SHARED CARE GUIDELINE

Homerton University Hospital NHS Foundation Trust

City and Hackney Teaching Primary Care Trust

LIRAGLUTIDE
TYPE 2 DIABETES MELLITUS

INTRODUCTION – INDICATION and LICENSING

Liraglutide is a stable analogue of GLP-1. It is indicated for treatment of Type 2 diabetes mellitus in combination with metformin and/or a sulphonylurea OR in combination with metformin and a thiazolidinedione in patients aged 18 years and over who have not achieved adequate glycaemic control on maximally tolerated doses of these oral therapies.

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

Liraglutide 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 liraglutide according to the following criteria:

1. As an **alternative to insulin** for the treatment of Type 2 diabetes:
   a. In **triple therapy regimen** in patients who are unable to achieve adequate glycaemic control (defined as HbA1c ≥ 7.5%) on a maximally tolerated regimen of metformin + a sulphonylurea or metformin + pioglitazone.
   b. In **dual therapy regimen** (with metformin or a sulphonylurea) in patients who are intolerant of either metformin **or** a sulphonylurea, or treatment with metformin **or** a sulphonylurea is contraindicated, **and**
      the person is intolerant of pioglitazone **and** dipeptidyl peptidase-4 (DPP-4) inhibitors, or treatment with pioglitazone **and** DPP-4 inhibitors is contraindicated

   AND where the patient has a
   c. **body mass index of > 35kg/m^2** in those of European descent (with appropriate adjustment for other ethnic groups) and specific psychological or medical problems associated with high body weight,
   OR
   d. **body mass index of < 35.0 kg/m^2**, and therapy with insulin would have significant occupational implications or weight loss would benefit other significant obesity-related co-morbidities.

2. All patients are assessed after **6 to 9 months treatment** with liraglutide and treatment only to be continued if they have achieved:
   - **weight loss of** ≥ 3% of initial body weight {an example of 3% weight reduction: weight of 80kg reduced to 77.6kg} **AND/ OR a percentage reduction in HbA1c of ≥ 1%** {an example of 1% reduction in HbA1c: HbA1c of 8% reduced to 7%} for TRIPLE THERAPY REGIMEN

   OR
   - **a percentage reduction in HbA1c of ≥ 1%** {an example of 1% reduction in HbA1c: HbA1c of 8% reduced to 7%} for DUAL THERAPY REGIMEN

   Patients who do **not lose at least 3%** of initial body weight and / or a reduction in HbA1c of at least 1% after 6 to 9 months (depending on the regimen – as above) should cease liraglutide, and be initiated alternative treatment e.g. insulin, by the hospital diabetes team.

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

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DOSE AND ADMINISTRATION AND STORAGE

- Liraglutide is administered by subcutaneous injection (SC) into the abdomen, thigh, or upper arm using a prefilled injection pen.
- The recommended initial dosage is 0.6 milligram once daily.
- After at least a fortnight, the dose should be increased to 1.2 mg. Most patients who respond at all, do so with the 1.2mg dose. Local experience suggests that increasing the dose further to 1.8mg is rarely needed.
- Daily doses higher than 1.8 mg are not recommended

Dose adjustment with combination treatment

- Liraglutide can be added to existing metformin or to a combination of metformin and thiazolidinedione therapy. The current dose of metformin and thiazolidinedione can be continued unchanged
- Liraglutide can be added to existing sulphonylurea or to a combination of metformin and sulphonylurea therapy. When liraglutide is added to sulphonylurea therapy, a **reduction** in the dose of sulphonylurea should be considered to reduce the risk of hypoglycaemia
- Self-monitoring of blood glucose is not needed in order to adjust the dose of liraglutide. However, when initiating treatment with liraglutide in combination with a sulphonylurea, blood glucose self-monitoring may become necessary to adjust the dose of the sulphonylurea

Storage

- Store in a refrigerator (2°C - 8°C).
- Do not freeze.
- Store away from the freezer compartment.
- *After first use*: Store below 30°C or store in a refrigerator (2°C - 8°C). Do not freeze.
- Keep the cap on the pen in order to protect from light.

CAUTIONS & CONTRAINDICATIONS

- Liraglutide should not be used in patients with type 1 diabetes mellitus or for the treatment of diabetic ketoacidosis.
- There is limited experience in patients with inflammatory bowel disease and diabetic gastroparesis and liraglutide is therefore **not recommended** in these patients. The use of liraglutide is associated with transient gastrointestinal adverse reactions, including nausea, vomiting and diarrhoea.
- Use of other GLP-1 analogues has been associated with the risk of pancreatitis. There have been few reported events of acute pancreatitis. If pancreatitis is suspected, liraglutide and other potentially suspect medicinal products should be discontinued.
- Thyroid adverse events, including increased blood calcitonin, goitre and thyroid neoplasm have been reported in clinical trials in particular in patients with pre-existing thyroid disease (see section 4.8).
- Patients receiving liraglutide in combination with a sulphonylurea or insulin may have an increased risk of hypoglycaemia. The risk of hypoglycaemia can be lowered by a reduction in the dose of sulphonylurea or insulin.

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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 prior to treatment, at months 3 and 6 and every 6 months thereafter.
- Thyroid Function Tests prior to treatment and routinely as required.

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 3% or 2.5kg weight loss and a reduction in HbA1c of at least 1.0% after 6 months should stop liraglutide, and be initiated on alternative treatment e.g. insulin, by hospital diabetes team

PREGNANCY AND LACTATION

Pregnancy

- There are no adequate data for the use of liraglutide in pregnant women. Studies in animals have shown reproductive toxicity. The potential risk for humans is unknown.
- Liraglutide should **not** be used during pregnancy
- If a patient wishes to become pregnant, or pregnancy occurs, treatment with liraglutide should be discontinued
- It is prudent to avoid using liraglutide in women who may become pregnant in the future, unless the benefits of treatment are very likely to outweigh the risks of pregnancy occurring during treatment with this agent.

Lactation

- Liraglutide should **not** be used if breast-feeding. It is unknown whether the drug is excreted in human milk

DRUG INTERACTIONS

- Few patients treated with liraglutide reported at least one episode of severe diarrhoea. Diarrhoea may affect the absorption of concomitant oral medicinal products
- *Insulin*: combination of liraglutide with insulin has not been evaluated

EVENTS AND ACTION

Adverse effects	Symptoms/signs	Actions
Acute pancreatitis	Persistent and severe abdominal pain	Stop liraglutide 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.
Thyroid events e.g. thyroid neoplasms	Increased blood calcitonin, goitre	Stop liraglutide. Seek advice from specialist immediately
Hypoglycaemia	Shaking & trembling, hunger, palpitation, confusion (amongst others)	Reduction in the dose of sulphonylurea should be considered for patients on concomitant sulphonylurea treatment.

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For further information on adverse effects as well as cautions, contra-indications and interactions, please refer to the current British National Formulary (www.bnf.org.uk) and Summary of Product Characteristics (www.medicines.org.uk).

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 liraglutide

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. Liraglutide 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 liraglutide
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/ or 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/or a reduction in HbA1c of 1.0% after 6 to 9 months may continue with liraglutide
6. Undertake all dose increments of liraglutide
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 any adverse events to the CHM where appropriate
10. Pancreatitis:
    a. Stop liraglutide if pancreatitis likely to have occurred
    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

- Liraglutide SCG. Draft guidance by JPG THPCT Medicines Committee & BLT Trust New Drugs Group. November 2010
- Liraglutide SPC: http://www.medicines.org.uk/emc/medicine/21986/SPC/ (Last accessed 29/12/2010)
- Liraglutide for Diabetes (type 2). TA 203 http://www.nice.org.uk/ta203