

Bath Clinical Area Partnership
Prescribing and Therapeutics Committee

Exenatide ▼ (Byetta®) Prescribing / Pathway

Traffic Light Status (TLS) – ‘amber without shared care’
Off label use (i.e in combination with insulin) or outside NICE CG 87 - TLS Red

Decision to use Exenatide

- Exenatide has to be initiated by a consultant and is classed as ‘amber without shared care’ (from February 2009) by BCAP PTC.
- The GP / diabetic specialist nurses will consult NICE guidance and discuss potential patients with consultants for suitability for exenatide before considering insulin therapy in Type 2 diabetic patients.
- NICE 2009 CG87 – Consider where BMI >35kg/m² (in people of European descent) and there are problems associated with high weight or where BMI < 35kg/m² but occupational considerations make insulin unacceptable or weight loss would benefit another co morbidity if HbA1c ≥7.5% after trial of metformin and sulphonylurea
- Licensed for use with metformin or sulphonylurea only (out of license in combination with glitazones and with insulin)
- Patient to be seen by consultant prior to commencing exenatide.
- Exenatide is not licensed with insulin therapy; though recently it has proved to be effective. If the patient is thought suitable to commence insulin with exenatide this has to be decided by the consultant, and the patient informed that the drug is not licensed for use with insulin **(on going prescribing to remain within Secondary Care).**

Obtaining supplies (NB exenatide is a fridge item)

- Email , fax consultant and/or telephone the consultants secretary with patient details, RUH number, GP, patient address and telephone number and which surgery the exenatide is to be delivered to.
- Initial prescription 1 x 5mcg pen, Then 1 x 10mcg pen
- If no side effects give 3 x 10 mcg pens
- The RUH pharmacy (01225 825869) will contact patient when delivering to GP surgery.
- Most surgeries accept deliveries but Widbrook (Trowbridge) do not and the patient will either have to collect from RUH or arrange community prescription with consultant to be dispensed from local pharmacy.

Diabetes Specialist Nurse Initial visit

- Instruction in safe injection technique, blood glucose monitoring, hypoglycaemia symptoms and treatment.
- May need to reduce total dose of sulphonylurea / insulin by 50% to reduce risk of hypoglycaemia
- Arrange prescription and repeat for pen needles and sharps box with GP
- Exenatide to be injected twice a day, within the hour before breakfast and evening meal - leaving at least 6 hours between injections. If experiencing nausea changing the injection timing maybe an option (i.e. injecting 15minutes before a meal)
- Starting dose 5micrograms exenatide twice daily for one month.
- Exenatide information pack to be given (Further packs available from Lilly Rep)
- Discuss driving and informing DVLA and insurance company (Give patient info letter).
- Discuss risks of pancreatitis including relative risk, symptoms and importance of stopping exenatide if occurs
- Give DSN contact details and advise of allowing at least 7 days to obtain supplies
- Complete audit form

DNS follow up - After 7-10 days

- Telephone contact to assess control.
- Increase sulphonylurea if blood glucose levels elevated Inform GP of dose changes to sulphonylureas
- Check side effects and if satisfactory arrange for progression to 10 microgram strength pen when completed 5microgram pen.

DNS follow up - One month (Discretion of DNS)

- DNS appointment - complete audit form as above and patient satisfaction scale.

DNS follow up -Two months

- Telephone to assess effectiveness of 10mcgs and arrange new prescription (3x10mcg) if tolerated.
- Discuss need for repeat HbA1c after three months on 10mcg and give form to patient to have taken 2 weeks before next appt.

DNS follow up - Three months (on 10mcg)

- Appointment to complete audit form as above with patient satisfaction scale and review HbA1C result.
- Discuss with consultant if doubts about efficacy.
- Discontinue at this stage if no improvement in HbA1c and no weight loss
- Contact GP with regard to taking on the prescribing of exenatide for the next 3 months until consultant review.

Consultant follow up- Six month (on 10mcg)

- Appointment to decide if treatment effective (HbA1c fall of $\geq 1\%$ and weight loss of $\geq 3\%$ at 6 months)
- Decide whether to continue with exenatide
- Inform GP of decision
- Complete audit form.

Consultant follow up - One year

- Appointment to decide if treatment effective (HbA1c reduction and weight loss sustained)
- Decide whether to continue with exenatide and frequency of subsequent FU
- Inform GP of decision
- Complete audit form.

Other factors to consider with exenatide

- Problems with indigestion consider timing of the injection as above.
- Discontinue if persistent nausea, vomiting or decrease to 5mcgs this has been effective for some patients.
- **Stop immediately if pancreatitis suspected**

Contact numbers for RUH & PCT Diabetic Specialist Nurses:

Trowbridge: 01225766161

Chippenham: 01249 456483

Bath: 01225 824173 / 825976

CLINICAL INFORMATION

Licensed indication

Exenatide is a novel injectable (subcutaneous) antidiabetic agent indicated for 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

Introduction

Exenatide is an incretin mimetic that exhibits several antihyperglycaemic actions of glucagon-like peptide-1 (GLP-1). The main effects are:

- Exenatide increases, on a glucose-dependent basis, the secretion of insulin from pancreatic beta cells. As blood glucose concentrations decrease, insulin secretion subsides. In trials when exenatide was used in combination with metformin alone, no increase in the incidence of hypoglycaemia was observed over that of placebo in combination with metformin.
- Exenatide also suppresses glucagon secretion, which is known to be inappropriately elevated in Type 2 diabetes. Lower glucagon concentrations lead to decreased hepatic glucose output. However, exenatide does not impair the normal glucagon response and other hormone responses to hypoglycaemia.

Contra-indications and cautions

- Exenatide **should not be used** in patients with type 1 diabetes mellitus or for the treatment of diabetic ketoacidosis.
- Exenatide is **not recommended for use in patients with end-stage renal disease or severe renal impairment (creatinine clearance <30ml/min)** or severe gastrointestinal disease.

Adverse effects

Include: nausea, vomiting, diarrhoea and hypoglycemia (if used in combination with a sulphonylurea or metiglinides – considering reducing doses of these drugs)

There are reports of an increased risk of **pancreatitis** with exenatide and patients should be warned of the characteristic symptoms of this and to seek medical help in this situation.

Exenatide should be discontinued immediately if a patient develops pancreatitis.

Effect on renal function- Reported events of altered renal function, including increased serum creatinine, renal impairment, worsened chronic renal failure and acute renal failure, sometimes requiring haemodialysis. Some of these events occurred in patients experiencing events that may affect hydration, including nausea, vomiting, and/or diarrhoea and/or receiving pharmacological agents known to affect renal function/hydration status.

Effect on gastric emptying - See below

Drug interactions

- The effect of exenatide to slow gastric emptying may reduce the extent and rate of absorption of orally administered medicinal products. Exenatide should be used with caution in patients receiving oral medicinal products that require rapid gastro-intestinal absorption and medicinal products with a narrow therapeutic ratio.
- Patients receiving orally administered medicinal products of either a **narrow therapeutic ratio** or that require careful clinical monitoring should be followed closely. If such medicinal products are to be administered with food, they should be taken with a meal when exenatide is not administered. Oral medicinal products that are dependent on threshold concentrations for efficacy, such as **contraceptives and antibiotics**, should be taken at least 1 hour before exenatide injection.
- **Gastroresistant formulations** containing substances sensitive for degradation in the stomach, such as proton pump inhibitors, should be taken at least 1 hour before or more than 4 hours after exenatide injection.
- **Digoxin:** No clinically relevant effects were noted on the maximum blood concentrations obtained or overall patient drug exposure, although there was a 2 hour delay in reaching the maximum concentration when administered 30 minutes after exenatide. It is however advisable to monitor digoxin concs in patients considered to be at increased risk of digoxin toxicity.

- Although not considered clinically significant, changes in lipid profiles may occur with concomitant use of exenatide and **statins**. Monitor lipid profiles regularly if taking statins.
- **Warfarin**: Increased INR has been reported during concomitant use of warfarin & exenatide. INR should be closely monitored during initiation & dose increase of exenatide therapy in patients on warfarin and/or coumarol derivatives.

Monitoring

- Unlike insulin, daily blood glucose monitoring is not routinely required for exenatide. However, blood glucose monitoring is necessary for patients initiating exenatide who are also taking sulphonylureas where a dose adjustment of the sulphonylurea may be necessary. In addition, it is considered appropriate for all patients initiating exenatide to monitor their blood glucose on a daily basis for the first 2 months as a measure of efficacy of a new treatment. Monitoring of HbA1c on a regular basis is necessary to assess continuing efficacy of treatment.

Pregnancy and lactation

- Exenatide **should not** be used in women who are pregnant or breast-feeding as there is insufficient information for use in these groups.

Cost

5 microgram / dose prefilled pen (60 doses) = £68.24

10 micrograms / dose prefilled pen (60 doses) = £68.24

Annual cost at a dose of 10micrograms twice a day is approximately £830 per patient

References

- [Byetta 5 micrograms solution for injection, prefilled pen. Byetta 10 micrograms solution for injection, prefilled pen. - Summary of Product Characteristics \(SPC\)](#)
- [medman.org > MTRAC > MTRAC Recommendations > Products \(A-E\)](#)
- [Drug Safety Update: Volume 2 Issue 8, March 2009 : MHRA](#)
- [CG87 Type 2 diabetes - newer agents: short guideline](#) May 2009
- [CG66 Diabetes - type 2 \(update\): full guideline](#) May 2008