SHARED CARE GUIDELINE

Homerton University Hospital NHS Foundation Trust

City and Hackney Teaching Primary Care Trust

EXENATIDE
TYPE 2 DIABETES MELLITUS

INTRODUCTION – INDICATION and LICENSING

Exenatide is an incretin mimetic structurally similarly to GLP-1. It is indicated for treatment of Type 2 diabetes mellitus in combination with metformin and/or sulphonylureas in patients aged 18 years and over who have not achieved adequate glycemic control on maximally tolerated doses of these oral therapies.

When exenatide is added to metformin therapy, the existing dosage of metformin can be continued as no increased risk of hypoglycemia is anticipated with such combination therapy. When added to sulphonylurea therapy, a reduction in the dose of the sulphonylurea may be considered to reduce the risk of hypoglycemia.

Exenatide can be initiated in primary or secondary care. Primary care providers who lack experience can consult the diabetes outreach team at Hackney Diabetes Center at 0208 550 5920 to undertake the initiation/ or request support for the initiation of Exenatide according to the following criteria:

1. As an alternative to insulin for the treatment of Type 2 diabetes:
    a. In patients who are unable to achieve adequate glycemic control (defined as HbA1c ≥ 9%) on a maximally tolerated regimen of metformin and with/ or without a sulphonylurea.
    AND
    b. Where the patient has a **body mass index of > 35kg/m2**

2. All patients are assessed after 6 to 9 months treatment with exenatide and treatment only to be continued if they have achieved a **weight loss of ≥ 3kg and a percentage reduction in HbA1c of ≥ 1.0%** (An example of 1.0% reduction in HbA1c of 9% reduced to 8%)

Patients who **fail** to achieve a 3kg weight loss and a reduction in HbA1c of at least 1.0% after 6 to 9 months should stop exenatide and be initiated on an alternative treatment e.g. insulin.

Patients who do achieve a weight loss of 3kg and a reduction in HbA1c of 1.0% after 6 to 9 months may continue with exenatide which can be prescribed by the GP under this shared care guideline.

Restricted use: The Joint formulary and Medicines Management Group has **approved the off license use of Exenatide WITH insulin** in carefully selected patients supervised by secondary care and /or the diabetes outreach team at Hackney Diabetes Center.

DOSE AND ADMINISTRATION AND STORAGE

- Exenatide is administered by subcutaneous injection (SC) into the abdomen, thigh or upper arm using a prefilled injection pen
- The recommended initial dosage is 5 micrograms twice daily, 60 minutes before the two main meals of the day, approximately 6 hours or more apart. **It should not be given after a meal**.
- Based on clinical response, the dosage of exenatide may be increased to a target dose of 10 micrograms twice daily one month after treatment initiation.
- Dose adjustment of a sulphonylurea is required when exenatide is added therefore a temporary increase in blood glucose monitoring may be required during dose adjustment only, due to increased likelihood of hypoglycemia
- NB exenatide is not licensed with a glitazones
- Storage:
    - Patients can keep the Exenatide prefilled pen at a temperature anywhere from 2 degrees C to 25 degrees C after first use
    - Until first use, Exenatide must continue to be stored in a refrigerator between 2 degrees C and 8 degrees C
    - Exenatide pens should be protected from light and never frozen

SHARED CARE GUIDELINE

CAUTIONS

(Conservative dose escalation required as limited clinical experience exists)

- Patients over 70 years old
- Moderate renal failure (GFR 30-50)

MONITORING STANDARDS, CONTRAINDICATIONS AND SIDE EFFECTS, DRUG INTERACTIONS

The following standards have been agreed for the monitoring of Exenatide

Pre-treatment

- HbA1c, weight and renal function

Minimum Monitoring

- HbA1c every 3 months on continuation
- weight at 3 and 6 months and every 6 months thereafter *

* Patients who fail to achieve a 2.5kg weight loss and a reduction in HbA1c of at least 1.0% after 6 months should stop exenatide, and be initiated on alternative treatment e.g. insulin, by hospital diabetes team

Contraindications

- Type 1 diabetes mellitus
- Stage 4 or 5 chronic kidney disease
- Severe gastrointestinal disease
- Treatment of diabetic ketoacidosis
- Under 18 years of age
- Pregnancy or during breast feeding
- Hypersensitivity to ingredients
- Intravenous or intramuscular injection of exenatide is not recommended

Caution

(Conservative dose escalation required as limited clinical experience exists)

- Patients over 70 years old
- Moderate renal impairment (GFR 30-50)

Drug interactions

- Proton pump inhibitors should be taken at least 1 hour before or more than 4 hours after Exenatide SC injection
- Increased INR has been reported during concomitant use of warfarin. INR should be closely monitored during initiation and dose increase of Exenatide therapy in patients on warfarin and/ or coumarol derivatives

EVENTS AND ACTION

Adverse effect	Symptoms/signs	Actions
Acute pancreatitis	Persistent and severe abdominal pain	Stop Exenatide if pancreatitis suspected. Seek advice from specialist immediately
Gastro-intestinal disorders	Nausea, vomiting, dyspepsia- which may lead to dehydration	Most episodes of nausea are mild to moderate and occur in a dose-dependent fashion. Gradual dose escalation important. With continued therapy, the frequency and severity decreases in most patients who initially experience nausea
Worsening of renal function/ acute renal failure	Nausea, vomiting, pruritis, confusion, increased serum creatinine, hyperkalaemia	Stop Exenatide and any concomitant nephrotoxic drugs e.g. NSAIDS, ACE inhibitors, and Angiotensin 2 receptor blockers. Seek advice from specialist immediately
Hypoglycaemia	Shaking, & trembling, hunger, palpitations, confusion	Reduction in the dose of sulphonylurea should be considered for patients on sulphonylurea treatment

SHARED CARE GUIDELINE

REMEMBER if unsure at any point: Contact the various Specialists and or Specialist Nurse/ Nurse Practitioner at Hackney Diabetes Center (020 8510 5920)

Share care guideline: is a document which provides information allowing patients to be managed safely by primary care, secondary care and across the interface. It assumes a partnership and an agreement between a hospital specialist, GP and the patient and also sets out responsibility for each party. The intention to shared care should be explained to the patient and accepted by them. Intrinsic in the shared care agreement is that the prescribing doctor should be appropriately supported by a system of communication and cooperation in the management of patients. The doctor who prescribes the medicine has the clinical responsibility for the drug and the consequence of its use.

Responsibility of clinician initiating Exenatide

1. Ensure that the patient/carer is an informed recipient in therapy
2. Ensure that patients understand their treatment regimen and any monitoring or follow up that is required (using advocacy if appropriate)
3. Ensure baseline investigations are appropriate before commencing treatment
4. Exenatide can be initiated in primary or secondary care. Primary care providers who lack experience can consult the diabetes outreach team at Hackney Diabetes Center at 0208 550 5920 to undertake the initiation/ or request support for the initiation of Exenatide
5. Ensure that a clear assessment of weight loss and HbA1c is undertaken every 6 to 9 months.
    - Patients who **fail** to achieve a 3kg weight loss and a reduction in HbA1c of at least 1.0% after 6 to 9 months should stop exenatide and be initiated on an alternative treatment e.g. insulin
    - Patients who **do achieve** a weight loss of 3kg and a reduction in HbA1c of 1.0% after 6 to 9 months may continue with exenatide
6. Undertake all dose increments of exenatide
7. Clinical and laboratory supervision of the patient by blood monitoring and routine clinic follow-up on a regular basis
8. Monitor patient's overall health and well-being
9. Report ant adverse events to the CHM where appropriate
10. Pancreatitis:
    a. Stop likely cases of pancreatitis
    b. Refer borderline cases to secondary care
    c. Report incidence of pancreatitis on MHRA yellow card

Responsibility of PCT

1. To provide feedback to trusts via Trust Medicines Committee
2. To support GPs to make the decision whether or not to accept clinical responsibility for prescribing
3. To develop and revise shared care guidelines
4. To support trusts in resolving issues that may arise

Patient responsibility

1. Report any adverse effects to their GP and/or specialist
2. Ensure they have a clear understanding of their treatment
3. Report any changes in disease symptoms to GP and/ or specialist
4. Alert GP and/or specialist of any changes of circumstances which could affect management of disease e.g. plans for pregnancy

References

1. Exenatide (Byetta ® 5 micrograms & 10 micrograms solution for injection, prefilled pen) Eli Lilly and Company Limited, Summary of product Characteristics (date of revision March 24, 2009). Last accessed April 26, 2009. http://emc.medicines.org.uk/medicine/19245