East Kent Prescribing Guidelines for the Management of Type 2 Diabetes

Document history:

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1	Judi Cross	September 2012	
2	Judi Cross	November 2012	Amendment to section on sulfonylureas
			Amendment on use in patients with history of hypoglycaemia Inclusion of information on most cost effective insulins
3	Judi Cross	January 2016	Updated to reflect NICE NG28
4	Judi Cross	February 2016	Amendments following feedback from stakeholders

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East Kent Prescribing Recommendations for the Management of Blood Glucose in Adults with Type 2 Diabetes

Introduction

These guidelines have been developed by an East Kent focus group to supplement NICE guidelines. Their purpose is to support evidence based, cost effective prescribing in East Kent.

It is intended that this document should be read in conjunction with NICE clinical guideline NG28 "Type 2 diabetes in adults: management".

NICE recommend that an individualised approach to diabetes care is adopted and is tailored to the needs and circumstances of adults with type 2 diabetes. This should take into account their personal preferences, comorbidities, risks from polypharmacy, and their ability to benefit from long-term interventions because of reduced life expectancy. Such an approach is especially important in the context of multimorbidity.

It is important to reassess the person's needs and circumstances at each review and think about whether to stop any medicines that are not effective.

Referral to DEREK group education is recommended at diagnosis and also if patient needs revision.

Rescue Therapy at Any Phase of Treatment

Treatment with insulin or a sulfonylurea should be considered in any patient who is symptomatically hyperglycaemic. Treatment should be reviewed when blood glucose control has been achieved.

Oral Hypoglycaemic Agents

Remember that diet and exercise messages should be reinforced at every review. The target HbA1c for a patient on diet and exercise control without medication is 48mmol/mol (6.5%) or lower.

Adherence with current therapy should always be assessed before any changes to medication are made.

a) Metformin

Metformin standard release is the drug of choice for first line treatment of adults with type 2 diabetes. Evidence shows that it has statistically greater effect than chlorpropamide, glibenclamide or insulin for reduction in diabetic complications, stroke and all-cause mortality. There is no such outcome data for the newer agents.

The dose of metformin should be titrated gradually in order to minimise the risk of gastrointestinal side effects. This should be done over several weeks.
If a patient develops side effects at any stage during this process they should remain on that dose for a further week before increasing the dose further.

Metformin slow release should be reserved for second line treatment. For those patients who still cannot tolerate metformin standard release despite slow titration, a trial of modified release metformin should be considered. It may be more cost effective to prescribe metformin MR by brand. At the current time Sukkarto is the recommended brand in East Kent.

The maximum dose of metformin is 2g if eGFR is below 45 and should be stopped if eGFR drops below 30.

b) Sulfonylureas

A sulfonylurea (SU) is an option in place of metformin in patients in whom metformin is contraindicated or not tolerated. They are also an option at first intensification in dual therapy and at second intensification in triple therapy.

Patients commenced on a sulfonylurea will need to monitor blood glucose in line with EK blood glucose testing guidelines and DVLA guidelines.

Aim to support patients on a sulfonylurea to aim for HbA1c of 53mmol/mol (7.0%).

Early treatment with a sulfonylurea may not be suitable for a patient with a significant degree of obesity.

In East Kent it is recommended that the following groups of patients may not be suitable for treatment with sulfonylurea due to the increased risk of hypoglycaemic attacks:

- Group 2 drivers (those who hold a licence to drive heavy goods vehicles or public service vehicles)
- Professional drivers (e.g. taxi drivers)
- Occupations where safety is critical, e.g. construction workers, steeplejacks
- Frail, elderly patients who live alone
- Those with severe renal impairment (eGFR less than 30mls/min)

Glibenclamide is not recommended as it is associated with a greater risk of hypoglycaemia due to its long half- life.

Gliclazide is the preferred first choice sulfonylurea in East Kent.

c) DPP4 Inhibitors
(Alogliptin, linagliptin,sitagliptin, vildagliptin, saxagliptin)

The preferred DPP4 inhibitor in East Kent is ALOGLIPTIN. Prescribers are reminded that the dose needs to be reduced in renal impairment. DPP4 inhibitors are recommended by NICE as an option in patients in whom metformin is contraindicated or not tolerated (despite slow titration of dose and a trial of metformin MR).

They are also recommended as an option in first intensification in combination with metformin and as an option in second intensification in combination with metformin and a sulfonylurea or metformin plus SGLT2 inhibitor.

For those that cannot tolerate metformin a DPP4 inhibitor can be used in combination with pioglitazone or a sulfonylurea in dual therapy (first intensification).

NICE NG28 recommends that where more than one drug in the same class is appropriate for treatment, the option with the lowest acquisition cost should be selected.

A summary of licensed indications, dose adjustment in renal failure and cost is attached in Appendix 1.

Patients should be informed of the goal of treatment when a DPP4 inhibitor is initiated. Arrangements must be in place for a follow up in 6 months with a view to stopping the drug if the treatment goal is not reached.
DPP4 inhibitors should be stopped if a GLP1 mimetic is commenced as they have a similar mode of action.

Dose of concomitant sulfonylurea or insulin may need to be reduced with DPP4.

d) Pioglitazone

Pioglitazone may be considered as an option in patients in whom metformin is contraindicated or not tolerated (despite slow titration of dose and a trial of metformin MR).

It is also recommended as an option in first intensification in combination with metformin and as an option in second intensification in combination with metformin and a sulfonylurea. Pioglitazone may be preferable to a DPP4 inhibitor for a patient who has marked insulin insensitivity.

Pioglitazone may cause an increase in weight and is not recommended for those in whom further weight gain would cause or exacerbate significant problems with a high body weight.

Pioglitazone is contraindicated in those with a history of heart failure, uninvestigated macroscopic haematuria, previous or active bladder cancer, diabetic ketoacidosis, hepatic impairment.

Patients should be informed of the goal of treatment when pioglitazone is initiated. Arrangements must be in place for a follow up in 6 months with a view to stopping the drug if the treatment goal is not reached

e) SGLT2 Inhibitors

(Dapagliflozin, canagliflozin, empagliflozin)

Adequate renal function is necessary for SGLT2 inhibitors to work (see Appendix 2 for details of individual drugs).

SGLT2 inhibitors are an option for use in some patients in dual therapy at first intensification and in triple therapy at second intensification.

SGLT2 inhibitors may be used in combination with insulin +/- other antidiabetic agents.

When a SGLT2 inhibitor is used in combination with a sulfonylurea or insulin the risk of hypoglycaemia may be increased and consideration should be given to reducing the dose of sulfonylurea / insulin.

An SGLT2 inhibitor may be an appropriate choice in combination with metformin for patients with adequate renal function and with a BMI>30 kg/m^2.

SGLT2 inhibitors are also recommended in dual therapy in combination with metformin for those in whom a DPP4 inhibitor or pioglitazone are contraindicated or not tolerated**.**

Patients should be informed of the goal of treatment when SGLT2 inhibitor is initiated. Arrangements must be in place for a follow up in 6 months with a view to stopping the drug if the treatment goal is not reached.

A comparison of SGLT2 inhibitors is attached in Appendix 2.

f) GLP-1 mimetics

(exenatide, liraglutide, lixisenatide, dulaglutide)

GLP1 mimetics are recommended in NG 28 for use in triple therapy only for those patients in whom triple therapy with metformin, sulfonylurea and pioglitazone or with metformin, sulfonylurea and a DPP4 inhibitor are not effective, tolerated or contraindicated. In these circumstances triple therapy with metformin, sulfonylurea and a GLP-1 mimetic may be considered in patients who:

- Have a BMI of 35kg/m^2 or higher **and** specific psychological or other medical problems associated with obesity.
- Have a BMI lower than 35kg/m^2 **and** for whom insulin therapy would have significant occupational implications, or weight loss would benefit other significant obesity-related comorbidities.

GLP-1 mimetics should not be used in combination with DPP4 inhibitors – the DPP4 inhibitor should be stopped if a GLP-1 mimetic is commenced.

Treatment should only be continued after 6 months if a reduction of 1% in HbA1c is achieved and a weight loss of 3% of initial body weight.

Patients should be informed of the goal of treatment when GLP-1 mimetic is initiated. Arrangements must be in place for a follow up in 6 months with a view to stopping the drug if the HbA1c has not fallen by at least a 1% point (11mmol/mol) and a weight reduction of at least 3% has not been achieved.

Choice of agent should depend on whether patient prefers daily or weekly administration.
The most cost effective agent within the class should be used unless there is a strong clinical reason to use an alternative agent.
Dulaglutide is the preferred weekly GLP-1 mimetic in East Kent.

If planning to initiate a GLP-1 mimetic in a patient with a low eGFR consideration should be given to specialised assessment to ensure an overview of all options.

GLP-1 mimetic should only be initiated in combination with insulin by experienced practitioners with advanced skills in diabetes management. For those with less advanced skills specialist advice should sought prior to commencing this treatment option as described in NG28.

g) Blood glucose monitoring

NICE guidelines advise the following:
Do not routinely offer self-monitoring of blood glucose levels for adults with type 2 diabetes unless:

- the person is on insulin or
- there is evidence of hypoglycaemic episodes or
- the person is on oral medication that may increase their risk of hypoglycaemia while driving or operating machinery or
- the person is pregnant, or is planning to become pregnant.

Studies have shown that there is no increase in the risk of hypoglycaemia when a DPP4 inhibitor, GLP-1 mimetic, SGLT2 inhibitor or pioglitazone is used in combination with metformin and there is no requirement for blood glucose monitoring. However there is an increased risk of hypoglycaemia when used in combination with a sulfonylurea or insulin and blood glucose testing guidelines should be referred to.

Short-term self-monitoring of blood glucose levels in adults with type 2 diabetes should be considered in the following circumstances (and reviewed as necessary):

- when starting treatment with oral or intravenous corticosteroids or
- to confirm suspected hypoglycaemia.

Be aware that adults with type 2 diabetes who have acute intercurrent illness are at risk of worsening hyperglycaemia. Review treatment as necessary.

If adults with type 2 diabetes are self-monitoring their blood glucose levels, carry out a structured assessment at least annually. The assessment should include:

- the person's self-monitoring skills
- the quality and frequency of testing
- checking the person knows how to interpret the blood glucose results and what action to take
- the impact on the person's quality of life
- the continued benefit to the person
- the equipment used.

The following blood glucose meters are recommended for use in type 2 diabetics in East Kent:

Glucomen Areo
GlucoRx Nexus
Omnitest 3

Other non-formulary meters should only be considered in exceptional circumstances where a patient has been shown to have difficulties with one of these meters.

h) Insulin Therapy – *for Type 2 Diabetics Only*

Please note that this does not apply to Type 1 diabetics

Insulins should be prescribed by brand name rather than generically.

Insulin-based treatment should be considered at second intensification as an alternative to triple therapy in:

- patients who are able to take metformin or after dual therapy in patients unable to take metformin
- when HbA1c remains above 58mmol/mol despite maximum intensification with other antidiabetic drugs.

Patients should be involved in the decision to start insulin and an individual HbA1c target should be agreed taking into account lifestyle, age, comorbidities risks from polypharmacy, and their ability to benefit from long-term interventions because of reduced life expectancy. Such an approach is especially important in the context of multimorbidity.

Practices are encouraged to have in-house clinics for this purpose. This helps to provide continuity of care and prevents delay of insulin treatment.

A structured programme is advised employing active dose titration and encouraging patients to self-manage. Continuing on-going support should be available from Practice Nurses and GPs including telephone consultations.

The dose of insulin to be taken should be stated clearly in units in the directions for basal insulins.

a. NPH Insulin – Insulatard, Humulin I , Insuman basal

NICE recommend that human NPH insulin, injected at bedtime or twice daily, is used first line except for the following groups:

- A patient needing assistance from a carer or healthcare professional to inject insulin, and in whom the use of an analogue would reduce injections from twice to once a day
- Whose lifestyle is significantly restricted by hypoglycaemia
- Who would otherwise need twice daily NPH insulin injections plus oral hypoglycaemic drugs
- Who cannot use their device to inject insulin.

In addition the following groups may be considered for a long acting analogue first line:

- Group 2 drivers (those who hold a licence to drive heavy goods vehicles or public service vehicles)
- Professional drivers (e.g. taxi drivers)
- Frail, elderly patients who live alone
- Those with severe renal impairment(eGFR less than 30mmls.min)

- Those who have a history of e hypoglycaemic episodes whilst on a sulfonylurea.

When starting insulin, review the continued need for other blood glucose lowering therapies.

Evidence shows that glargine and detemir are equivalent to NPH (and to each other) in terms of glycaemic control. Lower rates of hypoglycaemia, especially nocturnal hypoglycaemia have been demonstrated with glargine and detemir in comparison to NPH. However the incidence of severe hypoglycaemia was similar with both glargine and detemir when compared to NPH.

b. Long acting Insulin analogues – glargine (Abasaglar,Lantus,Toujeo), detemir (Levemir)

There is no evidence to demonstrate that either detemir or glargine is superior to the other. Some studies claim that weight gain is less with detemir rather than glargine but local experts generally feel that this is not significant.

Generally there is no clinical justification for the use of twice a day levemir in type 2 diabetics.

Patients should always be given a choice of device to suit their needs.

The most cost effective agent within the class should be used unless there is a strong clinical reason to use an alternative agent.

Insulin glargine (abasaglar) is the most cost effective long acting insulin analogue and is considered the first choice long acting analogue in East Kent. Abasaglar contains 100 units glargine per ml.

Toujeo is a high strength formulation of insulin glargine (300 units per ml). In East Kent use is restricted to patients requiring doses of insulin which exceed the end of their current delivery device (typically 60 to 80 units per day). Patients who experience difficulty with injections at doses greater than 40 units per day may also be considered for Toujeo on an individual patient basis

Toujeo is not bioequivalent to Lantus and is not directly interchangeable. Dose adjustment is needed when switching from Lantus or other basal insulins to Toujeo.

Switching from Lantus to Toujeo can be done on a unit for unit basis but a higher Toujeo dose may be needed to achieve target ranges for plasma glucose levels. For further information on dosing refer to the SPC (http://www.medicines.org.uk/emc/medicine/30586)

Insulin degludec (Tresiba) is not recommended for use in type 2 diabetes by NICE. Insulin degludec is NOT on the formulary in East Kent.

Xultophy (insulin degludec plus liraglutide) is NOT on the formulary in East Kent following the adoption by CCGs of a recommendation by the Policy Recommendation and Guidelines Committee that insulin degludec and liraglutide (xultophy) is not commissioned as the case for cost effectiveness vs. insulin glargine plus liraglutide was not proven.

i) Insujet

Insujet is generally not recommended as it can be quite painful to use despite being needle free. Any requests for insujet or any other needle- free device should be referred to a Diabetes Specialist Nurse (DSN).

Cost comparisons *(BNF 63 March 2012)*

NOTE – ALL INSULINS SHOULD NOW BE PRESCRIBED BY BRAND

Insulin Product	Cost and Pack Size	Cost/ml of insulin (100 units per ml)	Formulary Status
Insulatard® 10ml vial	£7.48 per 10ml vial	£0.75	On formulary
Insuman® Basal 5ml vial	£5.61 per 5ml vial	£1.12	On formulary
Humulin I® 10ml vial	£15.68 per 10ml vial	£1.57	On formulary
Lantus® (insulin glargine) 10ml vial	£30.68 per 10ml vial	£3.07	On formulary
Insuman® Basal 5 x 3ml cartridge for ClickSTAR®, Autopen® 24	**£17.50 for 5 x 3ml cartridge**	**£1.17**	**On formulary**
Humulin I® 5 x 3ml Cartridge for Autopen® Classic / HumaPen®	£19.08 per 5 x 3ml cartridge	£1.27	On formulary
Insulatard Penfill® 5 x 3ml cartridge for Novopen®	£22.90 for 5 x 3ml cartridge	£1.53	On formulary
Abasaglar (insulin glargine 100 units per ml) 5x 3ml cartridge for HumaPen Savvio	**£35.28 for 5 x 3ml cartridge**	**£2.35**	Preferred
Lantus® (insulin glargine 100 units per ml) 5x3ml cartridge for ClickSTAR®,Autopen®	£41.50 per 5 x 3ml cartridge	£2.77	On formulary for existing patients
Levemir® (insulin detemir) Penfill 5 x 3ml cartridge for NovoPen®	£42.00 per 5 x 3ml cartridge	£2.80	On formulary
Insuman® Basal Solostar® 5 x 3ml	**£19.80 for 5 x 3ml pre-filled disposable injection device**	**£1.32**	**On formulary**
Insulatard InnoLet® Prefilled Disposable Pen	£20.40 for 5 x 3ml prefilled disposable pen	£1.36	On formulary
Humulin I KwikPen® prefilled disposable pen	£21.70 for 5 x 3ml prefilled disposable pen	£1.45	On formulary
Abasaglar(insulin glargine 100 units per ml) 5 x 3ml KwikPen prefilled disposable pen	£35.28 for 5 x 3ml prefilled disposable pen	£2.35	Preferred
Lantus® (insulin glargine) SoloStar® 5 x 3ml prefilled pen	£41.50 per 5 x 3ml prefilled disposable pen	£2.77	On formulary for existing patients
Toujeo (insulin glargine 300 units per ml) SoloStar 5x 3ml prefilled pen	£33.13 for 3 x 1.5ml prefilled disposable pen	Equivalent to lantus	Restricted use – see full guidance
Levemir® (insulin detemir) Flexpen® 5 x 3ml prefilled disposable pen	£42.00 per 5 x 3ml prefilled disposable pen	£2.80	On formulary
Levemir® (insulin detemir) Innolet® 5 x 3ml prefilled disposable pen	£44.85 per 5 x 3ml prefilled disposable pen	£2.99	On formulary
Apidra (insulin glulisine) 10 ml vial	**£16.00**	**£1.60**	**Preferred**
Apidra Clikstar 5x 3ml prefilled disposable pen	**£28.30 per 5 x 3ml**	**£1.89**	**Preferred**
Apidra SoloStar 5 x 3 ml prefilled disposable pen	**£28.30 per 5 x 3ml**	**£1.89**	**Preferred**
NovoRapid (insulin aspart) 10ml vial	£16.28	£1.63	On formulary
NovoRapid Penfil cartridge 5 x 3ml	£28.31 per 5 x 3ml	£1.89	On formulary
NovoRapid FlexPen prefilled disposable pen	£32.13 per 5 x 3ml	£2.14	On formulary
Tresiba (insulin degludec) 100u and 200u flextouch disposable pen	£72.00 per 5 x 3ml £86.40 per 5 x 3ml	£4.80 N/A	Not recommened for prescribing in East Kent
Tresiba (insulin degludec) 100u cartridges	£72.00 per 5 x3ml	£4.80	
Xultophy (insulin degludec with liraglutide) disposable pen	£159.22 per 5 x 3ml	N/A	

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