

EXENATIDE (BYETTA®) IN TYPE 2 DIABETES

SHARED CARE CRITERIA

Patients will have been stabilised, receiving a therapeutic dose of EXENATIDE allowed for common adverse events and side effects to have occurred before referral to the GP. A minimum period of 1 month stabilisation is necessary prior to sharing care.

RESPONSIBILITIES

Consultant

1. Send a standard letter (giving patient pilot number) to GP requesting shared care for this patient.
2. Initiate treatment and prescribe the first 1 month treatment.
3. Clinical and laboratory supervision (as per proforma) of patient by routine clinic follow-up.
4. Advise GP on review, duration and discontinuation of treatment where necessary.
5. To discuss with patient the risks versus the benefits of the treatment.
6. Evaluation of any adverse effects reported by GP or patient.
7. Ensure that back-up advice is available at all times.

General Practitioner

1. Monitoring patient's overall health and well being.
2. Report any adverse events reported by the patient to consultant and CSM where appropriate.
3. Prescribe maintenance exenatide therapy as described above.
4. To return a copy of the standard letter to the consultant and Primary Care Trust accepting or declining shared care.

Primary Care Trust

1. To provide manage the audit process by ensuring that a copy of the letter to GP is sent to Rasila.shah@herts-pcts.nhs.uk giving patient i.d. and pilot number.
2. To support GPs in making the decision whether or not to accept clinical responsibility for prescribing.
3. To support trusts in resolving issues that may arise as a result of shared care.

LICENSED INDICATIONS (relevant to this Shared Care Guideline)

For the treatment of Type 2 diabetes mellitus in combination with metformin and/or sulphonylureas in patients who have not achieved adequate glycaemic control on maximally tolerated doses of these oral therapies.

DOSE AND ADMINISTRATION

Starting dose 5ug twice a day. Maximum dose 10ug twice a day

Inclusion criteria:

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

- Obese patients (BMI \geq 30kg/m²) who failed maximal dose of dual therapy (Metformin+Sulphonylurea, Metformin+Glitazone or Sulphonylurea+Glitazone)
 - i. with HbA1c above 8.4% and
 - ii. in whom add-on therapy of a drug in the third category is contraindicated or not tolerated and
 - iii. they would otherwise be considered for insulin therapy.
- Obese patients (BMI \geq 30kg/m²) who failed triple therapy (metformin+sulphonylurea+Glitazone)
 - with HbA1c between 8.4 and 10% who would otherwise need insulin therapy.
 - In these, patients, the addition of Exenatide will necessitate the withdrawal of Glitazone, as the later is not currently licensed with Exenatide

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- Professional drivers where insulin therapy may lead to withdrawal of their license.

Exclusion Criteria

- Patients older than 70 years (trial population); BMI < 30kg/m²; HbA1c < 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- Treatment failure (defined as failure to improve glycaemic control with less than 1% improvement in HbA1c after 6 months of maximum-dose therapy)
- 3- Patient's choice
- 4- Permanent occurrence of any of the exclusion criteria.
- 5- Failure to show significant improvement defined as a drop in HbA1c of 1% after 6 months.
- 6- Need for Insulin therapy or glitazone or gliptin. Exenatide is not licensed to be given with insulin, glitazone or gliptin.

Initiation, dosing and treatment monitoring (hospital-based):

- Assessment of patient's eligibility for treatment with Byetta will be undertaken by a consultant diabetologist in line with above criteria.
- Treatment should be initiated by a consultant diabetologist in the hospital at a starting dose of 5µg sc twice daily 60 minutes before meals for at least one month in order to improve tolerability.
- The dose can be increased to a maximum of dose of 10µg sc twice daily to further improve glycaemic control subject to absence of side effects or intolerance.
- Technical aspects of Byetta injection and training will be provided by the Diabetes Specialist Nurses in the secondary care and supervision of care and dose adjustment of Byetta and other concomitant diabetic therapies should be the responsibility of the Diabetes Team in the hospital.
- Comprehensive assessment at baseline and follow-up to be undertaken on the enclosed proforma.
- Decision to introduce exenatide therapy should be clearly justified and communicated to patient's GP in line with inclusion criteria.
- Progress will be monitored in the specialist diabetes clinic in the hospital every 3 months or more frequently if necessary.
- The outcome of each review should be communicated to the GP.

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ADVERSE EFFECTS (+ see BNF)

Body system/adverse reaction terms	Frequency of occurrence	
	Common	Very common
Reactions		
Metabolism and nutrition disorders		
Hypoglycaemia (with metformin and a sulphonylurea)**		x
Hypoglycaemia (with a sulphonylurea)		x
Decreased appetite	x	
Nervous system disorders		
Headache**	x	
Dizziness	x	
Gastrointestinal disorders		
Nausea		x
Vomiting		x
Diarrhoea		x
Dyspepsia	x	
Abdominal pain	x	
Gastroesophageal reflux disease	x	
Abdominal distension	x	
Skin and subcutaneous tissue disorders		
Hyperhidrosis**	x	
General disorders and administrative site conditions		
Feeling jittery	x	
Asthenia**	x	

Adverse Drug Reactions reported post-marketing

Immune system disorders: Anaphylactic reaction, very rarely.

Metabolism and nutritional disorders: Dehydration, generally associated with nausea, vomiting and/or diarrhoea, some reports associated with elevation of serum creatinine.

Nervous system disorders: Dysgeusia, somnolence.

Gastro-intestinal disorders: Eructation, constipation, flatulence. Pancreatitis, cases have been reported.

Skin and subcutaneous tissue disorders: Macular rash, papular rash, pruritis, urticaria, angioneurotic oedema.

CONTRAINDICATIONS

Hypersensitivity to the active substance or to any of the excipients. Byetta should not be used in patients with type 1 diabetes mellitus or for the treatment of diabetic ketoacidosis and is not recommended for use in patients with end-stage renal disease (creatinine clearance < 30ml/min), severe renal impairment or severe gastrointestinal disease. Byetta should not be used in patients with type 2 diabetes who require insulin therapy due to beta-cell failure. Intravenous or intramuscular injection of Byetta is not recommended.⁵

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COST

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.

Exenatide is cheaper than adding insulin to glitazones. Compared to insulin alone, exenatide is more expensive, unless dose of insulin exceed about 70 units of analogue insulin (insulin glargine).

CONTACT NUMBERS

East & North Hertfordshire NHS Trust	West Hertfordshire NHS Trust
Dr. Ken Darzy QEII hospital Dr. Peter Winocour QEII hospital Dr. Felicity Kaplan Lister hospital Dr. Lez Borthwick Lister hospital	Dr Colin Johnson Hemel Hampstead hospital Dr Chantal Kong Hemel Hampstead hospital Dr Arla Ogilvie Watford general hospital Dr Michael Clements Watford general hospital Dr Julia Ostberg Watford general hospital
Out of Hours Contact number: Through switchboard	Out of Hours contact number: Through switchboard

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