This policy statement is approved by Halton, Knowsley, Liverpool, Southport and Formby, South Sefton, St Helens, Warrington and West Lancashire CCGs

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PAN MERSEY APC

PAN MERSEY AREA PRESCRIBING COMMITTEE
PRESCRIBING POLICY STATEMENT
REF: PS88 FINAL
APC BOARD DATE: 27 JUL 2016

NHS
Pan Mersey
Area Prescribing Committee

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

GREEN

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

The current Pan Mersey recommended DPP-4 inhibitors are alogliptin (Vipidia®▼), linagliptin (Trajenta®), saxagliptin (Onglyza®) and sitagliptin (Januvia®) 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 $HbA_{1c} \geq$ 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 $HbA_{1c} \geq$ 58mmol/ml (7.5%) despite dual therapy with metformin and a sulfonylurea
- as monotherapy if $HbA_{1c} \geq$ 48mmol/ml (6.5%) despite lifestyle interventions and metformin is contraindicated or not tolerated.
- as dual therapy with either pioglitazone or a sulfonylurea if $HbA_{1c} \geq$ 58mmol/mol (7.5%) despite monotherapy

Note: Patients who are not eligible for treatment under this policy 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. If appropriate an exceptional funding request will be required following the usual locally defined process.

GLIPTINS (Dipeptidylpeptidase-4 (DPP-4) inhibitors)

EFFECTIVENESS

DPP-4 inhibitors act by increasing insulin secretion and lowering glucagon secretion.[6] NICE states that recommendations that cover DPP-4 inhibitors refer to the group of drugs at a class level.[1]

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).[1]

SAFETY

NICE note the lack of long-term safety data.

Discontinue if symptoms of acute pancreatitis occur (persistent, severe abdominal pain).[6] 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

COST per annum [6]

Alogliptin	£345.80
Linagliptin	£432.38
Saxagliptin	£410.80
Sitagliptin	£432.38

NICE states that if 2 drugs in the same class are appropriate, the option with the lowest acquisition cost should be chosen.[1]

PATIENT FACTORS [2,3,4,5,7]

Renal impairment: see Prescribing Information box

Hepatic impairment:

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

PRESCRIBING INFORMATION

DPP-4 inhibitors are recommended in accordance with NICE and their licensed indications.[1,2,3,4,5,]

	With MF	With MF & SU	With Insulin & MF	Monotherapy	With PG	With SU	With insulin
Alogliptin	Yes	Yes, but see below *	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 *Combination licensed, but SPC states that the safety and efficacy of alogliptin when used as triple therapy with metformin and a sulfonylurea have not been fully established[7]

Dosage Reductions in renal impairment[2,3,4,5,6]

	Standard Dose	eGFR 30-50 ml/min/1.73m^2	eGFR 15-29 ml/min/1.73m^2	eGFR < 15 ml/min/1.73m^2
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.[7]

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 25/5/16 Type 2 diabetes in adults: management
2. Summary of Product Characteristics. Januvia : Accessed 14/4/16 at http://www.medicines.org.uk/emc/
3. Summary of Product Characteristics. Trajenta: Accessed 14/4/16 at http://www.medicines.org.uk/emc/
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5. Summary of Product Characteristics. Vipidia: Accessed 14/4/16 at http://www.medicines.org.uk/emc/
6. British National Formulary. Accessed 14/4/16. Medicines Complete - BNF
7. Summary of Product Characteristics, Galvus: Accessed 14/4/16 at http://www.medicines.org.uk/emc/