

## GLIPTINS (Dipeptidylpeptidase-4 [DPP-4] inhibitors)

The Pan Mersey Area Prescribing Committee recommends the prescribing of  
DPP-4 inhibitors in accordance with  
NG28-Type 2 diabetes in adults: management

GREEN

The current Pan Mersey recommended DPP-4 inhibitors are alogliptin (Vipidia<sup>®</sup>), linagliptin (Trajenta<sup>®</sup>), saxagliptin (Onglyza<sup>®</sup>) and sitagliptin (Januvia<sup>®</sup>) in accordance with their licensed indications

- > NICE guideline 28 [Type 2 diabetes in adults: management](#) recommends considering a DPP-4 inhibitor in the following situations:
- > as dual therapy with metformin if HbA1c > 58mmol/mol (7.5%) despite patient taking maximum tolerated dose of metformin or modified release metformin
- > as triple therapy with metformin and a sulfonylurea if HbA1c > 58mmol/ml (7.5%) despite dual therapy with metformin and a DPP-4 inhibitor.
- > as monotherapy if HbA1c > 48mmol/ml (6.5%) despite lifestyle interventions and metformin is contraindicated or not tolerated.
- > as dual therapy with either pioglitazone or a sulfonylurea if HbA1c > 58mmol/mol (7.5%) despite monotherapy
- > [Algorithm for blood glucose lowering therapy in adults with type 2 diabetes](#)

**Note:** Patients who are not eligible for treatment under this statement may be considered on an individual basis where their GP or consultant believes exceptional circumstances exist that warrant deviation from the rule of this policy. In this situation, follow locally defined processes.

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### Effectiveness

DPP-4 inhibitors act by increasing insulin secretion and lowering glucagon secretion.<sup>6</sup> NICE states that recommendations that cover DPP-4 inhibitors refer to the group of drugs at a class level.<sup>1</sup> NICE note that there is limited evidence in relation to the long-term effects (at least 5 years) of blood glucose lowering therapies, particularly newer agents, in terms of efficacy and adverse events (for example, cardiovascular outcomes).<sup>1</sup>

### Cost <sup>7</sup>

Alogliptin	£346.75
Linagliptin	£433.57
Saxagliptin	£411.93
Sitagliptin	£433.57

NICE states that if 2 drugs in the same class are appropriate, the option with the lowest acquisition cost should be chosen.<sup>1</sup>

### Safety

NICE note the lack of long-term safety data.

Discontinue if symptoms of acute pancreatitis occur (persistent, severe abdominal pain).<sup>6</sup> The MHRA issued an alert in 2012 [Dipeptidylpeptidase-4 inhibitors: risk of acute pancreatitis](#)

For full prescribing information, consult the Summary of Product Characteristics (SPC) for the individual drug at [Electronic Medicines Compendium](#)

### Patient factors

**Renal impairment:** see Prescribing Information box

**Hepatic impairment:**

- > Alogliptin, no dose adjustment necessary in mild to moderate, not been studied in severe therefore not recommended
- > Linagliptin, pharmacokinetic studies suggest no dose adjustment but clinical experience is lacking.
- > Saxagliptin, caution in patients with moderate, not recommended in severe.
- > Sitagliptin, no dose adjustment necessary in mild to moderate, not been studied in severe, care should be exercised.

### Prescribing information

DPP-4 inhibitors are recommended in accordance with NICE and their licensed indications.<sup>1,2,3,4,5</sup>

	With MF	With MF and SU	With Insulin and MF	Monotherapy	With PG	With SU	With insulin
Alogliptin	Yes	Yes *	Yes	No	Yes	Yes	Yes
Linagliptin	Yes	Yes	Yes	Yes	No	No	Yes
Saxagliptin	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Sitagliptin	Yes	Yes	Yes	Yes	Yes	Yes	Yes

MF = metformin SU = sulfonylurea PG = pioglitazone

\* SPC states alogliptin has not been formally studied in combination with metformin and a sulphonylurea <sup>5</sup>

### Dosage Reductions in renal impairment <sup>2,3,4,5,6</sup>

	Standard Dose	eGFR 30-50 ml/min/1.73m <sup>2</sup>	eGFR 15-29 ml/min/1.73m <sup>2</sup>	eGFR < 15 ml/min/1.73m <sup>2</sup>
Alogliptin	25mg	Reduce dose to 12.5mg	Reduce dose to 6.25mg	Reduce dose to 6.25mg
Linagliptin	5mg	No dose change	No dose change	No dose change
Saxagliptin	5mg	Reduce dose to 2.5mg	Reduce dose to 2.5mg	Not recommended
Sitagliptin	100mg	Reduce dose to 50mg	Reduce dose to 25mg	Reduce dose to 25mg

### Implementation notes

Vildagliptin is not currently recommended due to the requirement to regularly monitor liver function tests.<sup>8</sup>

## SUPPORTING INFORMATION

### References

1. National Institute for Health and Clinical Excellence. Type 2 diabetes in adults: management of type 2 diabetes. NICE guideline 28. December 2015. Accessed 04/12/18 [Type 2 diabetes in adults: management](#)
2. Summary of Product Characteristics. Januvia : Accessed 11/12/18 at <http://www.medicines.org.uk/emc/>
3. Summary of Product Characteristics. Trajenta: Accessed 04/12/18 at <https://www.medicines.org.uk/emc/>
4. Summary of Product Characteristics. Onglyza: Accessed 11/12/18 at <http://www.medicines.org.uk/emc/>
5. Summary of Product Characteristics. Vipidia: Accessed 04/12/18 at <http://www.medicines.org.uk/emc/>
6. British National Formulary. Accessed 11/12/18 [Medicines Complete - BNF](#)
7. Drug Tariff. Accessed 11/12/18 [NHS Electronic Drug Tariff](#)
8. Summary of Product Characteristics, Galvus: Accessed 04/12/18 at <http://www.medicines.org.uk/emc/>