SHARED CARE GUIDELINE

Drug: Dapagliflozin

For the treatment of insufficiently controlled type 1 diabetes mellitus as an adjunct to insulin in adults with BMI ≥ 27 kg/m2, when insulin alone does not provide adequate glycaemic control despite optimal insulin therapy

Introduction	**Indication:**
	
	This shared care agreement applies to the use of dapafliflozin in accordance with NICE TA 597 **ONLY.**
	
	NICE TA 597
	
	NICE recommends the licensed use of dapagliflozin only if:
	• patients are on insulin doses of 0.5 units/kg of body weight/day or more and
	• patients have completed a structured education programme that is evidence based, quality assured, delivered by trained educators and includes information about diabetic ketoacidosis, such as:
	  ○ how to recognise its risk factors, signs and symptoms
	  ○ how and when to monitor blood ketone levels
	  ○ what actions to take for elevated blood ketones and
	• treatment is started and supervised by a consultant physician specialising in endocrinology and diabetes treatment, and haemoglobin A1c (HbA1c) levels are assessed after 6 months and regularly after this.
	
	Background to shared care arrangements:
	
	The best interest, agreement and preferences of the patient should be at the centre of any shared care agreement and their wishes followed wherever possible. Patients should be able to decline shared care if, after due consideration of the options, they decide it is not in their best interests.
	Please note:
	• **The provision of shared care prescribing guidelines does not necessarily mean that the GP must agree to and accept clinical and legal responsibility for prescribing; they should only do so if they feel clinically confident in managing that condition.**
	
	• **Referral to the GP should only take place once the GP has agreed to this in each individual case, and the hospital or specialist will continue to provide prescriptions until a successful transfer of responsibilities has occurred. The GP should confirm the agreement and acceptance of the shared care**

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	prescribing arrangement and that supply arrangements have been finalised. The secondary/tertiary provider must supply an adequate amount of the medication to cover the transition period. The patient should then be informed to obtain further prescriptions from the GP. **This shared care guideline excludes the use of dapagliflozin for the following indications:** Triple therapy for treating type 2 diabetes (NICE TA418), combination therapy for treating type 2 diabetes (NICE TA288) and monotherapy for treating type 2 diabetes (NICE TA390)
Form	Oral tablet
Dose and administration (please refer to BNF / SPCs for full details)	Treatment with dapagliflozin is to be initiated and supervised by specialists in type 1 diabetes. The recommended dose is 5 mg once daily (10 mg are not licensed for use in type 1 diabetes). Dapagliflozin must only be administered as an adjunct to insulin.
Common Adverse Effects (please refer to BNF / SPCs for full details)	**Please refer to the SPC or BNF for full list.** **Common (≥ 1/100 to < 1/10) or very common (≥ 1/10)** Back pain; balanoposthitis; diabetic ketoacidosis (discontinue immediately); dizziness; dyslipidaemia; hypoglycaemia (in combination with insulin or sulfonylurea); increased risk of infection; rash; urinary disorders. **Uncommon (≥ 1/1,000 to < 1/100)** Constipation; dry mouth; genital pruritus; hypovolaemia; thirst; vulvovaginal pruritus; weight decreased. **Rare (≥ 1/10,000 to < 1/1,000) or very rare (< 1/10,000)** Angioedema; Fournier's gangrene (discontinue and initiate treatment promptly).
Contraindications / Cautions (please refer to BNF / SPCs for full details)	**Contraindications** Hypersensitivity to the dapagliflozin or any of its excipients. **Cautions** • **Renal function** - The glycaemic efficacy of dapagliflozin is dependent on renal function, and efficacy is reduced in patients who have moderate renal impairment and is likely absent in patients with severe renal impairment. Dapagliflozin should not be initiated in patients with a eGFR < 60 mL/min and should be discontinued at eGFR persistently below 45 mL/min. • **DKA** - Dapagliflozin should be used with caution in patients with increased risk of DKA. Patients who may be at higher risk of DKA include patients with a low beta-cell function reserve (e.g. type 1 diabetes patients, or patients with a history of pancreatitis), patients with conditions that lead to restricted food intake or severe dehydration, patients for whom insulin doses are reduced and patients with

	increased insulin requirements due to acute medical illness, surgery or alcohol abuse.- • **Volume depletion and/or hypotension** - Caution should be exercised in patients for whom a dapagliflozin-induced drop in blood pressure could pose a risk, such as patients on anti-hypertensive therapy with a history of hypotension or elderly patients. In case of intercurrent conditions that may lead to volume depletion (e.g. gastrointestinal illness), careful monitoring of volume status (e.g. physical examination, blood pressure measurements, laboratory tests including haematocrit and electrolytes) is recommended. Temporary interruption of treatment with dapagliflozin is recommended for patients who develop volume depletion until the depletion is corrected. • **Hepatic function** - Dapagliflozin exposure is increased in patients with severe hepatic impairment. • **Insulin therapy** - Insulin therapy should be continuously optimised. When needed to prevent hypoglycaemia, insulin dose reduction should be done cautiously to avoid ketosis and DKA. In the event of a marked reduction of insulin need, discontinuation of dapagliflozin should be considered. • **Necrotising fasciitis of the perineum (Fournier's gangrene) -** Patients should be advised to seek medical attention if they experience a combination of symptoms of pain, tenderness, erythema, or swelling in the genital or perineal area, with fever or malaise. Uro-genital infection or perineal abscess may precede necrotising fasciitis. If Fournier's gangrene is suspected, dapagliflozin should be discontinued and prompt treatment should be instituted. • **Urinary tract infections -** Urinary glucose excretion may be associated with an increased risk of urinary tract infection; therefore, temporary interruption of dapagliflozin should be considered when treating pyelonephritis or urosepsis. • **Lower limb amputations -** An increase in cases of lower limb amputation (primarily of the toe) has been observed with another SGLT2 inhibitor. Like for all diabetic patients it is important to counsel patients on routine preventative foot care.
Potentially Serious Drug Interactions (please refer to BNF / SPCs for full details)	**Diuretics** - Dapagliflozin may add to the diuretic effect of thiazide and loop diuretics and may increase the risk of dehydration and hypotension. **Insulin** - In patients with a known risk of frequent or severe hypoglycaemia, it may be necessary to reduce the insulin dose at the time of initiating treatment with dapagliflozin to decrease the risk of hypoglycaemia. When needed, insulin dose reduction should be done cautiously to avoid ketosis and DKA.
Secondary Care Responsibilities	1) Record the person's preferences and concerns in their treatment plan. Patients should be able to decline shared care if, after due consideration of the options, they decide it is not in their best interests. Patients should provide explicit consent and this should be recorded in both the patients notes and on the shared care agreement form. 2) Provide information about the medication to patients, including common side effects, necessary monitoring, and where that monitoring will take place. Also, to keep the patient informed of the process at all stages to ensure continuity of treatment.

	3) Retain prescribing for three-months. During this period all necessary physical health monitoring should be conducted, including effectiveness of the medication and adverse effects, which should be document in the person's notes. 4) Continue to provide prescriptions until a successful transfer of responsibilities to the GP has occurred. The secondary/tertiary provider must supply an adequate amount of the medication to cover the transition period. With consent of the patient, the shared care template letter or equivalent information should forwarded in a timely manner to the patients GP. 5) Once shared care has been agreed the patient should then be informed to obtain further prescriptions from the GP after the transition period and must be made fully aware of all necessary monitoring requirements. 6) Review the patient at six-months post initiation as per NICE TA 597. 7) Conduct an annual face to face medication review for all patients covered by this shared care guidance. 8) Contact the GP within 3 days of a patient missing a specialist face to face appointment to advise whether treatment should be withheld. 9) Accept referrals back from primary care for medication discontinuation. 10) Resume prescribing and monitoring of the patient when a decision for managed withdrawal of treatment has been taken. 11) Continue to provide emergency appointments where patients are receiving prescriptions from their GP and they feel that a prompt assessment or review of their treatment is required. 12) Provide prompt on-going advice to General Practitioners as required without necessarily requiring a new referral. 13) Provide advice to the GP as to the changes in parameters that should trigger urgent referral back to the specialist 14) Telephone details and (if appropriate) secure email addresses for both Secondary and Primary Care should be exchanged and recorded. This should include out-of-hours contact numbers. Patients and their carers should also be provided with contact details for support and help if required; both in and out of hours. 15) Ensure that adequate training and educational support is in place for the primary care multidisciplinary team (in collaboration with the local commissioner of the service pathway i.e. CCG)
Primary Care Responsibilities	**Clinical responsibility for prescribing is held by the person signing the prescription, who must also ensure adequate monitoring.** 1) To consider requests to prescribe under shared care arrangements and reply in a timely manner. 2) To provide continuation prescriptions, or identify any concerns about the request to the prescriber in the specialist team. It is expected that primary care prescribers will not make changes to the dose/formulation, unless it is in consultation with the specialist team. 3) To monitor the patient in accordance with Appendix A and contact the specialist team if results give rise to concern. Any ongoing monitoring requirements for individual patients discharged from secondary care will be identified by the specialist service as part of the discharge information to the GP.

4) To contact specialists within the team where concerns arise about a patient's presentation or when advice is needed.

5) To refer back to secondary care if withdrawal of treatment might be indicated. This could be because:

   a. Impaired renal or hepatic function

   b. Hypotension or volume depletion

Circumstances for discontinuation of treatment in Primary Care

1) As a joint decision with specialist team providing specific advice in case of adverse effect pending assessment.

2) Following non-attendance at annual specialist team review pending that review taking place or if there is failure to engage with the review process.

Monitoring

Monitoring

Ketones

During the initial one to two weeks of treatment with dapagliflozin, ketones should be monitored on a regular basis, then the frequency of ketone level testing should be individualized, according to the patient's lifestyle and/or risk factors. Patients should be advised to take the following actions in response to ketone testing:

Blood Ketone (beta-hydroxybutyrate)	**Clinical stage and actions**
0.6-1.5 mmol/L	**Ketonaemia** - The patient may need to take extra insulin and drink water. The patient should measure blood glucose and consider taking extra carbohydrates if the glucose levels are normal or low. Ketone levels should be measured again after two hours. The patient should immediately seek medical advice and stop taking dapagliflozin if levels persist and symptoms present.
> 1.5-3.0 mmol/L	**Impending DKA** - The patient should immediately seek medical advice and stop taking dapagliflozin. The patient may need to take extra insulin and drink water. The patient should measure blood glucose and consider taking extra carbohydrates if the glucose levels are normal or low. Ketone levels should be measured again after two hours.
> 3.0 mmol/L	**Probable DKA** - The patient should go to emergency department without delay and stop taking dapagliflozin. The patient may need to take extra insulin and drink water. The patient should measure blood glucose and consider taking extra carbohydrates if the glucose levels are normal or low.

Renal function

Monitoring of renal function is recommended as follows:

- Prior to initiation of dapagliflozin and at least yearly, thereafter.
- Prior to initiation of concomitant medicinal products that may reduce renal function and periodically thereafter.
- For renal function with GFR < 60 mL/min, at least 2 to 4 times per year.

Dapagliflozin should not be initiated in patients with a GFR < 60 mL/min and should be discontinued at GFR persistently below 45 mL/min.

APPENDIX A

Monitoring Required	
Ketones	Regularly during the first 14 days of treatment. Then the frequency of ketone level testing should be individualized, according to the patient's lifestyle and/or risk factors – to be advised by the specialist service.
Renal function	Prior to initiation of dapagliflozin and at least yearly, thereafter. Prior to initiation of concomitant medicinal products that may reduce renal function and periodically thereafter. For renal function with GFR < 60 mL/min, at least 2 to 4 times per year.

Bibliography

[1] Royal Pharmaceutical Society, “British National Formulary,” Pharmaceutical Press, 2019. [Online]. Available: https://bnf.nice.org.uk/. [Accessed 23rd September 2020].

[2] AstraZeneca UK Limited, “Forxiga 10 mg film-coated tablets,” Electronic Medicines Compendium, 2nd January 2020. [Online]. Available: https://www.medicines.org.uk/emc/product/7607/smpc#gref. [Accessed 23rd September 2020].

Optional Shared Care Agreement form

Request by Specialist Clinician for the patient's GP to enter into a shared care agreement

PLEASE NOTE: The use of this form is not compulsory, but the same information must be communicated between the specialist service and primary care in advance of entering into a shared-care agreement.

Part 1 - To be signed by Consultant / Associate Specialist / Speciality Trainee or Specialist Nurse (who must be a prescriber)

Dear Doctor:	Click or tap here to enter text.
Name of Patient:	Click or tap here to enter text.
Address:	Click or tap here to enter text.
	Click or tap here to enter text.
	Click or tap here to enter text.
Date:	Click or tap to enter a date.
Patient NHS Number:	Click or tap here to enter text.
Patient Hospital Number:	Click or tap here to enter text.
Diagnosed Condition:	Click or tap here to enter text.

I request that you prescribe:

(1) Click or tap here to enter text.
(2) Click or tap here to enter text.
(3) Click or tap here to enter text.
(4) Click or tap here to enter text.

for the above patient in accordance with the LMMG shared care guideline(s) (Available on the LMMG website).

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Last Prescription Issued:	Click or tap to enter a date.
Next Supply Due:	Click or tap to enter a date.
Date of last blood test (if applicable):	Click or tap to enter a date.
Date of next blood test (if applicable:	Click or tap to enter a date.
Frequency of blood test (if applicable:	Click or tap here to enter text.

I confirm that the patient has been stabilised and reviewed on the above regime in accordance with the Shared Care guideline.

If this is a Shared Care Agreement for a drug indication which is unlicensed or off label, I confirm that informed consent has been received from the patient.

I will accept referral for reassessment at your request. The medical staff of the department are available if required to give you advice.

Details of Specialist Clinicians

Name:	Click or tap here to enter text.
Date:	Click or tap to enter a date.
Position:	Choose an item.
Signature:	Click or tap here to enter text.

(An email from the specialist clinician will be taken as the authorised signature)
In all cases, please also provide the name and contact details of the Consultant.

When the request for shared care is made by a Specialist Nurse, it is the supervising consultant who takes medicolegal responsibility for the agreement.

Consultant	Click or tap here to enter text.

Contact Details	
Telephone Number	Click or tap here to enter text.
Extension	Click or tap here to enter text.
Email Address	Click or tap here to enter text.

Part 2 - To be completed by Primary Care Clinician (GP)

I agree to prescribe and monitor Click or tap here to enter text. for the above patient in accordance with the LMMG shared care guideline(s) commencing from the date of next supply / monitoring (as stated in Part 1 of the agreement form).

Name:	Click or tap here to enter text.
Date:	Click or tap to enter a date.
Signature:	Click or tap here to enter text.

*Please sign and return a copy **within 14 calendar days** to the address above* **OR**

If you **do not** agree to prescribe, please sign below and provide any supporting information as appropriate:

I **DO NOT** agree to enter in to a shared care agreement on this occasion.

Name:	Click or tap here to enter text.
Date:	Click or tap to enter a date.
Signature:	Click or tap here to enter text.
Further information:	Click or tap here to enter text.