

HERTFORDSHIRE MEDICINES MANAGEMENT COMMITTEE (HMMC)

LIXISENATIDE (GLP-1 MIMETIC) FOR TYPE 2 DIABETES

RESTRICTED RECOMMENDATION

Name: generic (trade)	What it is	Indication	Date decision last revised	Decision status	NICE / SMC Guidance
Lixisenatide (Lyxumia®)	Glucagon-like peptide-1 mimetic agent (GLP-1)	Treatment of Type 2 diabetes-to increase insulin secretion, suppress glucagon secretion and slow gastric emptying	September 2013	Final	NICE – No recommendation. SMC – accepted for restricted use

HMMC Recommendation:

Recommended in the same place in therapy as other GLP-1 mimetic agents. (Other GLP-1 mimetic agents: Exenatide 10mcg bd; exenatide 2mg weekly; liraglutide 1.2mg od)

Position of GLP-1 mimetics in line with NICE:

1. As DUAL therapy (in combination with one oral treatment) in patients:

- Who are intolerant of or have contra-indications to all oral therapies that would be used as add-on treatments (add-on therapies may be: metformin or a sulfonylurea or thiazolidinediones (pioglitazone) or dipeptidyl peptidase-4 (DPP-4) inhibitors (gliptins).
- Treatment with lixisenatide in a dual therapy regimen should only be continued if a 1% reduction in HbA1c is obtained 6 months after treatment is initiated.

2. As TRIPLE therapy in combination with metformin and a sulfonylurea, or metformin and thiazolidinedione, (triple therapy) for adult patients with type 2 diabetes mellitus **only when control of blood glucose remains or becomes inadequate (HbA1c ≥ 7.5% [59 mmol/mol], or other higher level agreed with the individual), **and the person has:****

- a body mass index (BMI) $\geq 35 \text{ kg/m}^2$ in those of European descent (with appropriate adjustment for other ethnic groups) and specific psychological or medical problems associated with high body weight, **or**
- a BMI $< 35 \text{ kg/m}^2$, but **therapy with insulin would have significant occupational implications or weight loss would benefit other significant obesity-related co-morbidities.**
- Treatment with Lixisenatide in a triple therapy regimen **should only be continued** if there has been **at least** a reduction of 1% [11 mmol/mol] in HbA1c **and** a weight loss of 3% of initial body weight at 6 months.

3. The use of lixisenatide added to basal insulin, with or without oral glucose-lowering medicinal products is supported in accordance with the locally agreed initiation and discontinuation criteria for GLP-1 mimetic agents. **Initiation must be under specialist supervision only.**

N.B. The SPC for lixisenatide states that lixisenatide should not be given in combination with basal insulin and a sulfonylurea due to increased risk of hypoglycaemia. Use in this circumstance is therefore not recommended and sits outside of shared care arrangements.

Patients who do not achieve the outcomes with lixisenatide may be switched to another GLP-1 mimetic agent.

Rationale for recommendation

EFFICACY

- Results from trials suggest that the addition of lixisenatide to existing therapy reduces HbA1c by 0.6 to 1.0%. This reduction was approx 0.3 to 0.5% greater than placebo.
- Beneficial effects were also seen in other parameters e.g. 2-h postprandial glucose; % patients reaching target HbA1c.
- Lixisenatide was found to be non-inferior to exenatide bd in a 24-week comparative study.

SAFETY

- No long term safety data.
- Main side effect is nausea, vomiting and diarrhoea.
- Hypoglycaemia occurred when lixisenatide was combined with sulphonylurea and basal insulin.

COST

Lixisenatide is cheaper than currently available GLP-1 mimetics by about 15-20%.

PATIENT FACTORS

- Once a day s/c injection as opposed to twice a day with exenatide.

Key points to note:

- Fully published trial evidence to support the use of lixisenatide in triple therapy and dual therapy (***in combination with a sulphonylurea***) is currently lacking. However, the licensed indication of the drug is wide and seems to allow for all drug combinations.
- A network meta-analysis undertaken as part of TA 203 (liraglutide) showed that the mean difference (95% CI) in **HbA1c versus placebo** for other GLP-1 mimetics approved by NICE were as follows: weekly prolonged-release exenatide (-1.15% [-1.31 to -1.00]), liraglutide 1.2 mg (-1.01% [-1.18 to -0.85]) and exenatide twice daily (-0.82% [-0.94 to -0.70])⁵

1) Clinical Effectiveness

See information above

2) Cost of Treatment and Cost effectiveness

Studies evaluating cost-effectiveness were not identified during the literature search.

Drug & Dosage	30 day cost/per patient	Annual Cost per patient
Lixisenatide, (Lyxumia®) 20micrograms/day	£58.01	£696.12
Liraglutide, (Victoza®) 1.2mg/day	£78.48	£941.76
Exenatide (Byetta®) 5 or 10 micrograms twice daily	£68.24	£818.88
Exenatide (Bydureon®) 2mg once weekly	£73.36	£880.32

N.B. Doses are for general comparison and do not imply therapeutic equivalence

3) Need of the population

The need for healthcare is low as two other GLP-1 mimetics are available and there are a number of other treatment options for patients.

4) Needs of the community

The needs of the community may be considered high as the incidence of diabetes is increasing nationally, but it is less expensive than current treatment options and therefore needs are low.

5) Equity

No issues identified

6) Policy drivers

NICE Clinical Guideline 87, NICE TAGs 203 and 248

7) Implement ability

No issues identified.

Comments received from:

Endocrinologists at WHHT, E&NHT and Barnet and Chase Farm Hospitals NHS Trust.

References

1. http://www.gpref.bedfordshire.nhs.uk/media/98458/Lixisenatide_for_Type_2_DM_final_JPC_bulletin_184.pdf. Appendix 3 of this document gives the details of the GET-GOAL trials
2. Implementing key therapeutic topics: 3, Type 2 diabetes (2012) MeReC Bulletin 22(5)
3. National Institute for Health and Clinical Excellence (2012) Type 2 diabetes: does intensive blood glucose control improve renal outcomes? Medicines Evidence Commentary 21
4. National Institute for Health and Clinical Excellence (2010) Liraglutide for the treatment of type 2 diabetes mellitus. NICE technology appraisal guidance 203
5. National Institute for Health and Clinical Excellence (2012) Extended (prolonged release) exenatide for the treatment of type 2 diabetes mellitus. NICE technology appraisal guidance 248.
5. National Institute for Health and Clinical Excellence (2009): Type 2 Diabetes – Newer agents (partial update of CG 66). NICE clinical guideline CG87.

**Produced by Hertfordshire Pharmacy and Medicines Optimisation Team
Hertfordshire, Bedfordshire and Luton Commissioning Support
NHS Central Eastern Commissioning Support Unit**

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.