HERTFORDSHIRE MEDICINES MANAGEMENT COMMITTEE

NHS Hertfordshire

GLUCAGON-LIKE PEPTIDE-1 (GLP-1) ANALOGUES (EXENATIDE OR LIRAGLUTIDE) ADDED TO PATIENTS ALREADY ON INSULIN WHO HAVE POORLY CONTROLLED TYPE 2 DIABETES - RECOMMENDED FOR RESTRICTED USE JULY 2012

HMMC RECOMMENDATION:

The addition of a GLP-1 analogue to patients already on insulin who have poorly controlled type 2 diabetes is recommended for restricted use in the following circumstances:

- **Patients fulfil the criteria for initiation of treatment as set out in the shared care guidelines (SCG). In particular (but see SCG for full details - http://www.hertfordshire.nhs.uk/pharmacy/index.php/local-decisions-about-medicines/6-hmmc):**
  - patient has seen a dietitian and demonstrated an attempt to lose weight over previous 6 months
  - obese with a BMI > 35 kg/m^2
  - poor blood glucose control with a HbA1c ≥ 69 mmol/mol
  - willing to switch from insulin analogue to human insulin product (unless they are in a group who should not switch – see link below)

- **Patients fulfil the criteria for continuation of treatment as set out in the SCG. In particular (but see SCG for full details):**

  - Stopping criteria at 6 months

⇒ Treatment with a GLP-1 analogue should be stopped if the HbA1c has not fallen by at least 5mmol/mol and there is no weight loss or change in insulin dose.

  - Continuation criteria at 12 months

⇒ Improvement in HbA1c ≥ 11mmol/mol AND weight reduction ≥ 3% OR
⇒ Improvement in HbA1c ≥ 11mmol/mol AND insulin dose reduction ≥ 50% OR
⇒ Improvement in HbA1c ≥ 5mmol/mol AND weight reduction ≥ 10%

  - Stopping criteria beyond 12 months

⇒ GLP-1 analogues will be withdrawn if the HbA1c, weight or insulin dose deteriorates to a point where the patient would not have met the 12 month continuation criteria.

AND

- **Primary care prescribers may take on prescribing responsibility for combination therapy under the arrangements set out within the SCG.**
- **All existing patients on this combination are referred to the Hertfordshire Community NHS Trust Community Diabetes Service for review for continuation of treatment in line with the criteria in the SCG.**
- All patients requiring this combination are seen in the Hertfordshire Community Diabetes Service and followed up by this service.
- An audit by specialists of patients on this combination to be submitted to the HMMC by Feb 2013.

IN ADDITION

- Patients with type 2 diabetes, who require insulin, will be initiated on human insulin, in line with the locally agreed criteria (see separate document – http://www.hertfordshire.nhs.uk/pharmacy/index.php/local-decisions-about-medicines/6-hmmc).

The addition of insulin to patients on GLP-1 analogues has not been considered by HMMC, is NOT approved for use in Hertfordshire and is not covered by the SCG.

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Assessment against Ethical Framework

EFFICACY	SAFETY
• Small RCT in patients with type 2 diabetes demonstrated a reduced HbA1c of 0.69% and weight of 2.7kg for insulin + exenatide therapy compared to insulin + placebo at 30 weeks. • Surrogate endpoints only have been reported. • Long term efficacy of combination is not known.	• Combination therapy may be associated with: higher rates of discontinuation, hypoglycaemia and gastrointestinal side effects. • Long term safety of combination therapy is not known.
COST	**PATIENT FACTORS**
• Additional cost of 1year's treatment with GLP-1 analogues is approximately £1,000. • No cost-effectiveness analysis of combination therapy available. • There are potential cost savings if combination therapy results in insulin dose reduction and/or the stopping of oral hypoglycaemic drugs.	

Evidence of Clinical Effectiveness

- RCT in patients with type 2 diabetes (mean BMI 33-34 kg/m^2 & HbA1c 8.3-8.5%) has shown that adding exenatide to insulin glargine resulted in the following statistically significant differences compared to placebo at 30 weeks:
  - HbA1c reduction of 0.69%
  - Weight loss of 2.7kg
- The Association of British Clinical Diabetologists (ABCD) undertook a nationwide audit of the use of exenatide in clinical practice and reported mean reductions from baseline in HbA1c, weight and insulin dose in patients treated with insulin and exenatide (median follow-up of 34 weeks).
- Safety - combination treatment may be associated with: higher rates of discontinuation, hypoglycaemia and gastrointestinal side effects.
- Surrogate endpoints (eg HbA1c and weight reduction) only have been reported. Data has not been reported for patient orientated outcomes (macrovascular or microvascular).
- Long term efficacy/safety of combination is not known.

Cost of treatment and Cost Effectiveness

- No cost-effectiveness analysis available.
- Cost of 1year's treatment with GLP-1 analogues is approximately £1,000.
- There are potential cost savings if insulin dose can be reduced and oral hypoglycaemic drugs are stopped.
- Additional cost per year for combination therapy for Herts population has been estimated at approximately £100,000.
- Savings from other area have been identified to try to ensure that the use of combination therapy is cost neutral.

The Needs of the population

- The needs of the population appear to be low as this is a relatively small group of diabetic patients who were started on insulin before GLP-1 analogues were a treatment option.

The Needs of the community

- If combination therapy was widely used this would create a cost pressure which may have an impact on the local health economy which already has to identify savings.

Equity

- No impact anticipated.

Policy Drivers

- The management of type 2 diabetes is guided by NICE. This combination has not been assessed by NICE.

Implementability

- GP practices will need to identify all existing patients on this combination and refer to the Hertfordshire Community Diabetes Service for review for continuation of treatment in line with the criteria in the SCG.
- New patients are eligible for treatment in accordance with the initiation and continuation criteria in the SCG.

References

- John B. Buse et al, Use of Twice-Daily Exenatide in Basal Insulin–Treated Patients With Type 2 Diabetes, Ann Intern Med. 2011;154:103-112.
- REJ Ry der et al, The Association of British Clinical Diabetologists (ABCD) nationwide exenatide audit, Practical Diabetes Int 2010; 27(8): 352–357
- K. Y. Thong et al, Safety, efficacy and tolerability of exenatide in combination with insulin in the Association of British Clinical Diabetologists nationwide exenatide audit, Diabetes, Obesity and Metabolism 2011
- NICE Technology Appraisal Diabetes (type 2) – liraglutide http://guidance.nice.org.uk/TA203
- NICE Clinical Guidelines Type 2 Diabetes - newer agents http://guidance.nice.org.uk/CG87
- NPC Therapeutics, other therapeutics, Obesity - Key slides http://www.npc.nhs.uk/therapeutics/other/obesity/index.php