Supplementary Information for Lothian Diabetes MCN
Type 2 Diabetes Prescribing Guidance for Primary Care

The Lothian Diabetes MCN prescribing guidance for primary care is a much-simplified version of the attached ADA/EASD guidelines. They are intended to illustrate the recommended treatment algorithm for adults with type 2 diabetes (T2D). However, there will inevitably be times where it is appropriate for health care professionals to deviate from the algorithm and use alternative anti-diabetic agents, e.g. if there are contra-indications to recommended medicines, concern about side effects or possible interactions. The full ADA/EASD guidance should be consulted as appropriate (along with the BNF and SPCs of relevant medicines) and advice is always available from the three diabetes centres in Lothian, through their advice email services:

SJH Clinadvdiab@nhslothian.scot.nhs.uk
WGH WGH.DiabeticAdvice@nhslothian.scot.nhs.uk
RIE RIE.DiabetecAdvice@nhslothian.scot.nhs.uk

Q: What is the basic premise of the algorithm?
A: The purpose of the algorithm is to focus prescribing in T2D around medicines that:

- are potent anti-diabetic agents
- are not associated with hypoglycaemia
- promote weight loss
- are associated with reduction in cardiovascular events
- have beneficial effects in chronic kidney disease and heart failure (SGLT2 inhibitors)

Q: What patient resources are available to support this algorithm?
A: Patient information leaflets for the recommended oral anti-diabetic agents are available to print off from the Lothian Diabetes MCN website.

NICE Guidance 2022
NICE guidance from 2022 has suggested that for people with established cardiovascular disease, chronic kidney disease (CKD) with albuminuria (specific thresholds apply*) and/or heart failure and in those with a QRISK2 Score >10%, an SGLT2 inhibitor should be commenced immediately after Metformin has been started and its tolerability confirmed. Thus, the initiation of SGLT2 inhibitors in these individuals, should occur irrespective of whether or not glycaemic targets have been reached. This approach has been endorsed in new prescribing guidelines for NHS Scotland.
*More information is available on RefHelp: Diabetes CKD – RefHelp (nhslothian.scot)

Q: What advice should be given to patients following commencement of an SGLT2 inhibitor?
A: Genital Washing
Genital thrush usually occurs early in the course of treatment with an SGLT2 inhibitor, especially when glycaemic control is poor, although realistically only 1:16 women and 1:32 men get and extra dose of thrush in a number of years.

- Initial treatment should be with topical/pessary anti-year agents
- If thrush recurs/persists, then oral fluconazole can be very effective

- There would also be no harm in pausing treatment until the infection resolves.
- Genital washing patient leaflets are available.

Sick Day Rules

SGLT2 inhibitors have also been associated with euglycaemic ketoacidosis, particularly in the context of intercurrent illness. The MCN does not currently recommend that people on SGLT2 inhibitors have blood or urine ketone test strips, but strong advice should be given to **pause** these medicines during intercurrent dehydrating illness.

Additional Patient Information Leaflets are available.

Q: Are there any concerns prescribing dapagliflozin to a patient with a low eGFR?

A: Prescribing an SLGT2 inhibitor for a patient with an eGFR of around 29 is perfectly acceptable and is a good thing. The concern should be when an eGFR is down to 25, a second opinion should be sought as it is likely the patient will need referred to the joint diabetes / renal clinic for a discussion about renal replacement therapy.

Q: Are there any concerns that SGLT2's may cause or worsen existing peripheral vascular disease (PVD)?

A: No, the Diabetes MCN would recommend putting patients with PVD on an SGLT2i where clinically appsropriate. There is a small increased risk of distal amputation on patients who already have an ulcer however, the vast majority of studies would not suggest that there is a greater risk of this. In most of the studies, PVD was an inclusion criteria. Caution and possible second opinion should be noted if the patient has and active effective ulcer.

Q: What is Rybelsus?

A:
- Rybelsus is an oral formulation of semaglutide and is recommended as the first choice GLP-1 receptor agonist.
- The initial dose is 3mg once daily, increasing automatically to 7mg once daily after 4 weeks.
- The maximum dose is 14mg once daily.
- Its special formulation means it has to be taken on a daily basis on an empty stomach with a sip of water, with nothing to eat or drink for 30 minutes afterwards. Efficacy is significantly compromised if these administration instructions are not followed.

Caution

- Semaglutide has been associated with progression of diabetic retinopathy, so should be avoided in people with pre-existing retinopathy (unless discussed and agreed with the local secondary care diabetes team).
- Caution should be taken when prescribing to patients who utilise a dosette box; oral semaglutide should taken on an empty stomach, swallowed whole with a sip of water and patients should wait at least 30 minutes before eating or drinking or taking other oral medicinal products.

Q: What is the place of injectable GLP-1 receptor agonists?

A: Injectable GLP-1 receptor agonists (e.g.dulaglatide and semaglutide) have a very important role in T2D (subject to availability). The injectable agents are likely to be more potent than Rybelsus and so are indicated if glycaemic targets have not been met on this medicine, or if patients are not able to adhere to the oral administration guidance. Injectable agents may be initiated in primary care if there is suitable staff expertise (training courses for practices are provided by the Diabetes MCN). Referral to secondary care will otherwise be required to initiate the injectable agents.

Q: Is there still a place for Gliclazide (or other sulphonylureas) in the management of T2D?

A: Gliclazide is a potent anti-diabetic agent that stimulates endogenous insulin production. It is associated with weight gain and hypoglycaemia; it is not associated with a reduction in cardiovascular disease. It remains very useful in the following situations:

- individuals with BMI <25kg/m^2 (providing type 1 diabetes has been excluded)
- significant hyperglycaemia at the time of diagnosis of T2D (providing type 1 diabetes has been excluded)
- steroid-induced diabetes or where pre-existing diabetes is worsened by steroids
- individuals with significant liver or kidney disease
- certain rare genetic forms of diabetes

Q: Is there still a place for Gliptins (e.g. Sitagliptin) and Pioglitazone?

A: Gliptins are weak anti-diabetic agents. They are weight neutral and do not reduce cardiovascular disease. They have a low side effect profile and do not cause hypoglycaemia; therefore, they have a place in the management of frail individuals, where a modest reduction in hyperglycaemia may improve osmotic symptoms. Pioglitazone is associated with weight gain, fluid retention, atypical osteoporotic fractures, and an increased risk of bladder cancer. Its role should be limited to individuals with contra-indications or intolerance to multiple anti-diabetic agents and where insulin therapy is not desirable.

Q: Should therapy be changed in individuals with stable, good glycaemic control?

A: The algorithm is primarily intended for individuals with above-target glycaemic control where escalation of therapy is indicated. It is not necessary to modify therapy in individuals who are on regimens that include agents such as Gliclazide, Gliptins or Pioglitazone if glycaemic control is at target, with no significant side effects. An exception to that is individuals with established cardiovascular disease, those at high risk of cardiovascular disease (QRISK2 score >10%), heart failure or chronic kidney disease, where a change of therapy should be considered. Additionally with canagliflozin no longer on the East Region Formulary, currently there would be no immediate need to modify therapy unless patients are having a difficulties with canagliflozin – if this was the case then a straight swap to dapagliflozin would be appropriate.

Q: What HbA1c targets should be aimed for in T2D?

A: The MCN recommends a target **HbA1c of 48 mmol/mol** for individuals managed with therapies that do not cause hypoglycaemia and a target **HbA1c of 53 mmol/mol** for individuals who require treatments that can cause hypoglycaemia (insulin and/or sulphonylureas).

Higher glycaemic targets are recommended for frail individuals - a target HbA1c of 64 mmol/mol for individuals with moderate-severe frailty and 70 mmol/mol for those with very severe frailty.

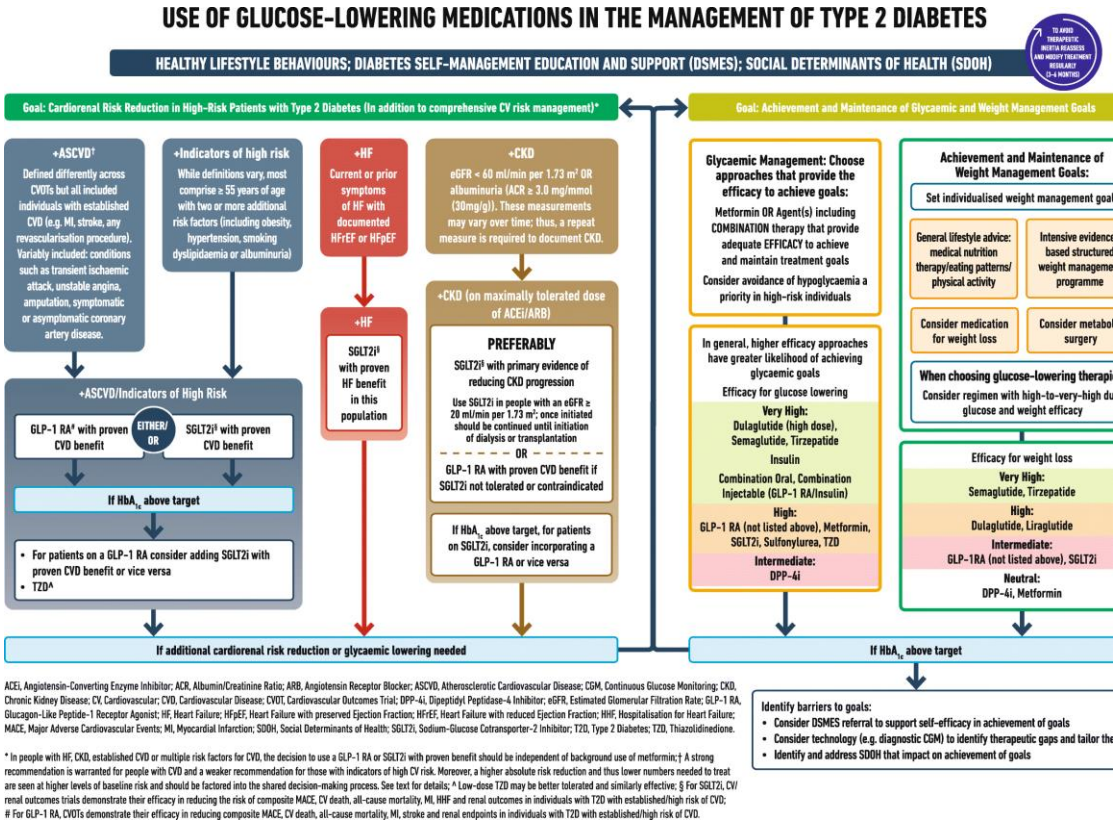
Referral to secondary care

Please see RefHelp for full referral guidance. Urgent/emergency referral is required when Type 1 diabetes is suspected and in children/young adults with a new diagnosis of diabetes.

Referral to secondary care diabetes services is likely to be needed for individuals with a BMI<25 kg/m^2, as they are likely to have a degree of insulin deficiency and the therapeutic options are more limited (usually a sulphonylurea and insulin). SGLT2 inhibitors and GLP-1 receptor agonists are contra-indicated in pregnancy (and sulphonylureas are not advised); therefore all women considering pregnancy should be referred and caution should exercised prescribing these agents in women of childbearing age (meaning that secondary care referral is also likely to be required). Referral is also indicated if there is uncertainty of the cause of diabetes or if glycaemic control is above target on maximally-tolerated oral therapy.

Q: What should we be aware of in women of childbearing age who have T2DM?

A: This issue is becoming more prevalent with more Type 2 being diagnosed in the younger population. The Diabetes MCN advises that metformin and insulin are safe in pregnancy. There is however limited data on women who have fallen pregnant whilst on oral diabetes medications and until there is more data, we should ensure that patients are aware of the limited research and discuss the use of contraception to avoid getting pregnant whilst being prescribed oral diabetes treatments.



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