forxiga®
(dapagliflozin)

Important Safety Information about Forxiga (dapagliflozin) - for type 1 diabetes mellitus only

Guide for Healthcare Professionals to minimise the risk of Diabetic Ketoacidosis (DKA)

Please read:

- **this booklet in full AND**
- **the Summary of Product Characteristics (SmPC).**

This booklet only explains specific side effects for particular indications. It does not replace the Summary of Product Characteristics (SmPC) which contains the full prescribing information.

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AstraZeneca

What is in this guide

Healthcare Professional Checklist

This guide relates to patients with type 1 diabetes only.

Healthcare Professional Checklist -
to be completed for type 1 diabetes patients only

Eligibility check before starting Forxiga

☐ **Treatment with Forxiga is to be initiated and supervised by a specialist in type 1 diabetes**

☐ **Patient is a Type 1 diabetic on insulin treatment**

☐ **Patient BMI: _____**
(patient is eligible for treatment if BMI ≥ 27 kg/m^2)

☐ **Patient has not achieved adequate glycaemic control despite optimal insulin therapy.**

Last HbA1C value: ____ **Date of last HbA1C value: ____**

Current insulin usage / day:

_____
_____
_____

☐ **Confirmed absence of the following risk factors which place patients at higher risk of DKA. If any risk factor is present DO NOT start dapagliflozin.**

a. Patients with low insulin needs
b. Patient not on optimal insulin dose or who have recent issues with noncompliance or recurrent errors with insulin dosing and who are unlikely to maintain adequate insulin dosing.
c. Patients with increased insulin requirements due to acute medical illness or surgery.
d. Patients who insist on maintaining caloric restriction, carbohydrate restriction or ketogenic diet or who chronically under-dose insulin (e.g. in order to remain in a lipolytic state).
e. Patients with recent or recurrent history of DKA.
f. Patients with excessive alcohol consumption or who use illicit drugs.

☐ **Patient is able and willing to monitor ketones.**

Advise the patient to establish their baseline ketone level 1 to 2 weeks before treatment initiation.

Where possible, measurement of blood ketones is preferred to measurement of urine ketones.

At Forxiga initiation

- ☐ **Conduct a dedicated education session with the patient in which you will:**
  - ☐ **Give out the Patient Alert Card and Patient and Carer Guide**
  - ☐ **Review Patient and Carer Guide with patient advising them of the following:**
    - ☐ Signs or symptoms of DKA and when it can happen, emphasising that DKA may occur in patients treated with Forxiga even if blood glucose levels are below 14 mmol/L (250 mg/dL)
    - ☐ How to recognise DKA risk factors
    - ☐ How to manage 'sick days'
    - ☐ When to discontinue/interrupt Forxiga treatment
    - ☐ How/when to measure ketone levels and actions to be taken if ketosis/DKA suspected

Note: The Education Worksheet in the Patient and Carer Guide can be used to write down any guidance for patients

- ☐ **Patient has demonstrated the willingness and ability to monitor ketone levels.**

☐ The patient has established their baseline ketone level 1 to 2 weeks before treatment initiation.

☐ Advise the patient to monitor ketones regularly for 1-2 weeks after starting treatment and to individualise the frequency thereafter

- ☐ **Ketone level check:**

Method of ketone testing:_____

Ketone value: _____ **Date of ketone check:** _____

Important. DO NOT start Forxiga if ketone levels are elevated (blood ketones ≥0.6 mmol/L or urine ketones ≥1+). Wait until levels are normal.

- ☐ **Patient has no signs/symptoms of volume depletion prior to initiation of dapagliflozin.**
- ☐ **Optimise insulin therapy**
  Consider reducing the first mealtime bolus insulin by 20% with the first dose of Forxiga to avoid hypoglycaemia
- ☐ **Users of insulin infusion pumps** [n/a if patient is not a user of insulin infusion pump]
  - ☐ Patient is experienced with pump use
  - ☐ Patient is familiar with common trouble-shooting strategies when interruptions of insulin delivery via pump occur (issues with insertion site, clogged tubing, empty reservoir, etc.)
  - ☐ Patient has ability to use supplemental insulin injections with pen or syringe as needed in case of pump failure

This guide relates to patients with type 1 diabetes only.

During Forxiga treatment

- ☐ **Continuously optimise insulin therapy**
- ☐ **If insulin reduction is needed to prevent hypoglycaemia - reduce cautiously to avoid ketosis/DKA**
- ☐ **Reassess ketone monitoring frequency according to patient lifestyle/risk factors**
- ☐ **Consider circumstances when Forxiga needs to be stopped or interrupted**
  - ☐ Stop Forxiga treatment if DKA is suspected.
  - ☐ Dapagliflozin treatment should be temporarily stopped before surgical procedures or in case of hospitalisation for acute serious illness.
  - ☐ If addition of dapagliflozin leads to marked reduction of insulin need, discontinuation of dapagliflozin should be considered to avoid high risk of DKA.
- ☐ **Check that the patient has the alert card**

1. About this guide

Forxiga is used as an adjunct to insulin in adult patients with BMI ≥27 kg/m^2 when insulin alone does not provide adequate glycaemic control despite optimal insulin therapy. Forxiga is not a substitute for insulin.

Treatment with Forxiga is to be initiated and supervised by specialists in type 1 diabetes.

This guide:

- Is only relevant to type 1 diabetes patients.
- Is for Healthcare Professionals (HCPs) – for example, specialists in type 1 diabetes, diabetes nurses and pharmacists.
- Explains how to minimise the risk of Diabetic KetoAcidosis (DKA) in patients with type 1 diabetes being treated with Forxiga.

This guide will help you to:

- Understand DKA in type 1 diabetes patients taking Forxiga.
- Understand risk factors for DKA and how to minimise the risk.
- How to treat possible DKA.
- Conduct a dedicated education session with patients and/or carers.

Please read:

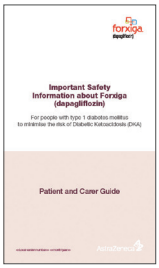
- **this booklet in full AND**
- **the Summary of Product Characteristics (SmPC).**

This booklet only explains specific side effects for particular indications. It does not replace the Summary of Product Characteristics (SmPC) which contains the full prescribing information.

2. Conducting a dedicated education session

A dedicated education session must be held with each patient when initiating Forxiga. You may want to record any guidance for the patient from the session in the optional 'Education Worksheet' on page 9 of the Patient and Carer Guide.

During this education session, you need to give all patients taking Forxiga for type 1 diabetes:

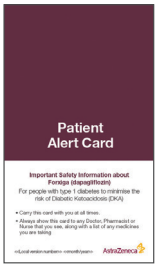


A) A Patient and Carer Guide: use the guide to help you discuss DKA with patients and carers, including:

- The signs or symptoms of DKA and when it can happen.
- How to recognise DKA risk factors.
- How to manage 'sick days'.
- When to discontinue/interrupt Forxiga treatment.
- How and when to measure and interpret ketone levels – including which actions to take if ketosis/DKA is suspected.

Note: Where possible, measurement of blood ketones is preferred to measurement of urine ketones.

AND



B) Patient Alert Card: a wallet-sized card

- The patient must carry this with them at all times.
- The patient must show the card to any other HCP who treats them.

This guide relates to patients with type 1 diabetes only.

3. What Forxiga is

Forxiga (dapagliflozin) is an 'SGLT-2 inhibitor'.

- The recommended dose of Forxiga in type 1 diabetes is 5 mg once daily.
- Forxiga is **not** a substitute for insulin and does not alter insulin sensitivity.
- It improves both fasting and post-prandial plasma glucose levels - by reducing renal glucose reabsorption leading to urinary glucose excretion.
- The amount of glucose removed by the kidney in this way depends on the blood glucose concentration and glomerular filtration rate.
- Forxiga does not impair normal endogenous glucose production in response to hypoglycaemia - and acts independently of insulin secretion and insulin action.

To maintain treatment benefit, insulin therapy should be continuously optimised. It is recommended that Forxiga therapy is regularly evaluated in the individual patient - weighing the treatment benefit against the risks.

4. Risk of DKA in patients with type 1 diabetes

What you need to be aware of

There is a high background risk of DKA in patients with type 1 diabetes. This is because patients with type 1 diabetes mellitus are dependent on administered insulin. DKA can happen if patients do not take their insulin – or if they do not take enough insulin. The risk of DKA is increased with dapagliflozin treatment

Patients and medical staff should both be:

- **aware that while taking Forxiga glucose levels may not adequately reflect insulin needs.**
  - **DKA may occur in patients treated with Forxiga even if blood glucose levels are below 14 mmol/L (250 mg/dL) – this is called euglycaemic DKA.**
- **able to recognise the signs of DKA early so that treatment is not delayed – early DKA detection is crucial to reduce and prevent metabolic deterioration.**

The risk of DKA must be considered in the event of non-specific symptoms such as nausea, vomiting, anorexia, abdominal pain, excessive thirst, difficulty breathing, confusion, unusual fatigue or sleepiness. Assess patients for DKA immediately if these symptoms occur - regardless of blood glucose level.

4. Risk of DKA in patients with type 1 diabetes (continued)

Findings from clinical studies

In clinical studies where people with type 1 diabetes mellitus were using Forxiga:

- There were more DKA events compared with placebo in the entire study population.
- There were several events where the measured blood glucose level was in the euglycaemic range.

In the pooled 52-week data, events of DKA were reported in 22 (4.0%) patients in the dapagliflozin 5 mg group and 6 (1.1%) patients in the placebo group, with corresponding incidence rates per 100 patient years of 4.62 for dapagliflozin 5 mg and 1.27 for placebo.

DKA events occurred evenly distributed over the clinical study period.

Inadequate insulin doses (missed insulin dose or insulin pump failure) were the most common precipitating factors. 6 of 23 events of DKA in the dapagliflozin 5 mg group occurred in patients with blood glucose in the euglycaemic range (< 14 mmol/l or 250 mg/dl).

Patients with DKA events responded to conventional treatment for DKA (see section 4.4 of the SmPC for more details).

5. Minimising the risk of DKA

Before starting Forxiga:

Before you start, the treatment benefits need to be weighed against the risk of DKA in each individual patient.

- Forxiga is restricted to adult patients with BMI ≥27 kg/m^2 when insulin does not provide adequate glycaemic control despite optimal insulin therapy.
- Forxiga should not be initiated in patients with risk factors that may predispose them to DKA, including:
  - Sub-optimal insulin dose or low insulin needs
  - Poor compliance or recurrent errors with insulin dosing and unlikely to maintain adequate insulin dosing
  - Recent or recurrent history of DKA
  - Increased insulin requirements due to acute medical illness, surgery
  - Excessive alcohol consumption or illicit drug use
  - Caloric restriction, carbohydrate restriction, ketogenic diet or chronic under-dosing of insulin
- Educate eligible patients on how and when to monitor ketone levels.
  - Advise patients to obtain several baseline ketone levels over 1-2 weeks before Forxiga initiation and become familiar with how their behaviours and circumstances affect their ketone levels

A summary of recommendations for patients can be found in the HCP Checklist (pages 3-5) and in the Patient and Carer Guide.

At Forxiga initiation:

In addition to conducting a dedicated education session:

- Ensure that the patient is able and willing to monitor ketone levels
- Ensure that the patient has access to ketone testing materials and immediate access to a clinician if ketone levels are elevated
- Ensure that ketone levels are normal (blood <0.6 mmol/L or urine <1+)
- Advise patients to monitor ketones regularly for 1-2 weeks after Forxiga initiation and individualise frequency thereafter based on patient's behaviour and circumstances including pump use
- Correct volume depletion in the patient, where required
- Optimise insulin therapy
- Consider reducing the first mealtime bolus insulin by 20% with the first dose of Forxiga to avoid hypoglycaemia (refer to SmPC 4.2)

Do not start Forxiga if ketone levels are elevated (blood ketones ≥0.6 mmol/L or urine ketones ≥1+). Wait until levels are normal. Where possible, measurement of blood ketones is preferred to measurement of urine ketones.

Reminder that insulin infusion pump users:

- Have a higher risk of DKA.
- Should only take Forxiga if they are experienced in use and trouble shooting strategies in the event of insulin interruptions.
- Should consider monitoring ketones 3-4 hours after changing pump materials and with any suspected insulin interruption, regardless of glucose level.
- Should take insulin injections within 2 hours of unexplained high glucose/ketones.

5. Minimising the risk of DKA (continued)

During Forxiga treatment:

- Continuously optimise insulin therapy.
- If insulin reduction is needed to prevent hypoglycaemia - reduce the dose cautiously to avoid ketosis/DKA.
- Reassess ketone monitoring frequency according to patient lifestyle/risk factors.
- Consider recommending an increase in carbohydrate intake in circumstances where ketones are raised and glucose is normal.
- Check that the patient still has the alert card.

Glucose monitoring must continue to be supplemented by ketone monitoring.

Consider when to interrupt/stop Forxiga treatment:

- Stop Forxiga treatment if DKA is suspected.
- Interrupt Forxiga treatment:
  - In settings of reduced oral intake, such as during acute illness
  - In patients who are hospitalised for major surgical procedures or acute serious medical illness.

  Treatment with Forxiga may be restarted once the patient's condition has stabilised
- Consider discontinuing Forxiga if a marked reduction in insulin need occurs.

6. If you suspect DKA/euglycaemic DKA and how to treat it

If DKA/euglycaemic DKA is suspected:

- get the patient immediate medical attention
- immediately stop Forxiga.

DKA/euglycaemic DKA should be treated as per standard of care which includes the use of insulin, intravenous fluids and glucose as appropriate.

Do not stop or interrupt insulin treatment under any circumstances.

Restarting SGLT-2 inhibitor treatment in patients with previous DKA while on SGLT-2 inhibitor treatment is not recommended until the patient is metabolically compensated and any clear precipitating factor is identified and resolved.

7. Reporting Adverse Reactions

Reporting suspected adverse reactions after authorisation of a medicine is important. It allows continual monitoring of the benefit and risk balance of the medicine to patients.

When reporting adverse reactions, please provide as much information as possible including:

- information about the patient's medical history
- any other medicines they are taking and
- that the patient has type 1 diabetes.

Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store. Adverse events should also be reported to AstraZeneca on 0800 783 0033

More information on Forxiga and this material are available online at goto.az/forxiga-hcp-uk

The Patient and Carer Guide and Patient Alert Card are available online at goto.az/forxiga-pat-uk

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