2 diabetes mellitus (T2DM) in adults. There are currently 5 gliptins licensed in the UK: **alogliptin, linagliptin, sitagliptin, saxagliptin, and vildagliptin.**

Indication

In line with NICE guidelines on the management of type 2 diabetes in adults, NG28, gliptins are indicated in patients with T2DM (and who are not at high cardiovascular disease risk) as monotherapy (if metformin is inappropriate), or in combination with other antidiabetic drugs (including insulin) if existing treatment fails to control HbA1c to below the person's individually agreed threshold.

Notes: alogliptin is not licensed for monotherapy. Gliptins should not be prescribed in conjunction with GLP-1 RAs as they both work on the same pathway.

Clinical Effectiveness

Meta-analyses of gliptins (used as monotherapy) show they all provide similar, modest reduction in HbA1c. Gliptins have no effect on weight or renal outcomes, nor do they improve cardiovascular outcomes.

Preferred Gliptin in Kent and Medway – generic sitagliptin

NG28 recommends that if two drugs in the same class are appropriate for a patient, then the drug with the lowest acquisition cost should be chosen (where all other factors are equal). Currently, **generic sitagliptin is the most cost-effective gliptin**.

Table 1: Current gliptin prices

Gliptin	Strength	September 2024 Drug Tariff (DT) Price
Alogliptin	6.25mg	£26.60 (28)
	12.5mg	£26.60 (28)
	25mg	£26.60 (28)
Sitagliptin	25mg	£1.88 (28)
	50mg	£2.49 (28)
	100mg	£3.08 (28)
Linagliptin	5mg	£33.26 (28)
Vildagliptin	50mg	£28.23 (56)
Saxagliptin	2.5mg	£31.60 (28)
	5mg	£31.60 (28)

Table 2: Formulary statuses of gliptins in Kent and Medway and links to SPCs

DPP-4 inhibitor (gliptin)	Formulary status across Kent and Medway	SPC link
Sitagliptin (generic)	**First line/preferred cost-effective gliptin** Generic sitagliptin is first line for all eligible patients/new initiations. Where existing patients are prescribed a different gliptin, and ongoing prescribing of a gliptin is indicated following diabetes review, switch to generic sitagliptin if appropriate	Click here
Linagliptin	**Second line** Linagliptin is the second line gliptin to be used only after sitagliptin has been tried, or if eGFR <45ml/min/1.73m^2	Click here
Alogliptin (Not licensed as monotherapy)	**Not recommended** Where existing patients are prescribed alogliptin, and ongoing prescribing of a gliptin is indicated following next diabetes review, switch to generic sitagliptin if appropriate	Click here
Saxagliptin	**Not recommended**	Click here
Vildagliptin	**Not recommended**	Click here
Gliptin combination products	**Not recommended**	

Table 3: Recommended gliptin doses for adults above 18 years of age

Gliptin	Recommended Daily dose (maximum):
Alogliptin	25mg once daily
Linagliptin	5mg once daily
Sitagliptin	100mg once daily
Saxagliptin	5mg once daily
Vildagliptin	50mg twice daily. When used with a sulfonylurea, reduce to 50mg once daily (morning)

Review

- Patients should be reviewed against treatment targets (e.g. HbA1c reduction/metabolic benefit), as well as overall diabetes care assessed, to ensure gliptin use is appropriate and to maximise patient outcomes, in line with NG28. Adequate review/audit arrangements should be in place, as with other oral antidiabetic drugs.
- NG28 recommends stopping medicines that have had no impact on glycaemic control or weight, unless there is an additional clinical benefit from continued treatment e.g. cardiovascular or renal protection. If targets have not been met, review the gliptin and optimise therapy for the management of the patient/T2DM, considering alternative therapies in line with NG28 and local guidelines where appropriate e.g. if patients meet criteria for SGLT2i.

Implementing cost-effective prescribing of generic sitagliptin

- **Changing sitagliptin prescribing from brand to generic**: all patients prescribed sitagliptin by brand (Januvia®) should be reviewed and changed to the more cost-effective generic sitagliptin where clinically appropriate.
- **Changing existing patients from other gliptins to generic sitagliptin:** patients can be opportunistically switched, where ongoing prescribing of a gliptin is indicated following a review as per "**Review**" section above. E.g., appropriate switching of linagliptin (e.g. where eGFR >45 mL/min/1.73m^2) and alogliptin to generic sitagliptin.
- **Monitoring:** ensure that patients who are switched have HbA1c rechecked 3 to 6 months after starting sitagliptin.

Renal Impairment

Gliptins have a good safety and tolerability profile in patients with impaired kidney function. Dosing of gliptins is based on renal function; thus, patients' renal function must be known to allow switching to the appropriate dose of sitagliptin. **Table 4** should be used to ensure dosing is appropriate for renal impairment. Renal function should be monitored as part of annual checks required for T2DM.

For patients with an eGFR <45ml/min/1.73m^2, linagliptin may be preferred (hepatically metabolised, only gliptin where no dose adjustment is required in renal impairment). However, sitagliptin is licensed for use in patients with mild, moderate and severe renal impairment with appropriate dose reductions and can also be considered for patients currently on linagliptin with stable eGFR (refer to SPC).

Table 4: Renal Impairment dose adjustments and dose equivalence if changing to generic sitagliptin

Renal function (eGFR ml/min/1.73m^2)	Change from Alogliptin	Change from Linagliptin (only one strength available (5mg)	Change to Sitagliptin (if renal function stable on current gliptin)
>50ml/min/1.73m^2	25mg OD	5mg OD	100mg OD
45-50ml/min/1.73m^2	12.5mg OD	5mg OD	100mg OD
30-44ml/min/1.73m^2	12.5mg OD	5mg OD	50mg OD
15-29ml/min/1.73m^2	6.25mg OD	5mg OD	25mg OD
ESRD including dialysis (<15ml/min/1.73m^2)	6.25mg OD	5mg OD	25mg OD

Note: gliptin SPCs use creatinine clearance (CrCl)/GFR rather than eGFR for dosing; eGFR can be used for gliptins.

Safety & Cautions/Contraindications (see SPCs for further information)

- The adverse effects of the gliptins are broadly similar.
- Saxagliptin and alogliptin: use with caution in patients with heart failure. Saxagliptin: caution in patients at risk of hospitalisation for heart failure. (Sitagliptin and linagliptin have a neutral effect on risk of heart failure).
- The MHRA reported an increased risk of acute pancreatitis for all gliptins.
- Vildagliptin is associated with rare cases of hepatic dysfunction, so requires liver enzyme monitoring and cannot be used in patients with hepatic impairment, unlike the other gliptins.