Bedfordshire Clinical Commissioning Group

Luton Clinical Commissioning Group

BEDFORDSHIRE AND LUTON JOINT PRESCRIBING COMMITTEE (JPC)

Overarching Shared Care Guideline for Glucagon-like peptide 1 (GLP 1) agonists.

PATIENT'S NAME: PATIENT'S ADDRESS: HOSPITAL NAME AND NUMBER / PATIENT IDENTIFIER: CONSULTANT'S NAME: GP's NAME:

There are currently 5 Glucagon-like peptide (GLP 1) agonists licensed for use by subcutaneous injection:- Liraglutide (Victoza®), Semaglutide (Ozempic®), Dulaglutide (Trulicity®), Exenatide (Byetta®;Bydureon®), Lixisenatide (Lyxumia®). In addition an oral preparation of Semaglutide (Rybelsus®) has been licensed for use.
This is the overarching shared care guideline which outlines the shared care responsibilities of the Healthcare professionals involved in the care of patients receiving GLP 1 agonists. Drug specific factsheets have been produced for all GLP 1 agonists and these are available as separate embedded documents in appendix 2:-

Preferred Formulary Choices (**New patients from December 2020, existing patients may remain on current choices)** - :-

Joint first line choices:-

Subcutaneous injection preparations of:-

- Dulaglutide (Trulicity®)
- Liraglutide (Victoza®) - NB maximum recommended dose of liraglutide is 1.2mg except in very exceptional circumstances and only after consultation with the Specialist Diabetes Team

Approved by the Bedfordshire and Luton Joint Prescribing Committee, February 2017, Updated September 2019 and December 2020.

- Semaglutide (Ozempic®)

Second line choice (if the subcutaneous injection preparations outlined above are unsuitable)

- Oral Semaglutide (Rybelsus®)

Non Formulary (no new initiations/existing patients may remain on these medicines):-

- Exenatide (Bydureon®)- once weekly preparation
- Exenatide (Byetta®) – twice daily preparation
- Lixisenatide (Lyxumia®)

Not recommended:-

- Xultophy® (insulin degludec/liraglutide combination)

Although Lixisenatide and Exenatide (Byetta®/Bydureon®) have been removed from the Formulary, the factsheets have been retained as historical patients may still be receiving these medicines.

Definitions

Throughout this document, the following definitions will apply wherever the following terms appear in bold**:**

Diabetes Specialist Team – Integrated Community Diabetes Service [ICDS], Specialist [Diabetes] Primary Care Pharmacists [with access to dietetics support], Secondary/Tertiary Care Specialist Diabetes Teams.

General Practice Diabetes Specialist – Healthcare professional in General Practice with appropriate specialist expertise in management of diabetes (Excludes Specialist [Diabetes] Primary Care Pharmacists who are covered by the 'Diabetes Specialist Team' definition above).

JPC Recommendations:

Place in therapy of GLP 1 agonists

1) As per the NICE Guideline on the management of type 2 diabetes in adults (NG28 – December 15) https://www.nice.org.uk/guidance/ng28 as follows:

- Use of GLP 1 agonists is supported (as part of the second intensification step including consideration of insulin treatment) in combination with metformin and sulfonylurea in patients with type 2 diabetes who:-
    - have a BMI of 35 kg/m^2 or higher (adjusted accordingly for people from black, Asian and other minority ethnic groups) and specific psychological or other medical problems associated with obesity

or

    - have a BMI lower than 35 kg/m^2, and for whom insulin therapy would have significant occupational implications, or weight loss would benefit other significant obesity-related comorbidities.

2) The NICE Clinical Guideline does not cover the complex patients seen by **Diabetes Specialist Team** and at this stage in therapy there is little to guide us in terms of absolute evidence. With the exception of subcutaneous preparations, which may be initiated by a **General Practice Diabetes Specialist (**see appropriate section below), use of a GLP1-agonist post NICE second intensification step should be in accordance with recommendations by, and under the supervison of, the **Diabetes Specialist Team,** with healthcare professionals in General Practice prescribing under shared care. **N.B.** Use of GLP 1 agonists in this setting is likely to involve multiple treatment combinations including insulin which may sit outside of the NICE Clinical Guideline and licenses for the GLP 1 agonists
3) GLP 1 agonists and insulin – recommended in line with NICE Guideline 28 i.e. combination only to be used when initiated and supervised by a Specialist with the GP practice taking on prescribing under shared care. (**See appendix 2 for Local Criteria for use)**

4) Specialist use (combined use with insulin and/or use outside of NICE Guidance /product license) is subject to annual audit, reported to the JPC.

Dietetic support is necessary in whatever setting GLP-1 agonist initiation occurs

Initation of GLP 1 agonist - subcutaneous injection preparations

Healthcare professionals in General Practice without specialist diabetes expertise should only initiate in accordance with NICE Guideline 28 up to the second intensification (see first bullet point above); they should not initiate GLP 1 agonist / insulin combinations at any stage.

Post NICE second intensification step, a subcutaneous GLP1-agonist preparation should only be initiated by the **Diabetes Specialist Team** or a **General Practice Diabetes Specialist**, or in accordance with their recommendations

Initiation of Oral Semaglutide (Rybelsus®)

As patient selection is key, initiation of oral semaglutide should be undertaken by the **Diabetes Specialist Team** only.

Patients receiving GLP1 agonist only (i.e. not in combination with insulin) :- **Criteria for continuation of therapy**

- Only continue GLP-1 agonist therapy if the person with type 2 diabetes has had a beneficial metabolic response (a reduction of at least 11 mmol/mol [1.0%] in HbA1c and a weight loss of at least 3% of initial body weight in 6 months.

- Criteria for continuation at 12 months and beyond – Consider discontinuing treatment if the response at 6 months is not maintained, taking into consideration the progressive nature of type II diabetes.

Patients receiving insulin/GLP 1 agonist combination :-

Criteria for continuation of therapy

6 month review

The GLP 1 agonist should be stopped if the HbA1c has not fallen by at least 5mmol/mol.

12 month review

The GLP 1 agonist should be stopped if none of the following apply

- Improvement in HbA1c ≥ 11mmol/mol [1.0%] **and** weight reduction ≥ 3%

Or

- Improvement in HbA1c ≥ 11mmol/mol [1.0%] **and** patient is taking human insulin

Or

- Improvement in HbA1c ≥ 5mmol/mol [0.5%] **and** weight reduction ≥ 10%

Beyond 12 months

Consider discontinuing treatment if the response at 12 months is not maintained, taking into consideration the progressive nature of type II diabetes.

Responsibilities for Prescriber Initiating therapy:

1. Assessment and confirmation of the need for GLP- 1 agonist, prescribing in compliance with the Bedfordshire and Luton Joint Prescribing Committee (JPC) recommendations– see above.

2. Ensure patient has received relevant patient information material and discuss the potential benefits and risks of the GLP 1 agonist to allow the patient to make an informed decision on treatment.

3. Initiate the GLP 1 agonist (see above for preferred Formulary choices) as per dosage instructions in the summary of product characteristics. **NB** Note maximum recommended dose of liraglutide is 1.2 mg unless otherwise advised by the **Diabetes Specialist Team**.

4. Educate the patient on the use of the delivery device, injection technique, storage and safe disposal of sharps if the GLP-1 agonist is injectable.

5. If initiated by the **Diabetes Specialist Team**, continue prescribing until the dosage is stabilised (1 original pack of medication to be provided). NB. Specialist [Diabetes] Primary Care Pharmacists will initiate and continue prescribing.

6. The Bedford ICDS team and the Luton ICDS team review process differs slightly. Healthcare professionals in General Practice who initiate treatment may follow either of these recommendations dependent on the support services available to them:-
    - Bedford ICDS - Each patient to be reviewed at 1 week, then between 2 and 4 weeks after initiation of treatment, then 3 monthly for 6 months, then on a 6 monthly basis for response to treatment and adverse effects as per the monitoring requirements outlined below.[1]
    - Luton ICDS – Each patient to be reviewed by telephone 1 week after commencing treatment and if necessary at week 2 or 3 for dose titration. Currently, all patients initiated on a GLP-1 agonist within Luton ICDS are referred to the ICDS Dietitian, who aims to see them within the first 6 weeks of starting a GLP-1 agonist and to further provide new patients with intensive 4-6 weekly follow up for the 6 month duration, to support them in meeting the weight and HbA1c targets; for patients already under the care of the Dietician prior to staring a GLP-1 agonist, these review timeframes may be altered depending on the individual. At 3 months the HbA1c and weight is reviewed by the Diabetes Specialist Nurse and if target reached, the patient is discharged to their General Practice. If the patient is progressing to target, 4-6 weekly dietetics review continues until 6 months when the weight and HbA1c is reviewed. If target is reached the patient is discharged to their General Practice. If target is not reached, the patient's treatment is stopped/reviewed.[2]

7. Discontinue treatment if the patient doesn't fulfill the **continuation criteria** (see above).

8. If the **Diabetes Specialist Team** (other than a healthcare professional from General Practice) has initiated treatment, all clinical assessments including results of any investigations will be reported to the patient's GP following each visit to the hospital/community diabetes clinic.

[1] The Bedford ICDS team may pass the monitoring of the patient to the GP after 3 months only if the patient has already reached the expected 6 month target for continuation of therapy. Otherwise, monitoring of the treatment should be retained by the by the ICDS team until after the 6 month review.

[2] Moving forward, the plan is for joint clinics in GP practices where follow-ups will be with the GP/Practice Nurse, overseen by the ICDS team. (This is similar to the current Bedfordshire model)

9. To report all suspected reactions to established drugs that are serious, medically significant, or result in harm to the MHRA. For medicines showing the black triangle symbol, **all** suspected reactions (including those considered not to be serious) should be reported to the MHRA. Reporting is through the Yellow Card Scheme using the electronic form at www.mhra.gov.uk/yellowcard.

General Practice Responsibilities*:

1. To continue to have overall responsibility for the routine care of the patient and if there are any concerns to liaise with the **Diabetes Specialist Team.**

2. Where the **Diabetes Specialist Team** has initiated treatment, take over prescribing of the GLP 1 agonists after the dosage is stabilised (minimum one month after initiation). If a healthcare professional from General Practice has initiated therapy, continue to prescribe.

3. To ensure all communication with the **Diabetes Specialist Team** is reviewed and actioned.

4. Monitor response to treatment and refer back or seek advice from the **Diabetes Specialist Team** if the patient has not met agreed outcome criteria.

5. Healthcare professionals in General Practice may be asked to discontinue treatment with support from the **Diabetes Specialist Team**.

6. To report all suspected reactions to established drugs that are serious, medically significant, or result in harm to the MHRA. For medicines showing the black triangle symbol, **all** suspected reactions (including those considered not to be serious) should be reported to the MHRA. Reporting is through the Yellow Card Scheme using the electronic form at www.mhra.gov.uk/yellowcard

When should Healthcare professionals in General Practice refer back to the Diabetes Specialist Team

1. Report to and seek advice on any aspect of patient care that is of concern and may affect treatment.
2. Referral back to/seek advice from the **Diabetes Specialist Team** is particularly advised if:-

- Problems arise tolerating the GLP 1 agonist or if the GLP 1 agonist has to be discontinued for other medical reasons.
- Diabetes control becomes unstable.
- Patient develops any acute/serious diabetes complications.
- The patient is a women with diabetes who is planning a pregnancy or becomes pregnant. If the patient becomes pregnant, treatment should be stopped immediately and the patient urgently referred to the **Diabetes Specialist Team**.
- The patient is receiving liraglutide at a dose of 1.2 mg and dosage increase in being considered.
- Use of a GLP 1 agonist post NICE second intensification is being considered.

***Where the Diabetes Specialist Team member is the Specialist [Diabetes] Primary Care Pharmacist, some of these responsibilities will be retained by this Healthcare Professional and some actions relating to the General Practice will be unnecessary (for agreement at Practice level).**

Patient responsibilities:

1. To attend for all blood tests and clinical reviews.
2. To advise all relevant Health care professionals (primary and secondary care) of current medication (prescribed and over the counter) being taken.
3. To report any adverse effects of treatment and/or deterioration in diabetes control to their General Practice and/or Specialist.
4. To advise their General Practice and Specialist if a pregnancy is planned or occurs.

Monitoring Requirements

1. HbA1c levels. Monitor every 3 months until HbA1c stable for 6 months, then at least every 6 months thereafter.
2. Weight, height & BMI – any weight reduction or increase should be recorded at 3 months, 6 months and 12 months. BMI should be calculated at each visit.
3. Insulin requirements (if insulin is prescribed) – any reduction in insulin dose at 6 and 12 months should be calculated and recorded at 6 and 12 months.
4. Renal function.

<u>Discontinuation/Continuation Criteria</u>

Stopping Criteria (applicable at any time point)

- Patient choice
- Drug intolerance

- Occurrence of any contra-indication to treatment
- Failure to meet continuation criteria
- Failure to attend for blood tests and clinical reviews
- Pregnancy or planning a pregnancy

Criteria for continuation of therapy – See JPC recommendations

Contact Details for Diabetes Specialist Teams:-

Bedford Hospital

Consultants:

Dr Alison Melvin Dr Rajeev Kumar

Dr Mustafa Khan Dr Shwe Pan

Telephone: 01234 792287

Fax: 01234 792180

Diabetes Specialist Nurses:

Claire Springall **Nurse advice line**: 01234 730586

Fax: 01234 792180

Jo Long

Luton & Dunstable Hospital

Consultants

Dr Shiu-Ching Soo - 01582 497564 Dr Banerjee – 01582 497204

Dr Rehman – 01582 497202 Dr Naziat – 01582 497204

Diabetes Specialist Nurses

Emma Glastonbury

Jos Garchitorena

Sheila Mallari

Telephone: 01582 718050

North and Central Beds - Integrated Community Diabetes Service

Consultants

Dr Nick Morrish

Telephone: 01234 792287

Diabetes Nurse Consultant

Mrs Julia Pledger

Telephone: 01234 792297
Fax: 01234 792180

Community Diabetes Specialist Nurses

Sally Graham
Jackie Walton
Andrea Wetherhill
Sharon White
Telephone: 01234 792013
Fax: 01234 792180

South Bedfordshire- Integrated Community Diabetes Service

Consultants

Dr Shiu-Ching Soo

Telephone : 01582 497564

Diabetes Specialist Nurses

Lucy Joseph
Aksana Uzkurniene
Telephone: 01582 718431

Luton - Integrated Community Diabetes Services

Community Diabetes Specialist Nurses

Frances Moss

Cathy Doyle
Juliet Davies
Patience Kyereh-Chamba

Telephone: 0333 405 31

Appendix 1

As NICE Guideline 28 contained very little detail pertaining to the use of insulin in combination with GLP 1- agonists. The JPC agreed to the following updated criteria agreed Nov 2016 between the JPC and local **Diabetes Specialist Teams**.

Inclusion Criteria for use of GLP1 agonists in combination with insulin in patients with type 2 diabetes:-

- Clinician needs to be satisfied that the patient demonstrates clinical signs of "proactive self-management of glucose and body weight " i.e. patient has been seen by a dietician and has demonstrated an attempt to lose weight over the previous 6 months
- Clinician should give consideration to the length of time a patient has been receiving insulin / duration of time since diagnosis of diabetes as GLP 1 agonists potentiate endogenous insulin secretion and therefore may have limited efficacy in patients with limited ß-cell functional capacity.
- Consider patient acceptability (insulin and GLP 1 agonist regimens will involve multiple daily injections)
- DPP4 inhibitors should be stopped when adding a GLP 1 agonist.
- Patients who are on an insulin analogues should be reviewed and switched to human insulin where possible (and if appropriate) before a GLP 1 agonist is started.
- Review dose of basal insulin before starting a GLP 1 agonist – consider reducing the dose of basal insulin in patients at increased risk of hypoglycaemia when adding a GLP 1 agonist.

- The patient must fit **all** of the following criteria for starting a GLP 1 agonist:

1) a body mass index (BMI) ≥ 35 kg/m^2 in those of European family origin (with appropriate adjustment for other ethnic groups) and specific psychological or medical problems associated with high body weight **or**
a body mass index (BMI) < 35 kg/m^2, and intensification of existing insulin regimen would have significant occupational implications or weight loss would benefit other significant obesity-related comorbidities.

2) Patient has a HbA1c of > 60mmol/mol (7.6%) or other higher level agreed with the individual), **AND ONLY IF:**

- there are concerns associated with intensifying the insulin regimen (e.g. clinical reasons, practical reasons or patient refuses).

or

- further weight gain (expected with intensification of insulin) would be of significant concern (e.g. pt has obesity co-morbidities – sleep apnoea, mobility / musculoskeletal issues / CHD / heart failure/ NASH)

or

- previous attempts at intensification of insulin regimen have been unsuccessful in reducing HBA1c to acceptable target.

3) Agreement that the GLP-1 agonist will be discontinued at 6 month or 12 month review date, and beyond if the required criteria for continuation are not met.

Appendix 2

Drug Specific Fact sheets

There is a separate fact sheet for each of the following drugs:-

(Listed In order of preferred Formulary choices)

Formulary

- Dulaglutide (Trulicity®)
- Liraglutide (Victoza®)
- Semaglutide (Ozempic®)
- Semaglutide Oral (Rybelsus®)

Non-Formulary – use in existing patients only

- Exenatide (Bydureon®)- once weekly preparation
- Exenatide (Byetta®) – twice daily preparation
- Lixisenatide (Lyxumia®)

These are available as separate documents on the BLMK Medicines Management Team Website - click on links below:-

https://medicines.blmkccg.nhs.uk/guideline/dulaglutide-information-sheet/

https://medicines.blmkccg.nhs.uk/guideline/liraglutide-information-sheet/

https://medicines.blmkccg.nhs.uk/guideline/semaglutide-ozempic-information-sheet/

https://medicines.blmkccg.nhs.uk/guideline/semaglutide-oral-rybelsus-prescribing-information/

https://medicines.blmkccg.nhs.uk/guideline/exenatide-twice-daily-information-sheet/

https://medicines.blmkccg.nhs.uk/guideline/exenatide-once-weekly-information-sheet/

https://medicines.blmkccg.nhs.uk/guideline/lixisenatide-information-sheet/