Association of British Clinical Diabetologists (ABCD) and Diabetes UK joint position statement and recommendations on the use of sodium-glucose co-transporter inhibitors with insulin for treatment of type 1 diabetes (updated October 2020)

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Abstract

Dapagliflozin (sodium-glucose co-transporter (SGLT-2) inhibitor) and sotagliflozin (SGLT-1/2 inhibitor) are two of the drugs of the SGLT inhibitor class which have been recommended by the National Institute for Health and Care Excellence (NICE) in people with type 1 diabetes with body mass index ≥27 kg/m^2. Dapagliflozin is licensed in the UK for use in the NHS while sotagliflozin may be available in future. These and possibly other SGLT inhibitors may be increasingly used in people with type 1 diabetes as new licences are obtained. These drugs have the potential to improve glycaemic control in people with type 1 diabetes with the added benefit of weight loss, better control of blood pressure and more time in optimal glucose range. However, SGLT inhibitors are associated with a higher incidence of diabetic ketoacidosis without significant hyperglycaemia. The present ABCD/Diabetes UK joint updated position statement is to guide people with type 1 diabetes and clinicians using these drugs to help mitigate this risk and other potential complications. Particularly, caution needs to be exercised in people who are at risk of diabetic ketoacidosis due to low calorie diets, illnesses, injuries, starvation, excessive exercise, excessive alcohol consumption and reduced insulin administration, among other precipitating factors for diabetic ketoacidosis.

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Recommendations for use of SGLT inhibitors in type 1 diabetes

1. In the UK, one of the sodium-glucose co-transporter 2 (SGLT-2) inhibitors (dapagliflozin) is now licensed in people with type 1 diabetes with body mass index (BMI) ≥27 kg/m^2. The National Institute for Health and Care Excellence (NICE) has recommended it as an addition to insulin in people with type 1 diabetes who are not adequately controlled on insulin alone as long as BMI is ≥27 kg/m^2, insulin requirement is ≥0.5 units/kg body weight, and the treatment is started by a specialist after an educational course and stopped if the HbA_{1c} does not show a sustained drop of 0.3% or 3 mmol/mol in six months.[1] NICE has also made similar recommendations for the SGLT-1/2 inhibitor sotagliflozin, which might be available for use in the UK in future.[2] We support the NICE recommendations for managing health in people with type 1 diabetes.[3]
2. SGLT inhibitor treatment may be a useful addition to insulin treatment to lower HbA_{1c}, increase time in target glucose range and lower glucose variability. In people with BMI ≥27 kg/m^2, it may also support weight loss and lower the insulin dose without increasing the incidence of hypoglycaemia.
3. We support the recommendation from NICE that any use of SGLT inhibitors in people with type 1 diabetes must be started

and regularly supervised by a consultant physician specialising in endocrinology and diabetes treatment. HbA_{1c} levels should be assessed after 6 months of starting such treatment and regularly after that.[1]

4. People with type 1 diabetes should be actively involved in their care planning with the additional use of SGLT inhibitors to get maximum informed engagement.
5. We support the international consensus on risk management of diabetic ketoacidosis in people with type 1 diabetes treated with SGLT-2 inhibitors.[4]

- All people with type 1 diabetes should receive adequate education about how to prevent, recognise and treat diabetic ketoacidosis (DKA) reinforced with educational prompts (eg, wallet card, fridge magnets).
- People with diabetes should be advised of the precipitating factors for DKA (ie, excessive carbohydrate restriction, ketogenic diet, excessive alcohol, use of illicit drugs, surgical procedures, vigorous exercise, vomiting, acute medical illness including infections and infarctions, insulin pump failure, missed or reduced insulin doses and travel with disrupted insulin regimen/schedule).
- People with diabetes should be informed of the risks of DKA precipitated by taking SGLT inhibitors in specific situations. DKA has been reported in about 4% of people with diabetes taking SGLT inhibitors per year, particularly those in whom the insulin dose was reduced by more than 20% according to some studies. Many of these people with DKA had blood glucose levels within range or that were only mildly raised.
- We recommend temporarily suspending SGLT inhibitors before any surgical or medical procedures (at least for 24 hours) and in people with diabetes who are acutely ill, hospitalised, unable to eat or have any nausea, vomiting or abdominal discomfort.
- We recommend stopping SGLT inhibitors in patients suspected of COVID-19 infection.
- We recommend withholding SGLT inhibitors in people with diabetes whose insulin therapy is being changed (eg, injections to pump or manual mode to auto mode or automated insulin delivery).
- We recommend stopping SGLT inhibitors in people with type 1 diabetes who are not able to come for regular supervision by their specialist team.
- Inform people with diabetes that SGLT inhibitors should be used with caution in people with peripheral vascular disease or neuropathic ulcers.
- Inform people with diabetes and educate all health professionals that there have been six reports of Fournier's gangrene through the yellow card system between 2012 and January 2019 in about 550,000 person-years of treatment with SGLT inhibitors in people with diabetes in the UK. Inform people with diabetes taking SGLT inhibitors to seek immediate medical attention if they experience pain, redness, swelling or discomfort in the perineal area. The treatment may include prompt antibiotics and may require surgical debridement. Given that the absolute risk of this complication is low, clinicians should not be discouraged from using this class of drug in people with type 1 diabetes who may benefit.
- Inform people with diabetes that SGLT inhibitors can cause mild diuresis and nocturia and the importance of maintaining adequate hydration to prevent dehydration which would increase the risk of hypovolaemia. For those on concomitant diuretic therapy, the dose may need to be adjusted.
- The smallest possible dose of SGLT inhibitors (eg, dapagliflozin 5 mg daily or sotagliflozin 200 mg when available for use in the UK) should be used to minimise the risk of ketoacidosis.
- People with type 1 diabetes should be provided with a blood ketone monitor and trained to use it. Ketone test strips and appropriate meters should be provided by primary care. Blood ketones should be checked if feeling unwell, even when the capillary glucose levels are not particularly high. Blood ketones should also be measured with changes in diet, activity, insulin dose or events known to precipitate ketoacidosis such as infections, dehydration, surgery, injury, pump occlusion/malfunction or stress.
- We recommend checking blood ketones before starting SGLT inhibitors in people with type 1 diabetes. The SGLT inhibitors should be avoided if blood ketones are ≥0.6 mmol/L. Individuals may become eligible if their ketone level reduces at a later date.
- Discontinue SGLT inhibitors in people with type 1 diabetes if the ketones are above 0.6 mmol/L. Additional insulin along with carbohydrate (15–30 g rapidly absorbed) and adequate oral hydration (300–500 mL/hour) may avoid frank DKA and hospitalisation in people with diabetes with mild ketosis (0.6–1.5 mmol/L).
- People with diabetes with blood ketones above 1.6 mmol/L should seek medical attention. People with diabetes on an insulin pump should return to injectable insulin and trouble shoot the pump to ensure it is delivering insulin before they restart it. Some people with diabetes may require treatment with intravenous fluids and intravenous insulin.
- All people with diabetes should be issued a medical alert card and advised to carry it with them at all times. If hospitalisation is required for treatment of ketoacidosis, they should inform the medical personnel that they have type 1 diabetes, they are taking SGLT inhibitors and they are at risk of DKA with non-elevated glucose levels. Urine ketones may not be reliable. There should be a low threshold for evaluation by blood gases, bicarbonate, anion gap and blood ketones.
- All healthcare professionals should be educated about various SGLT inhibitors, the risk of DKA associated with this class of medication even when the glucose levels are not elevated and urine ketones are absent. Such euglycaemic DKA may require treatment with glucose as well as insulin.
- In people with type 1 diabetes with an HbA_{1c} <58 mmol/mol (7.5%), 10–20% insulin dose reduction may be needed when SGLT inhibitors are started but this should be accompanied by frequent capillary blood glucose (CBG) monitoring or continuous glucose monitoring (CGM) along with easy access to a healthcare provider. Carbohydrate intake may need to be

flexibly increased or decreased to avoid excessive or inadequate reduction in insulin dose.
- SGLT inhibitors are not suitable for people with diabetes on very low insulin doses. We suggest an insulin requirement of at least 0.5 IU/kg body weight before considering adding SGLT inhibitors. Adjustment in insulin doses should be made every 24–48 hours.
- For people with diabetes with an HbA_{1c} ≥58 mmol/mol (7.5%), no reduction in prandial or basal insulin may be necessary based on CBG, CGM data, hypoglycaemia history and awareness.
- SGLT inhibitors should not be used in pregnancy as pregnancy is associated with an increased risk of ketoacidosis which is known to be associated with a higher risk of fetal mortality. There are insufficient data in relation to the use of SGLT inhibitors in pregnancy. In women of reproductive age with type 1 diabetes, SGLT inhibitors should not be used if there is a risk of pregnancy.
- Insufficient data are currently available to advocate use in people with type 1 diabetes aged <18 years or >75 years.

SGLT inhibitors and current licensed indications

SGLT inhibitors are an established class of drugs which effectively lower glucose levels in people with type 2 diabetes, with additional cardiac and renal benefits. These drugs reduce blood glucose by preventing renal reabsorption of glucose, a mechanism which is insulin independent but glucose dependent.[5] An additional positive effect on lowering blood pressure by natriuresis and weight loss might partly mediate the cardiovascular benefit recently observed in clinical trials in people with type 2 diabetes, although other mechanisms are possible.[6–9] Dapagliflozin was the first SGLT-2 inhibitor to be approved for use in Europe in 2011 and in the UK in 2012. NICE has also approved the use of add-on dapagliflozin in people with type 1 diabetes with BMI ≥27kg/m^2 when insulin alone is not sufficient to manage their diabetes, as long as their insulin requirement is at least 0.5 units/kg body weight. The medication can be continued as long as it results in sustained reduction in HbA_{1c} of 3 mmol/mol (0.3%) after 6 months.[1] There are currently four SGLT-2 inhibitors licensed in the UK: dapagliflozin, canagliflozin empagliflozin and ertugliflozin. Only dapagliflozin has obtained a licence for use in people with type 1 diabetes in the UK. Sotagliflozin is a dual SGLT-1 and 2 inhibitor and has had a favourable NICE technology appraisal guidance but is not yet available in the UK.[2] These developments have prompted an update of the previous position statements.[10,11] This update is in accordance with the RIGHT statement for practice guidelines.[12] The term SGLT has been used when relating to both SGLT-2 and dual SGLT-1/2 inhibitors, whereas SGLT-2 has been used when the intention is to refer to SGLT-2 inhibitors only.

We searched PubMed, Google Scholar, Cinahl and Embase databases with the search words 'SGLT inhibitors' AND 'type 1 diabetes' and recent meta-analyses from 2020 were included for up-to-date evidence to the information already available in the previous version of the position statement. The evidence and recommendations were shared widely amongst the writing group and consensus was obtained electronically. The views and preferences were sought from people with type 1 diabetes selected from personal contacts and changes were made where appropriate. The limitation of these recommendations is that evidence can change quickly in this area and therefore regular update may be required.

Potential role in type 1 diabetes

Optimal management of type 1 diabetes remains a challenge in the UK. Recent data show that the percentage of people achieving the NICE recommended targets (ie, HbA_{1c} <58 mmol/mol (7.5%), blood pressure <140/80 mmHg, cholesterol <5 mmol/L) is 32.1%, 73.1% and 72.8%, respectively. All three targets combined were achieved in only 20.1% of the people.[3,13,14]

There are considerable data showing higher cardiovascular[15,16] and renal risk[17] in people with type 1 diabetes. There is therefore scope for achieving tight glycaemic management with appropriate insulin therapy and any potential adjunct therapy for people with type 1 diabetes that may help improve risk factor and/or cardiovascular and renal outcomes.

Our previous ABCD position statements outline the standards of care for people with type 1 diabetes.[18,19] Intensified insulin therapy is often used to manage hyperglycaemia in people with type 1 diabetes on the basis of studies which showed a link between hyperglycaemia and micro and macrovascular complications of diabetes.[20] This intensification, however, may increase the risk of hypoglycaemia, weight gain and associated adverse cardiovascular profile.[21]

Metformin is inexpensive and useful in some people with type 1 diabetes with BMI ≥25 kg/m^2, but it does not improve HbA_{1c} in the long term.[22,23] Compared with metformin at week 26, SGLT inhibitors like dapagliflozin (5 mg), sotagliflozin (200 mg) and empagliflozin (10 mg) had greater reductions in HbA_{1c} (MD –3 mmol/mol (–0.24%), –3 mmol/mol (–0.23%) and –4 mmol/mol (–0.35%), respectively) and weight.[24]

GLP-1 analogues and receptor agonists may be helpful in subgroups of people with type 1 diabetes, but the reductions in HbA_{1c} are modest (MD –3 mmol/mol (–0.24%) with liraglutide 1.8 mg) although weight reductions were significant (4.87 kg with liraglutide 1.8 mg), insulin dose reduced, hypoglycaemia reduced but not significantly (OR 0.80) and gastrointestinal adverse events increased significantly (OR nausea 4.70, vomiting 2.50).[25,26] Dipeptidyl peptidase-4 (DPP4) inhibitors added to insulin did result in a small but insignificant reduction in HbA_{1c} (1 mmol/mol (0.07%)) and no consistent effect on glucose variability in people with type 1 diabetes.[27] By contrast, SGLT inhibitors are oral glucose-lowering drugs with potential as long as they are used appropriately.[28,29]

Evidence for SGLT inhibitors in type 1 diabetes

There is considerable emerging evidence for use of SGLT inhibitors in people with type 1 diabetes. The initial studies which formed the basis of evidence are summarised in brief in Table 1. Details of subsequent studies are not included in this paper as they have not influenced the position paper. More recent meta-analyses, however, are outlined in the paragraphs below.[30–37]

Table 1 Summary of evidence for SGLT-2 inhibitors in type 1 diabetes

Author year	Participant features Age (years) BMI (kg/m^2) (n)	Type of study and duration	SGLT-2 inhibitor used vs. placebo plus insulin	Results	DKA (where reported)
Henry[30] 2015	Age 18–65 BMI 24.8 (70)	RCT (2 weeks)	Dapagliflozin 10 mg	↑ Urine glucose (109.10 g/24 h). No increase in hypoglycaemia	None
Pieber[31] 2015	Age 18–65 BMI 25.7 (75)	RCT (4 weeks)	Empagliflozin 25 mg	↓ Insulin dose (–0.98 IU). No increase in hypoglycaemia ↑ Ketones in 2 individuals (not an adverse event)	None
Dandona[32] 2017	Age 18–75 BMI 28.3 (833)	RCT (24 weeks)	Dapagliflozin 5 and 10 mg	↓ HbA_{1c} (–0.42% and –0.45%) ↓ Insulin dose (–8.8% and 13.2%) ↓ Body weight (–2.96% and 3.72%) No increase in hypoglycaemia (79%, 79% and 80%)	Similar in all groups 5 mg: 4/277 10 mg: 5/296 Placebo: 3/260 In people who had DKA insulin dose reduction vs. placebo in the above groups was –8.9%, –25.3% and –7.8% at the time of DKA.
Famulla[33] 2017	Age 18–65 BMI 18.5–35 (75)	RCT (4 weeks)	Empagliflozin 2.5, 10 and 25 mg	↓ Mean glucose under the median continuous glucose monitoring curve (–12.2, –30.3 and –33.0 mg/dL/h) ↓ Glucose variability	None
Rodbard[34] 2017	Age 25–65 BMI 21–35 (351)	RCT (18 weeks)	Canagliflozin 100 and 300 mg	↓ Mean glucose (–1.2, –0.7) with more time spent within target glucose range than outside	
Henry[35] 2015	Age 25–65 BMI 21–35 (351)	RCT (18 weeks)	Canagliflozin 100 and 300 mg	↑ Proportion of participants achieving HbA_{1c} reduction of over 0.4% without any increase in body weight (36.9% and 41.4% vs. 4.5%)	↑ DKA (4.3% and 6% vs. 0)
Biester[36] 2017	Age 12–21 BMI 18–35 (33)	Randomised crossover single-dose study (24 hours)	Dapagliflozin 10 mg	↓ Insulin dose (13.6%) and ↑ in glucose excretion (610%) irrespective of baseline HbA_{1c}	None. 5 treated with dapagliflozin vs. 1 placebo-treated participant had ↑ in betahydroxybutyrate levels
Dandona[37] 2018	Mean age 41.9, 42.7 BMI 28.4, 28.2 (747)	RCT (52-week extension from 24-week study)	Dapagliflozin 5 mg, 10 mg	↓ HbA_{1c} (–0.33% and –0.36%) ↓ Body weight (–2.95% and –4.54%) No increase in hypoglycaemia	↑ DKA (4.0% and 3.4% with dapagliflozin 10 and 5 mg vs 1.9% with placebo)

CBG, capillary blood glucose; DKA, diabetic ketoacidosis; RCT, randomised controlled trial

In a recent meta-analysis including over 7000 participants and 17 randomised controlled trials (RCTs), SGLT inhibitor therapy significantly reduced HbA_{1c} (4 mmol/mol (0.37%)) and body weight (2.88 kg).[38]

In another meta-analysis of seven RCTs, lower HbA_{1c} (–3 mmol/mol (–0.28%)), lower insulin dose (MD –0.89) and greater weight loss (–3.03) without any significant difference in hypoglycaemia[39] was seen in the sotagliflozin group.

The European Medicines Agency has accepted the application of a marketing authorisation variation for dapagliflozin for use as an oral adjunct treatment to insulin in people with type 1 diabetes.[40]

In a further RCT from a single centre, 30 people with type 1 diabetes on liraglutide and insulin were put on additional dapagliflozin or placebo.[41] In the dapagliflozin group, HbA_{1c} fell by 7 mmol/mol (0.66%) from 7.8% with no change ($p<0.01$) in the placebo group over 12 weeks.

Cautions in prescribing SGLT inhibitors in type 1 diabetes

Adverse effects of SGLT inhibitors

In a systematic review and meta-analysis of seven RCTs including 3,900 participants in comparison to the placebo group, the risk of genital infection (RR 3.22) and DKA (RR 2.66) was higher in the SGLT inhibitor-treated group.[42]

In another evaluation of the safety of SGLT-2 inhibitors covering 1,653 articles including eight RCTs, compared with

placebo, the SGLT-2 inhibitor group was found to have an increased incidence of DKA (OR 4.34), genital infections (OR 3.64), volume depletion (OR 2.10) and diarrhoea (OR 1.64). The risk of diarrhoea was dose-related. There was no increase in the incidence of urinary tract infections, cardiovascular events, renal events, liver injury and fractures.[43]

In a meta-analysis of 13 RCTs including 7,962 participants, there was a higher risk of DKA (RR 5.04), urinary tract infections (RR 1.2) and genital infections (RR 2.99) but not hypoglycaemia.[44]

Sotagliflozin meta-analysis of seven RCTs including nearly 3,600 participants showed a higher rate of DKA (RD 0.03) and genital mycotic infections (RD 0.06) but no increase in urinary tract infections compared with placebo.[39]

People with type 1 diabetes develop DKA in the absence of insulin. Insulin helps reduce glucose but also prevents lipolysis. SGLT inhibitors reduce glucose but have been associated with reports of DKA in people with type 1 diabetes and some people with type 2 diabetes through mechanisms which are not fully understood. The current evidence is presented below.

A study based on the US Food and Drug Administration Adverse Event Reporting System (FAERS) showed that the proportional reporting ratio of DKA in people on SGLT inhibitors was 7.9, was higher for type 1 diabetes and women, in a wide range of age and body weight. Duration of treatment varied and death was reported in 37 individuals (1.54%).[45]

Peters *et al* reported a series of case reports of DKA in people taking SGLT inhibitors. Thirteen cases of DKA were observed in nine people. Seven people had type 1 diabetes and two had type 2 diabetes. Four people had repeat episodes.[46]

A post-hoc re-evaluation of 17,000 participants in a canagliflozin development programme has been reported. Twelve cases of DKA were reported, four (0.07%) in the canagliflozin 100 mg group, six (0.11%) in the canagliflozin 300 mg group and two (0.03%) in the placebo comparator group. Six of the participants (50%) were reported to have either type 1 diabetes or latent autoimmune diabetes of adults (LADA).[47]

Another study by Perkins *et al* was an 8-week open-label proof of concept trial using SGLT-2 inhibitors in type 1 diabetes. Two of the 40 participants with type 1 diabetes (5%) had symptomatic ketosis or DKA.[48]

Putative mechanism of ketogenesis

A small but not insignificant rise in the incidence of DKA in people taking SGLT inhibitors is poorly understood. Several mechanisms have been suggested including excessive dose reduction of insulin, pre-existing propensity to DKA, reduced ketone excretion and shift in substrate metabolism with increased reliance on free fatty acids and ketone bodies rather than glucose and pyruvate.[49,50]

There is also a possibility that ketogenesis could occur due to the direct action of SGLT inhibitors on human pancreatic alpha cells increasing glucagon secretion.[51,52] As the glucose concentration can be closer to target levels, and as the urine ketones may not always be raised in some individuals, the diagnosis of DKA can be delayed or missed.

Effect of insulin dose reduction on ketosis

Insulin deficiency seems to be related to ketoacidosis in people with type 1 diabetes taking SGLT inhibitors. A post-hoc exploratory analysis has shown that ketone formation is increased when insulin dose reduction is >20% compared to when it is <20%.[53] Similarly, insulin pump failure and missed insulin doses were the most frequent risk factors in the cases of DKA seen in another study.[32] In another small study in people with type 1 diabetes using liraglutide and SGLT-2 inhibitors, two developed DKA. Both participants had a reduction in insulin dose >20% and both events occurred within 48 hours dose titration of dapagliflozin from 5 mg to 10 mg daily.[41] In addition, one participant had consumed a large amount of alcohol which is likely to be a factor in the development of euglycaemic ketoacidosis.

Risk of amputations and stroke

The risk of amputations and stroke remains unclear with the available current evidence in people with type 1 or type 2 diabetes. Canagliflozin in people with type 2 diabetes was associated with a higher rate of lower limb amputations mainly at the level of the toe and metatarsals.[8] There was a higher rate of fractures in the CANVAS study but not in the CANVAS-R study.[8] A recent meta-analysis has confirmed an excess risk of amputations with canagliflozin but not with other SGLT-2 inhibitors.[54] In a meta-analysis covering 12 RCTs and 18 observational studies, there was no significant association between SGLT inhibitor exposure and amputations, although there was an increased risk noted in the subgroup analysis with canagliflozin (n=2 RCTs, RR 1.59) but not with other gliflozins.[55] Another meta-analysis of five RCTs involving 21,395 participants on SGLT inhibitors has shown no significant increase in the risk of amputation (OR 1.31, NS) with any SGLT inhibitors including canagliflozin. Another trial level meta-analysis of six studies involving 51,713 participants with an event rate of amputation of 2.0% showed no significant association of empagliflozin, dapagliflozin or canagliflozin compared with controls (RR 1.24) including subgroups with or without peripheral artery disease.[56] A real-world evidence study looking at lower limb amputation in over 700,000 people in the USA also concluded that there was no increase in the risk of lower limb amputation with canagliflozin compared with other SGLT inhibitors or with non-SGLT inhibitor diabetes drugs in either the overall population or in the subset of people with established cardiovascular disease.[57] National advice from European, American and UK professional bodies and regulators is to be cautious with the use of all SGLT inhibitors in people with active foot disease as there may be a possible adverse class effect on foot health.[58–62]

Numerically, empagliflozin increased but canagliflozin reduced strokes in people with type 2 diabetes, although both were not significant and a subsequent meta-analysis is reassuring.[6,8,63,64]

Risk during COVID-19

SGLT inhibitors would theoretically be a high-risk strategy given the increased risk of DKA in unwell people with type 1 diabetes

Key messages

- Dapagliflozin (SGLT-2 inhibitor) and sotagliflozin (SGLT-1/2 inhibitor) have been recommended by the National Institute for Health and Care Excellence in people with type 1 diabetes with BMI ≥27 kg/m^2 when insulin alone is not sufficient for diabetes control and the insulin requirement is at least 0.5 units/kg of body weight
- SGLT inhibitors should only be started under supervision of a consultant physician specialising in endocrinology and diabetes after a structured educational programme for the person with type 1 diabetes including comprehensive information on diabetic ketoacidosis
- Such combination therapy can continue if there is sustained reduction in HbA_{1c} of at least 3 mmol/mol after 6 months
- Dapagliflozin is licensed in the UK for use in the NHS while sotagliflozin may be available in the future

infected with COVID-19. However, the potential benefits on heart and kidneys might make them useful in some patients. Further clinical trials will help us in this area.[65,66] The risks and benefits of SGLT use should be discussed with the person with diabetes as part of a care planning approach to consider individual circumstances and considerations.

Conclusions

Dapagliflozin is currently licensed and dapagliflozin and sotagliflozin are both recommended as an add-on therapy in people with type 1 diabetes with BMI ≥27 kg/m^2 in whom insulin alone is not sufficient to manage their diabetes.

SGLT inhibitors are tolerated well with very few side effects (eg, urinary and genital infections, dehydration and DKA). In general, the rate and prevalence of DKA in people with type 1 diabetes taking SGLT inhibitors is too low to quantify exactly, but may not be insignificant. In people with type 1 diabetes taking SGLT inhibitors, it would make pragmatic sense to anticipate and monitor for possible DKA in situations known to precipitate metabolic decompensation (eg, injury, infections, myocardial infarction, stroke, insulin deficiency, ketogenic diet, surgery, other stressful events and catabolic states). There should be prompts to identify individuals attending Emergency Departments or Medical Admissions Units who are prescribed SGLT inhibitors to warn of the possibility of euglycaemic DKA where the individual may be in diabetic ketoacidosis despite non-elevated glucose levels and low urine ketones. SGLT inhibitors should be stopped in people who are acutely ill or are admitted for elective surgery. SGLT inhibitors should also be discontinued in people who have developed DKA and should not be re-started unless a clear alternative cause of DKA is identified. Insulin doses should not be reduced more than 20% if SGLT inhibitors are added to insulin regimens.

It is recommended that regular monitoring of blood glucose and ketones should be undertaken in people with diabetes taking these drugs to avoid hypoglycaemia as well as ketosis. This Joint ABCD/Diabetes UK position statement will be reviewed following publication of any further evidence and research studies.

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