

BEDFORDSHIRE AND LUTON JOINT PRESCRIBING COMMITTEE (JPC)

Overarching Shared Care Guideline for Glucagon-like peptide 1 (GLP 1) agonists, February 2017.

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 available for use:- Albiglutide (Eperzan®), Dulaglutide (Trulicity®), Exenatide (Byetta®;Bydureon®), Lixisenatide (Lyxumia®), Liraglutide (Victoza®).

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 (except Albiglutide – not recommended locally) and these are available as separate embedded documents in appendix 3.

- Dulaglutide (Trulicity®)
- Liraglutide (Victoza®)
- Exenatide (Byetta®) – twice daily preparation
- Exenatide (Bydureon®)- once weekly preparation
- Lixisenatide (Lyxumia®)

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/m² 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/m², 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 the Specialist Diabetes Teams and at this stage in therapy there is little to guide us in terms of absolute evidence. Use of a GLP1 agonist post NICE second intensification step should be in accordance with the Specialist Diabetes Teams recommendations. Patients at this stage in therapy **must** be supervised by the Specialist Diabetes Team with GPs 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. See appendix 1 for London Medicines Evaluation Network overview of GLP1 agonists (published December 2016) which gives helpful information on GLP1 agonist evidence, individual product licences and NICE recommendations.
- 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 GP 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.

Initiation of GLP 1 agonists

Specialist Diabetes Team (this is defined as Integrated Community Diabetes Service [ICDS] or Secondary/Tertiary Care Specialist Diabetes Teams) initiation or GP initiation after consultation with specialist if the GP has access to dietetics support. **GPs should only initiate in accordance with NICE Guideline 28** (see first bullet point above) **up to the second intensification**, after that refer patient to the Specialist Diabetes Team which should be the ICDS in the first instance. **NB.** GLP 1 agonist/insulin combination – Specialist Diabetes Team initiation only.

Preferred GLP 1- agonist Formulary Choices (New patients from December 2016, existing patients to remain on current choices)

Dulaglutide and Liraglutide - **NB maximum recommended dose of liraglutide is 1.2mg** except in very exceptional circumstances and only after consultation with the Specialist Diabetes Team.

Not recommended:-

- Xultophy® (insulin degludec/liraglutide combination)
- Albiglutide

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 \geq 11mmol/mol [1.0%] **and** weight reduction \geq 3%
Or
- Improvement in HbA1c \geq 11mmol/mol [1.0%] **and** patient is taking human insulin
Or
- Improvement in HbA1c \geq 5mmol/mol [0.5%] **and** weight reduction \geq 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 advised by the Specialist Diabetes Team.

4. Educate the patient on the use of the delivery device, injection technique and storage and safe disposal of sharps.
5. If initiated by the Specialist Diabetes Team, continue prescribing until the dosage is stabilised (1 original pack of medication to be provided).
6. The Bedford ICDS team and the Luton ICDS team review process differs slightly. GPs 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. The patient is seen monthly by dietitian for weight check and diet discussion. At 3 months the HbA1c and weight is reviewed by the Diabetes Specialist Nurse and if target reached, the patient is discharged to GP. If the patient is progressing to target, monthly dietetics review continues until 6 months when the weight and HBA1c is reviewed. If target is reached the patient is referred back to the GP. 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 Specialist Diabetes Team 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.
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.

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)

GP 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 Specialist Diabetes Teams.
2. Where the Specialist Diabetes Team has initiated treatment, take over prescribing of the GLP 1 agonists after the dosage is stabilised (minimum one month after initiation). If the GP has initiated therapy, continue to prescribe.
3. To ensure all communication with the Specialist Diabetes Team is reviewed and actioned.
4. Monitor response to treatment and refer back or seek advice from the Specialist Diabetes team if the patient has not met agreed outcome criteria.
5. The GP may be asked to discontinue treatment with support from the Specialist Diabetes 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 the GP refer back to the Specialist Diabetes Team?

1. Report to and seek advice on any aspect of patient care that is of concern to the GP and may affect treatment.
2. Referral back to/seek advice from the Specialist Diabetes 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 Specialist Diabetes 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.

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 the GP and/or Specialist.
4. To advise the GP and Specialist if a pregnancy is planned or occurs.

Monitoring Requirements

1. HBA1c levels. Monitor at least 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.

Discontinuation/Continuation Criteria**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 Specialist Diabetes 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

Tessa Kidd

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

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South Bedfordshire- Integrated Community Diabetes Service

Consultants

Dr Shiu-Ching Soo

Telephone : 01582 497564

Diabetes Specialist Nurses

Lucy Joseph

Aksana Uzurniene

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

London Medicines Evaluation Network Overview: Glucagon- Like Peptide – 1 receptor analogues, published December 2016

<https://www.sps.nhs.uk/wp-content/uploads/2017/01/GLP-1-analogues.pdf>

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 β -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/m² 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/m², 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 > 60 mmol/mol (7.6%) or other higher level agreed with the individual), **AND ONLY IF:**
 - there are concerns associated with initiation of or intensifying the insulin regimen (e.g. clinical reasons, practical reasons or patient refuses).
- or**
- further weight gain (expected with initiation of or 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 3

Drug Specific Fact sheets

There is a separate fact sheet for each of the following drugs . Click the relevant embedded document below to access these.

- Dulaglutide (Trulicity®)
- Liraglutide (Victoza®)
- Exenatide (Byetta®) – twice daily preparation
- Exenatide (Bydureon®)- once weekly preparation
- Lixisenatide (Lyxumia®)



Dulaglutide

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