NHS Northamptonshire

Northamptonshire Shared Care Protocol for Glucagon-Like Peptide – 1 analogue therapy.

Part A

Background

Glucagon-Like Peptide-1 (GLP-1) analogues are a relatively new class of drugs that can be used in the treatment of Type 2 Diabetes. They have an impact on the incretin system. When administered subcutaneously, there is reduction in post-prandial glucose levels as a result of increased insulin secretion from pancreatic beta cells and simultaneously, a reduction in glucagon release from pancreatic alpha cells. The net effect is an increase in peripheral uptake of glucose and reduced glucose release from hepatic glycogen stores. GLP-1 also acts as a satiety signal, which can therefore potentially aid weight loss.

There are currently two GLP-1 analogues available: Exenatide (either as Byetta®, the twice daily product or as Bydureon®, the once-weekly modified release formulation) and Liraglutide (Victoza®).
Northamptonshire Prescribing Advisory Group (NPAG) recommends that a member of the Northamptonshire Diabetes Multidisciplinary Team (NDMT) initiates (or recommends initiation of) GLP-1 analogue therapy.

[NB Secondary care consultants may initiate GLP-1 agonists but this would no longer be the usual pathway for routine initiation.

The continued prescription and responsibility for monitoring may be transferred over to primary care physicians once the patient is stabilised on the maintenance dose.

Indications for initiation

NICE Clinical Guideline 87 recommends NPH Insulin as the usual 3rd line option for patients taking metformin and a sulphonylurea with sub-optimal glycaemic control. A DPP-4 inhibitor or pioglitazone can be considered for patients where insulin is unacceptable because of employment, social, recreational or other personal issues, or obesity. Alternatively GLP-1 analogues can be considered for patients with the following criteria:

- Body Mass Index (BMI) ≥ 35kg/m^2 in patients of European descent. For patients of other ethnic origin, adjustments need to be made and a lower BMI level is appropriate.
- Patients with BMI <35 kg/m^2 in whom therapy with insulin would have significant occupational difficulty due to withdrawal of their driving licence or weight loss would benefit other co-morbidities.
- HbA1C greater than 58mmol/mol (7.5%)

Doses and titration regimes

Exenatide:

Byetta®
Starting dose 5mcg twice daily before meals for 4 weeks, increased to maintenance dose of 10mcg twice daily if lower dose tolerated.

Bydureon®
2mg once weekly.
Patients changing from standard-release exenatide may experience initial transient increase in blood glucose.
Important – the effect of Bydureon® may persist for 10 weeks after discontinuation.

Liraglutide:
Starting dose 0.6mg once daily for at least one week, increased to a maintenance dose of 1.2mg once daily if lower dose tolerated.

If the patient is taking a sulphonylurea, consider a dose reduction to reduce the potential for hypoglycaemic episodes

Indications for continuing therapy

GLP-1 analogue treatment should normally only be continued beyond **6** months if **both** of the following criteria are met:

- HbA1c reduced by ≥ 11 mmol/mol (1% in old units) **and**
- Weight reduction by ≥ 3%

  If HbA1c is reduced by ≥ 16 mmol/mol (1.5% in old units) but the 3% weight loss has not been achieved there should be a discussion between the clinician and the patient about whether it is appropriate to continue the GLP-1 analogue

  Weight loss of >3% alone (without an accompanying fall in HbA1c of >11 mmol/mol ({1% in old units}) is not cost effective (NICE) and the GLP-1 analogue should be discontinued. However, if other blood glucose lowering medication was changed when the GLP-1 analogue was introduced (e.g. withdrawal of a glitazone) this may influence the HbA1c result and should be taken into account.

At 12 months NICE advises that the patient should have lost at least 5% of their body weight. Also, if at 12 months, HbA1c has started to rise again, this may prompt a decision to discontinue the GLP-1 analogue.

Adverse effects

- The commonest side effects are related to gastrointestinal upset with nausea being reported most commonly.
- There has been concern about the possibility of an increase in the incidence of acute pancreatitis. Whilst this has not been substantiated, it is recommended to advise patients that they should stop taking GLP-1 therapy if they experience continued severe abdominal pain and seek medical assistance.

Co- prescribing with insulin

Exenatide (Byetta®) is licensed as adjunctive therapy to basal insulin with or without metformin and/or pioglitazone in adults who have not achieved adequate glycaemic control with these agents

Bydureon®and liraglutide are not licensed for co-prescribing with insulin therapy.

Co-prescribing of (Byetta®) with insulin has yet to be assessed by NICE and its cost-effectiveness is not clear. **Co-prescribing is therefore not routinely commissioned.**

It may however, be felt by the specialist diabetologist in a secondary care setting, that co-prescribing may be clinically beneficial, for example to reduce total daily doses of insulin (usually when there is marked insulin resistance and daily doses are in excess of 1.5-2.0 units/kg) or even to facilitate the eventual withdrawal of insulin completely.

Patient potentially eligible for combination therapy (insulin and GLP-1 agonist)

- Type 2 diabetes
- BMI > 35 or obesity related co-morbidities (i.e. meet NICE criteria for initiation of GLP-1 analogue) AND currently taking large doses of insulin

In situations like this, patients should be referred to secondary care and remain under active follow up and not enter into the shared care protocol. There should also be clear documentation that the issue of off-licence prescribing, where applicable, has been discussed with the patient.

Co-prescribing with insulin should not be initiated within the NDMT; any co-prescribing must remain within secondary care. Both the GLP-1 and the insulin must be prescribed by the secondary care specialist.

Part B

Shared Care Protocol for GLP-1 analogue therapy

If the following criteria are satisfied, patients can be transferred to a shared care protocol:

- Meet NICE criteria for initiation of GLP-1 analogue therapy
- Have been initiated by the NDMT Established and tolerating maintenance dose of GLP-1 analogue therapy
- Not co-prescribed with insulin

Expectations of the NDMT

Initiation

- Patients who require GLP-1 therapy must be referred to the NDMT for initiation. The exception to this is for a GP or practice nurse with prior experience of initiating GLP-1 therapy within a specialist diabetes service environment (community or secondary care), in this situation it would be appropriate for these individuals to initiate a patient onto GLP-1 therapy and the NDMT be informed about the patient for auditing purposes
- At initiation, certain patient information will be recorded which will facilitate tracking of patient's progress. (See appendix 1). This information will be provided to the patient's GP.
- Patients are provided with the following information (written or verbal):
    - What the side effects of the drugs are
    - Requirements for continuing GLP-1 therapy i.e. that in 6 months they will be expected to have lost at least 3% of their body weight and HbA1c will have reduced by 1% and in 12 months their body weight will have reduced by 5% and HbA1c will remain at least 1% below baseline.
    - Which existing drugs that the patient is taking will be stopped
    - Which existing drugs that the patient is taking will be continued.
    - Lifestyle advice to assist them with their weight loss
    - When and how to use the pen device (for administering the drug)
    - How to use the diary given to them to record their progress
- Patients are provided with the first prescription of GLP-1 therapy by the NMDT nurse prescriber (the NDMT nurse prescriber allocates the prescription to the patient's GP practice code) or the patient's GP is asked to provide the initial prescription if the nurse is not a prescriber.
- Arrangements will be made for the patient to receive the appropriate training on administration either individually or as part of a "group start".
- Arrangements for reviewing their progress within the first month will be made in discussion with the DSN.
- For those patients on twice-daily exenatide, at one month, if the drug is well tolerated and there are no side effects the GP should be advised to provide a prescription for maintenance dose therapy and the patient may be discharged to primary care.
- For those patients on once-weekly exenatide, they may be discharged to primary if they are tolerating the therapy within the first month

- For those patients on Liraglutide, as the maintenance dose is achieved with the initial prescription after 1 week, they may be discharged to primary if they are tolerating the maintenance therapy within the first month
- **A patient must not be discharged into general practice if:**
    - The patient is prescribed both a GLP-1 analogue and insulin
    - NB This is only applicable to secondary care. The NDMT should not initiate co-prescribing.

Discharge to General Practice

- If the discharge to General Practice takes place the patient is provided with:
    - A letter detailing what the treatment is and a plan for weight loss and HbA1c targets at both six and 12 months (appendix 1).
    - Monitoring regime provided to both patient and primary care physician (keep a copy in NMDT records).
    - Information so that they understand what their responsibility is as part of the shared care protocol

General Practice responsibilities

- Continue to prescribe GLP-1 therapy once initiated / recommended by NMDT

6 Month Review

- At this review the following will happen:
    - Check and record HbA1c
    - Check and record weight
    - Remind patients of the potential side effects of using the drug and that if they become unwell to seek medical attention

GLP-1 analogue treatment should normally be discontinued at 6 months if both of the following criteria are not met:

- HbA1c reduced by ≥ 11 mmol/mol (1% in old units) **and**
- Weight reduction by ≥ 3%

The Shared Care Protocol supports the Primary Care Clinician to discontinue therapy at this stage if the above targets are not met.

The next step according to NICE would usually be to initiate human insulin but advice may be sought from the NMDT.

- However, if HbA1c is reduced by ≥ 16 mmol/mol (1.5% in old units) but the 3% weight loss has not been achieved there shouldl be a discussion between the clinician and the patient about whether it is appropriate to continue the GLP-1 analogue. Although NICE advises that there is no evidence of cost-effectiveness in this situation, NMDT opinion should be sought as to whether it may be clinically beneficial to continue with GLP-1 therapy

- Weight loss of >3% alone (without an accompanying fall in HbA1c of >11 mmol/mol {1% in old units}) is not cost effective (NICE) and the GLP-1 analogue should be discontinued.

12 Month Review

- At this review the following will happen:
    - HbA1c is checked. If the HbA1c has increased from the 6 month review, discontinuation of the GLP-1 analogue should be considered. NMDT advice may be sought at this stage.
    - Patient is weighed. (It is expected that weight loss of at least 5% will have been achieved - NICE).
    - Record the results (HbA1c and weight reduction) of the consultation.
    - Remind patients of the potential side effects of using the drug and that if they become unwell seek medical advice.

- **Other circumstances where GLP-1 therapy should be discontinued:**
    - In all cases where the patients HBA1c levels has risen from baseline
    - If pancreatitis is suspected
- If the patient has an occupation e.g. certain drivers and initiation onto insulin will lead to withdrawal of their licence then the case should be discussed with the NMDT
- If patients not meeting criteria for continuing therapy, primary care to discuss and agree options.

Monitoring Regime

- Baseline — Weight / BMI / HbA1c (NMDT)
- 6 Months — Weight / HbA1c (Primary Care)
- 6 Monthly thereafter — Weight / HbA1c (Primary Care)

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Appendix 1

Northamptonshire Shared Care Protocol for Glucagon-Like Peptide-1 therapy

Secondary care / NDMT to send a copy of this form to patient's GP

Today we have started / recommended a medicine called Exenatide (trade name Byetta or Bydureon) or Liraglutide (trade name Victoza) to help treat your type 2 diabetes.

Exenatide / Liraglutide has been prescribed for you to help reduce your blood glucose levels and help you to lose weight.

Exenatide / Liraglutide is not beneficial in everyone and the National Institute for Clinical Excellence (NICE) have advised that treatment should only be continued for patients who have a reasonable response; defined by NICE as a reduction in HbA1c (sometimes called the "H" test) of 11 mmol/mol (1% in old units) or more and a reduction in weight of 3% or more after 6 months of treatment.

Over the next 6 months we will ask your GP to monitor your HbA1c and weight to assess if you are one of the patients who benefits from Exenatide / Liraglutide. Exenatide/ Liraglutide will only usually be continued beyond 6 months in patients who have a reasonable benefit from the treatment as stated above.

In occasional cases, where there has been a very good reduction in HbA1c (above that suggested by NICE) but weight has not reduced , it may still be deemed beneficial to continue using Exenatide / Liraglutide.

Your latest HbA1c test is: _____mmol/mol

After 6 and 12 months your HbA1c should be below: _____mmol/mol

Your weight today is:_____Kg (BMI_____)

At 6 months, with 3% weight loss your weight would be: _____Kg

At 12 months, with 5% weight loss your weight would be: _____Kg

Patient Agreement

The information above has been explained to me and I understand that treatment with Exenatide / Liraglutide is unlikely to be continued after 6 months if the medicine does not appear to be having a reasonable benefit.

Patient Name: _____

Patient Signature: _____

Clinician Name: _____

Clinician Signature: _____

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Date: _____

Date of 6-month review: _____