

HERTFORDSHIRE MEDICINES MANAGEMENT COMMITTEE (HMMC)

November 2008

Exenatide (Byetta[®])

RECOMMENDED IN LINE WITH FOLLOWING CRITERIA

Inclusion criteria:

Patients aged between 40 years to 70 years who fit the following criteria

1. Obese patients (**BMI \geq 30kg/m²**) who failed triple therapy at maximally tolerated doses (metformin+sulphonylurea+Glitazone) **AND HbA1c \geq 8.4%**
 - who would otherwise need insulin therapy. In these, patients, the addition of Exenatide will necessitate the withdrawal of Glitazone, as the latter is not currently licensed with Exenatide.
2. Obese patients (**BMI \geq 30kg/m²**) who failed maximal dose of dual therapy (Metformin+Sulphonylurea, Metformin+Glitazone or Sulphonylurea+Glitazone) **AND**
 - **with HbA1c \geq 8.4% and**
 - in whom add-on therapy of a drug in the third category is contraindicated or not tolerated and who would otherwise be considered for insulin therapy

Exclusion Criteria

- Patients older than 70 years; BMI \leq 30kg/m²; HbA1c \leq 8.4%.
- Severe renal impairment (creatinine clearance < 30ml/min)
- Diabetic gastropathy with recurrent vomiting
- Gastro-intestinal disease with delayed gastric emptying and/or recurrent vomiting.
- Post myocardial infarction (insulin preferred) unless insulin therapy declined.
- Heart failure, pulmonary hypertension and liver failure (no safety data)
- History of pancreatitis
- Gall stones or heavy alcohol intake (risk of pancreatitis)

Criteria for stopping treatment:

- 1- Drug intolerance
- 2- **If a beneficial metabolic effect has not been obtained, defined less than 1% improvement in HbA1c after 6 months.**
- 3- Patient's choice
- 4- Permanent occurrence of any of the exclusion criteria.
- 5- Need for Insulin therapy or oral drug treatment – gliptin or glitazone. **Exenatide is not licensed as add-on therapy with insulin, glitazone or gliptin.**

ADVICE:

Initiation of treatment should be undertaken by specialists.

(Careful patient selection is necessary to minimise risk of pancreatitis). All patients should be on the hospital specialist managed database and outcomes to be recorded on this database.

Management by GPs: Under Shared-care with specialists.

REVIEW:

The results of the use of widespread use of exenatide will be reviewed in November 2009 together with final NICE guideline on new therapies.

The Drug

Exenatide is a glucagon-like peptide-1 (GLP-1) agonist administered by subcutaneous (SC) injection. It stimulates glucose-dependent insulin secretion/glucagon suppression and delays gastric emptying, thus lowering both fasting and post-prandial glycaemia and improving metabolic control (HbA_{1c}).

Exenatide remains a black triangle drug; any adverse effects must be reported. Information should also be submitted to your local endocrinologists for entry onto a national database.

Outcomes of the Pilot Study

The pilot was intended for 50 patients. To date 38 patients have entered the pilot. Of these, 3 patients had BMI <30kg/m² or not reported, 3 were too early for analysis.

Of the 34 evaluable patients, 5 withdrew because of side-effects (weight gain (1); acute illness and hospitalisation (1); sickness and gallstones (1); no response after 6 months (1) abdominal pain and nausea (1).

The results of the remaining 29 patients showed that, exenatide, added after triple therapy and prior to insulin:

- Reduces 5% or more weight in many patients who continue taking the treatment for 6 months, ***the greatest weight reduction achieved in patients with highest baseline BMI.***
- Reduces HBA1c by 1% or more in many patients – the highest reduction being in patients with highest baseline HBA1c.
- There is no correlation between weight loss and reduction in HBA1c.
- Side effects of nausea (50% patients), vomiting (18% of patients), diarrhoea, burping and bloating, reduced appetite – all occurred in 10% or more of patients.
- Compared to a pre-existing cohort of patients treated with insulin and pioglitazone, exenatide treatment achieved similar reduction in HBA1c and 5% weight loss compared to >5 weight gain in the insulin/pioglitazone cohort.

Cost and estimated Impact to the NHS

Drug	Usual daily dose range	Approx. annual cost (Drug Tariff Dec 08)
Metformin	1000-2000mg	£22.88 - £45.76
Metformin S/R	500mg od – 2g in divided doses	£41.06 - £166.40
Gliclazide	80-320mg	£13.91 - £55.64
Gliclazide SR	30mg – 120mg	£40.04 - £159.12
Glimepiride	1-4mg	£25.87 - £72.02
Glipizide	5-20mg	£16.38 - £65.52
Pioglitazone	15-45mg	£295.23 - £480.48
Sitagliptin	100mg	£432.38
Insulin glargine	See below	£253.50
Biphasic insulin aspart	See below	£191.30
Biphasic isophane insulin	See below	£130.52
Exenatide	20mcg	£887.12

Costs for insulin are calculated on cartridge costs, assuming the patient is using 50 units daily of short acting insulin or 25 units daily of longer acting insulin.

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