

## Dipeptidyl Peptidase-4 (DPP-4) inhibitors (Gliptins)

### Introduction

There are currently five DPP-4 enzyme inhibitors ('gliptins') licensed in the UK for the management of type 2 diabetes (T2DM). These are sitagliptin, linagliptin, alogliptin, vildagliptin and saxagliptin.

There are a number of differences between the gliptins including costs, licensed indications, monitoring requirements, interactions and the need for dose adjustment in renal and hepatic impairment.

Robust clinical outcome data for gliptins, particularly around their cardiovascular effects and long-term safety in people with T2DM is limited.

### Indication

- For T2DM as monotherapy for some patients (if metformin inappropriate), or in combination with other antidiabetic drugs (including insulin) if existing treatment fails to control glycated haemoglobin (HbA1c) to below the person's individually agreed threshold
- Co-prescribing a gliptin with a glucagon-like peptide-1 (GLP-1) agonist is not recommended as both work through the same (incretin) pathway
- Note: alogliptin is not licensed for monotherapy

### Mechanism of action

- Inhibits dipeptidylpeptidase-4 to increase insulin secretion and lower glucagon secretion in response to a meal
- Low risk of hypoglycaemia (unless combined with other hypoglycaemic medication) – useful option for elderly patients or in frailty
- **Weight neutral**

### Dosing and titration

- **Sitagliptin (100mg once daily) is the preferred first line gliptin.** Renal dose adjustment required, therefore assessment of renal function is recommended prior to commencing treatment and periodically thereafter. See below for dosage recommendations:
  - **50mg once daily:** eGFR between 30 and 45 mL/min
  - **25mg once daily:** eGFR between 15 and 30 mL/min, or with end-stage renal disease CKD 5 (eGFR less than 15 mL/min), including those requiring haemodialysis or peritoneal dialysis
- Linagliptin (5mg once daily) is second line option after sitagliptin has been tried. No dose adjustment is needed in impaired renal function
- Do not initiate alogliptin, saxagliptin or vildagliptin in new patients who require a gliptin. Renal dose adjustment may be required, further information can be found in [individual products licenses](#)
- Titration of dosing not required with gliptin therapy

- Prescribe generically

### Contraindications

- Diabetic ketoacidosis
- Hepatic impairment: avoid vildagliptin; avoid saxagliptin and alogliptin if severe hepatic impairment
- Heart failure: avoid vildagliptin if severe heart failure and alogliptin if moderate-to-severe heart failure

### Cautions

- Avoid in acute pancreatitis and use with caution in patients with history of pancreatitis
- [Pancreatitis](#) has been reported for all approved gliptins. Discontinue gliptin and other potentially suspect medicines if symptoms of acute pancreatitis occur such as persistent, severe abdominal pain
- There is limited experience with use of gliptins in patients with moderate or severe heart failure therefore use with caution

### Monitoring

No specific monitoring required for sitagliptin and linagliptin.

### MHRA/Safety alerts

[Dipeptidylpeptidase-4 inhibitors: risk of acute pancreatitis](#) (September 2012).

### Noteworthy Interactions ([Individual product license contains full list](#))

To reduce the risk of hypoglycaemia, a lower dose of sulfonylurea or insulin may be considered when used in combination with gliptins.

### Information on adverse effects ([Individual product license contains full list](#))

- Common side effects include gastrointestinal: constipation, vomiting, nausea, diarrhoea, dyspepsia, gastritis, and gastro-oesophageal reflux
- Headache, dizziness, and tremor (common with sitagliptin, saxagliptin, vildagliptin, and alogliptin)
- Modest HbA1c efficacy 7 to 9mmol/mol
- Acute pancreatitis is uncommon: see cautions and counselling
- Hepatic (rare): hepatitis and hepatic failure (with vildagliptin and alogliptin)
- Infections: increased risk with saxagliptin, alogliptin, and vildagliptin

### Sick Day rules

There are no specific requirements for gliptins. Follow general [sick day rules](#) for patients with T2DM.

## Blood Glucose Testing Strip Prescribing

### For patients prescribed metformin/gliptins/Sodium-glucose Cotransporter-2 Inhibitor (SGLT2i) only or in combination

Do not prescribe blood glucose strips for self monitoring unless short-term use advised by a specialist (e.g. when starting treatment with oral or intravenous corticosteroids or to confirm suspected hypoglycaemia). Advise patients can buy meters and blood glucose strips if they wish to.

### Counselling

- The tablets can be taken with or without a meal at any time of the day
- Patients treated with DPP-4 inhibitors should be informed of the characteristic symptoms of acute [pancreatitis](#): persistent, severe abdominal pain (sometimes radiating to the back) and encouraged to report these to their healthcare provider
- Report suspected adverse reactions through the [MHRA Yellow Card Scheme](#)

### References

- [A summary of oral diabetes medications 15<sup>th</sup> Edition June 2022](#) (Last accessed 08/09/2022)
- [BNF online](#) (Last accessed 21/10/2022)
- [Clinical Knowledge Summaries \(CKS\) DPP-4 inhibitors](#) (Last accessed 21/10/2022)
- [Combination therapy with once-weekly glucagon like peptide-1 receptor agonists and dipeptidyl peptidase-4 inhibitors in type 2 diabetes: a case series](#) (Last accessed 21/10/2022)
- [NICE guideline \[NG28\] Type 2 diabetes in adults: management](#) (Last accessed 21/10/2022)
- [SPCs for individual gliptins](#) (Last accessed 21/10/2022)

### Document History

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