NHS
Herts Valleys
Clinical Commissioning Group

NHS
East and North Hertfordshire
Clinical Commissioning Group

HERTFORDSHIRE MEDICINES MANAGEMENT COMMITTEE (HMMC)
ALOGLIPTIN FOR TYPE 2 DIABETES MELLITUS (T2DM)
RECOMMENDED FOR ROUTINE COMMISSIONING within license

Name: generic (trade)	What it is	Indication	Date decision last revised	Decision status	NICE / SMC Guidance
Alogliptin (Vipidia®)	Dipeptidyl peptidase 4 (DPP-4) inhibitor	Combination treatment with other glucose lowering products, including insulin, in adults with T2DM	June 2016 Previous decision April 2014	Final	NICE – ESNM20[1] SMC - Accepted for restricted use- dual therapy.

HMMC Recommendation: RECOMMENDED within license for prescribing in Hertfordshire.

New Patients

Alogliptin is recommended within license for new patients requiring gliptin therapy, unless the patient has impaired renal function. In these circumstances, linagliptin is the agent of choice as no dosage adjustment is required.

Existing Patients

Alogliptin may be considered as an option for patients on an alternative DPP-4 inhibitor within specific inclusion, exclusion and follow-up criteria as agreed by individual CCGs. HVCCG Position Statement available. ENHCCG do not currently support systematic switching from alternative gliptins to alogliptin.

Main issues considered by HMMC:

- Alogliptin is currently the least costly DPP-4 inhibitor (HMMC 2016).
- NICE guidance (NG28) for type 2 diabetes mellitus did not distinguish between the gliptins. There are no head to head trials confirming that one gliptin is more effective/safer than another (HMMC 2016).
- Alogliptin, although licensed for triple therapy, was not specifically trialled in combination with metformin and sulphonylureas, the most commonly prescribed triple therapy combination (HMMC 2014).

EFFICACY

- 5 randomised controlled trials of alogliptin as either dual or triple therapy over 26 weeks, and one trial of triple therapy over 52 weeks demonstrated a reduction in HbA1c of approximately 5.5mmol/mol (0.5%) over placebo[1].
- A randomised double blind trial over 104 weeks (ENDURE) studied metformin+alogliptin vs metformin+glipizide. The European Medicines Agency did not consider the primary endpoint of non inferiority had been met due to low glipizide dose and low starting HbA1c[2].

SAFETY

- In a pooled analysis of 13 trials, the most common adverse reaction was pruritus[5].
- Other common side effects reported in trials are upper respiratory tract infections, nasopharyngitis, headache, abdominal pain, gastrointestinal reflux and rash[5].
- Caution in patients who have known risk factors for heart failure. Discontinue in patients presenting with symptoms of heart failure
- Use of DPP-4 inhibitors has been associated with a risk of developing acute pancreatitis

COST

Drug	Usual dosage	Cost per year (excluding VAT)
Alogliptin	25mg od	£347
Sitagliptin	100mg od	£434
Linagliptin	5mg od	£434
Saxagliptin	5mg od	£412
Vildagliptin	50mg bd	£435

Costs taken from Drug Tariff, July 2016

PATIENT FACTORS

- None identified.

This HMMC recommendation is based upon the evidence available at the time of publication. The recommendation will be reviewed upon request in the light of new evidence becoming available.

Assessment against Ethical Framework

Evidence of Clinical Effectiveness and Safety

- Alogliptin has been studied in a number of add-on dual therapy and triple therapy trials, and has been shown to reduce HbA1c by approximately 5.5mmol/mol (0.5%) more than placebo.
- Alogliptin has been shown not to increase the risk of cardiovascular events in a study with median duration 18 months.
- Alogliptin has not been trialled specifically as add on triple therapy with metformin and a sulphonylurea.
- A double blind trial in 5380 diabetic patients with high cardiovascular risk showed non inferiority of alogliptin to placebo for the primary composite endpoint of death from cardiovascular causes, non-fatal myocardial infarction or non-fatal stroke[4].
- An FDA safety review has found that type 2 diabetes medicines containing saxagliptin and alogliptin may increase the risk of heart failure, particularly in patients who already have heart or kidney disease.In the UK, the MHRA have collated yellow card reports of heart failure (some fatal) for all the gliptins except alogliptin, although alogliptin has been available for a much shorter time.

Cost of treatment and cost effectiveness

- Alogliptin is currently the least expensive of the gliptins:
- The SMC considered that the economic case for alogliptin presented by the company had been demonstrated.

The needs of the population

The effect on the population receiving DPP-4 inhibitors is considered low. NICE recommends that drug treatment should be individualised and DPP-4 inhibitors are included in the drug treatment algorithm.

The needs of the community

The effect on the local health economy is moderate. The use of alogliptin instead of more costly gliptins may release funding for other treatments within the local health economies.

Equity

No impact anticipated.

Policy Drivers

SMC have approved alogliptin for restricted use in dual therapy. NICE guidance (NG28) for type 2 diabetes mellitus does not distinguish between the gliptins and there are no head to head trials confirming that one gliptin is more effective/safer than another. PrescQIPP recommends alogliptin as the least costly DPP-4 inhibitor. A number of other CCGs have approved alogliptin as a treatment option.

Implementability

No issues identified for new patients.
Switch protocol will be required for switching patients.

References

1. Evidence summary new medicine 20: Type 2 diabetes: alogliptin, 21 May 2013
http://www.nice.org.uk/mpc/evidencesummariesnewmedicines/ESNM20.jsp
2. Scottish Medicines Consortium: Alogliptin, 10 January 2014
http://www.scottishmedicines.org.uk/files/advice/alogliptin_Vipidia_FINAL_January_2014_Revised_16.01.14_FOR_WEBSITE.pdf
3. NICE Medicines Evidence Commentary: Type 2 diabetes: study finds no benefit from alogliptin on cardiovascular outcomes in people with recent acute coronary syndrome, October 2013
http://www.evidence.nhs.uk/document?ci=http%3A%2F%2Farms.evidence.nhs.uk%2Fresources%2FHub%2F1029671&q=Alogliptin&ReturnUrl=%2Fsearch%3Fq%3DAlogliptin
4. White WB, Cannon CP, Heller SR, et al. (2013) Alogliptin after acute coronary syndrome in patients with type 2 diabetes N Engl J Med DOI: 10.1056/NEJMoa1305889
5. eMC Summary of Product Characteristics, accessed 19.03.2014
http://www.medicines.org.uk/emc/medicine/28513/SPC/Vipidia+6.25mg%2c+12.5mg%2c+25mg+film-coated+tablets/
6. eMC Dictionary of Medicines and Devices Browser http://dmd.medicines.org.uk/DesktopDefault.aspx?AMPP=23636411000001100&toc=nofloat
7. FDA Safety Review April 2016 http://www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm494252.htm

Produced by Herts Valleys Pharmacy and Medicines Optimisation Team in consultation with E&NH Pharmacy and Medicines Optimisation Team on behalf of HMMC