AMBER RETAINED

NHS
Pan Mersey
Area Prescribing Committee

Pathway for addition of SGLT2 inhibitors to insulin therapy for patients with type 1 diabetes

Aims of treatment

- Reduction in HbA1c without increasing risk of hypoglycaemia
- Reduction in glucose variability
- Lower risk of diabetes complications due to improved glycaemic control (time in target)
- Minimise the risk of diabetic ketoacidosis (DKA) - the risk may be increased 5 to 15X in people with type 1 diabetes

Patient selection by consultant physician (diabetes and endocrinology) ONLY

Inclusion criteria (all apply)	Exclusion criteria	Additional surveillance/ baseline measures
• Adults 18-74 years • Type 1 diabetes • BMI ≥27 kg/m^2 • eGFR ≥60mL/min/ • Optimised insulin (MDI or insulin pump) • Insulin requirement ≥0.5 units/kg/day • HbA1c >60 and <86mmol/mol • Motivated patient to engage with pathway • Regular glucose monitoring • Willingness to measure blood ketones as advised • Willingness to take corrective action if raised blood ketones	• BMI <27 kg/m^2 • Pre-pregnancy planning /pregnancy/breast feeding • Low insulin requirement < 0.5 units/kg /day (suspect honeymoon period/concordance with medication) • Recent /recurrent DKA • Acute illness • Excess alcohol consumption/illicit drugs • Unable to monitor blood ketones and capillary blood glucose • Low calorific diet or ketogenic diet • Erratic diet with inconsistent calorific intake • Frequent non-attendance at clinic	• Baseline assessment • Renal function • HbA1c • Weight • Total daily insulin dose • DKA risk • Foot ulcers • Time in target if Libre/CGM • Frequency of hypoglycaemia

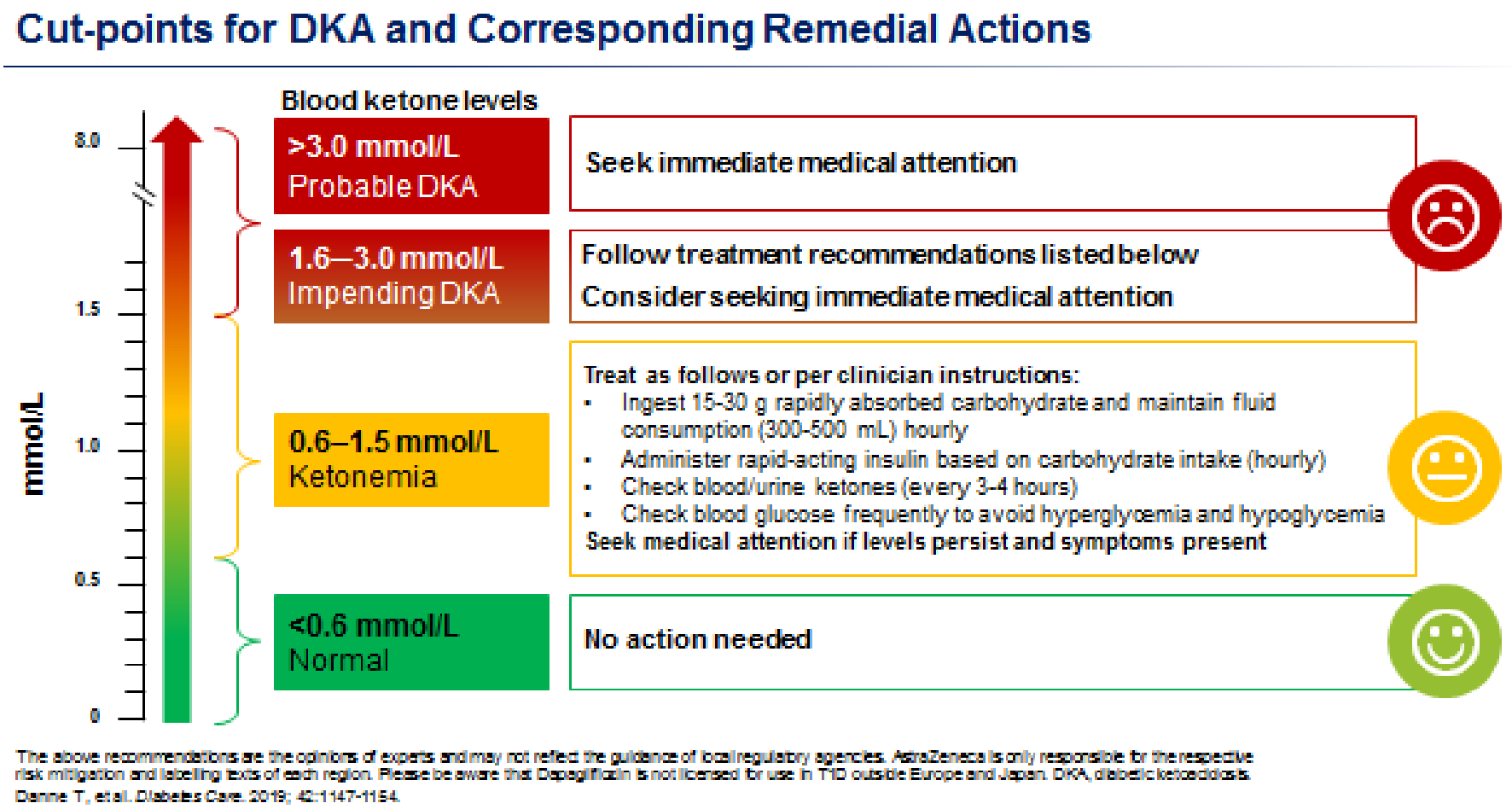
If appropriate for SGLT2 initiation refer to DSN and Specialist Dietitian

Visit 1: DSN and Dietitian Assessment	**Education**	**Notes**
• Assessment / education of risk factors for DKA • Exclude pregnancy (verbal confirmation) • Monitoring of **blood** ketones levels • Revision of insulin pump education with special consideration of DKA risk • programme • Dietary assessment by specialist dietitian	• Provision of approved combined glucose/ketone meter • Completion of structured education on the risk of DKA, how to recognise DKA risk factors, signs or symptoms, how and when to monitor ketone levels and what actions to take at elevated ketone readings • Provide treatment local protocol for addressing ketosis (see appendix 1) • Sick day management • Specific education if on insulin pump	***People with Type 1 diabetes using an insulin infusion pump have a higher risk of DKA*** • Should be experienced with pump use, common trouble-shooting strategies when interruptions of insulin delivery via pump occur (e.g. issues with insertion site, clogged tubing, empty reservoir, etc.) • Should use supplemental insulin injections with pen or syringe as needed in case of pump failure • Consider monitoring ketone levels 3 to 4 hours after changing pump materials • check their ketone levels with any suspected insulin interruption, regardless of blood glucose levels • Insulin injections should be given within 2 hours of an unexplained high blood glucose/ketone value and SGLT2 treatment should be interrupted
Visit 2: DSN Initiation of treatment	**Education**	**Notes**
• Review of recent blood glucose/ketone monitoring • Evidence of several baseline ketone level readings over 1 to 2 weeks prior to initiation of SGLT2i • Ensure hospital prescription of SGLT2 available for **6 weeks** supply	• Dose adjustment of first mealtime bolus up to 20% reduction • Reduction in basal insulin is not recommended when initiating SGLT2. Subsequently, basal insulin should be adjusted based on blood glucose results • SGLT2 treatment should be interrupted in patients who are hospitalised for	• Basal insulin should be adjusted based on blood glucose results • Urgent advice contact details Do not initiate SGLT2 if: • Pre-pregnancy planning/pregnancy • Significant drop in insulin requirement • Acute illness/major surgery • Worsening of renal function

	major surgical procedures or acute serious medical illnesses • STICH or STOP-DKA protocol as per local preference (see appendix 2) • Hypoglycaemia treatment and management	• New onset foot ulceration • Blood ketones >0.6 mmol/L
Visit 3: DSN and Dietitian **Review of treatment at 1 month**	**Education**	**Notes**
• Review of recent blood glucose/ketone monitoring • Frequency of follow up by DSN agreed including telephone contact	• Reassess insulin: carbohydrate ratios and insulin sensitivity factor once the patient is stabilised on the SGLT2 inhibitor • Sick day management	**Write to GP with outcome of review and request GP to start prescribing SGLT2 as regular medication** Discontinuation of SGLT2 if any of the following: • Pre-pregnancy planning/pregnancy • Significant drop in insulin requirement • Acute illness/major surgery • Worsening of renal function • New onset foot ulceration • Recurrent ketonaemia > 1.5 mmol/L without precipitating cause
Visit 4: DSN **Review of treatment at 3 months**	**Education**	**Notes**
• Review of recent blood glucose/ketone monitoring • Frequency of follow up by DSN agreed including telephone contact	• Reassess insulin: carbohydrate ratios and insulin sensitivity factor once the patient is stabilised on the SGLT inhibitor • Sick day management	Discontinuation of SGLT2 if any of the following: • Pre-pregnancy planning/pregnancy • Significant drop in insulin requirement • Acute illness/major surgery • Worsening of renal function • New onset foot ulceration • Recurrent ketonaemia > 1.5 mmol/L without precipitating cause

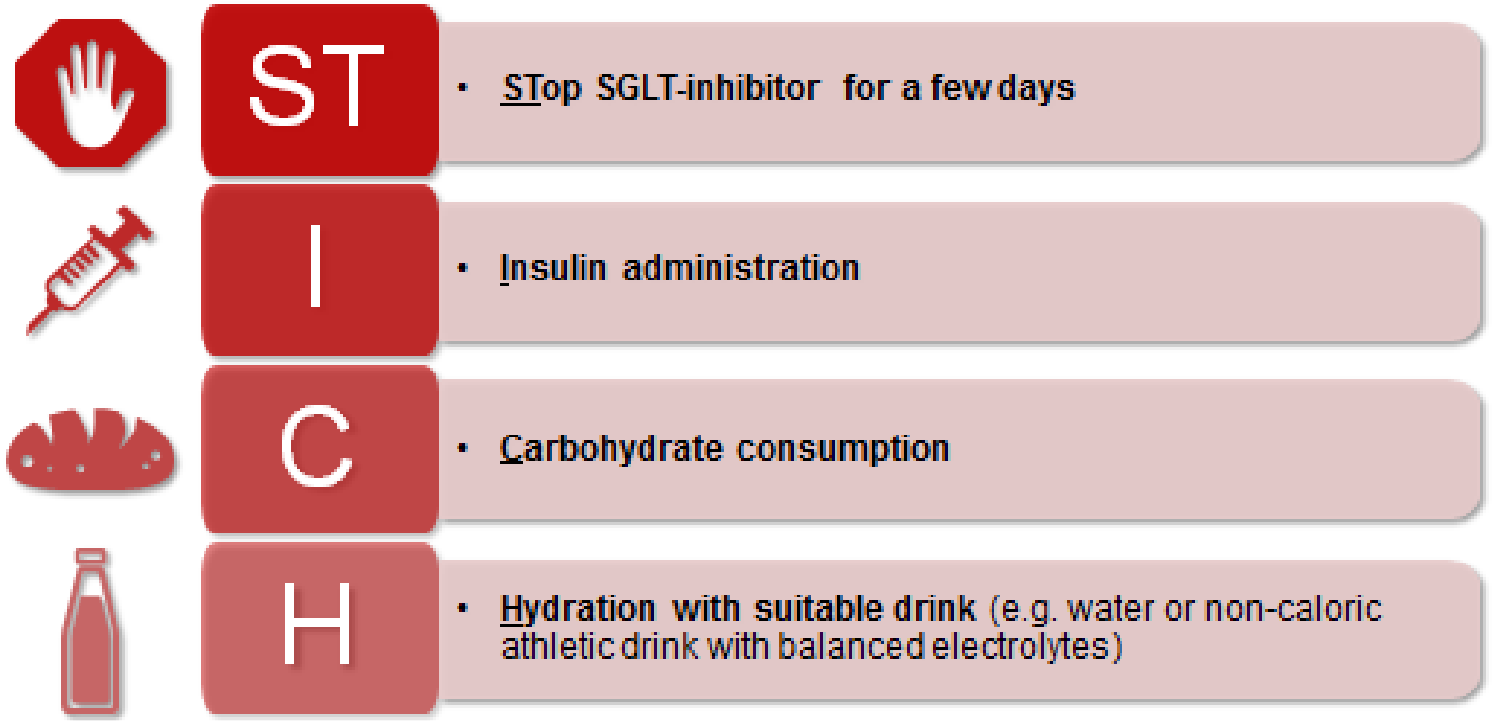
6 Month reassessment/review - Consultant (or speciality doctor with delegated responsibility, working within a consultant-led clinic)		
• Renal function • HbA1c (discontinue SGLT2 if less than 3 mmol/mol improvement) • Weight • Total daily insulin dose • DKA risk • Foot ulcers		Discontinuation of SGLT2 if any of the following: • Less than 3mmol/mol improvement in HbA1c • Pre-pregnancy planning/pregnancy • Significant drop in insulin requirement • Acute illness/major surgery • Worsening of renal function • New onset foot ulceration • Recurrent ketonaemia > 1.5 mmol/L without precipitating cause

Appendix 1


Cut-points for DKA and Corresponding Remedial Actions
Blood ketone levels
mmol/L
8.0
1.5
1.0
0.5
0
>3.0 mmol/L
Probable DKA
1.6–3.0 mmol/L
Impending DKA
0.6–1.5 mmol/L
Ketonemia
<0.6 mmol/L
Normal
Seek immediate medical attention
Follow treatment recommendations listed below
Consider seeking immediate medical attention
Treat as follows or per clinician instructions:
• Ingest 15-30 g rapidly absorbed carbohydrate and maintain fluid consumption (300-500 mL) hourly
• Administer rapid-acting insulin based on carbohydrate intake (hourly)
• Check blood/urine ketones (every 3-4 hours)
• Check blood glucose frequently to avoid hyperglycemia and hypoglycemia
Seek medical attention if levels persist and symptoms present
No action needed
The above recommendations are the opinions of experts and may not reflect the guidance of local regulatory agencies. AstraZeneca is only responsible for the respective risk mitigation and labelling texts of each region. Please be aware that Dapagliflozin is not licensed for use in T1D outside Europe and Japan. DKA, diabetic ketoacidosis.
Danne T, et al. Diabetes Care. 2019; 42:1147-1154.

Appendix 2

STICH Protocol – Recommended Treatment Strategies



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DKA, diabetic ketoacidosis; SGLT, sodium-glucose cotransporter.

Danne T, et al. *Diabetes Care*. 2019; 42:1147-1154.