forxiga®
(dapagliflozin)

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

Guide for Health Care 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

Health Care Professional Checklist

1. About this guide 4

2. Conducting a dedicated education session 4

3. What Forxiga is 5

4. Risk of DKA in patients with type 1 diabetes 5

5. Minimising the risk of DKA 6-7

6. If you suspect DKA and how to treat it 7

7. Reporting Adverse Reactions 8

This guide relates to patients with type 1 diabetes only.

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

Before starting Forxiga

- ☐ **Forxiga is restricted to adult patients with BMI ≥27 kg/m² when insulin alone does not provide adequate glycaemic control despite optimal insulin therapy**
- ☐ **Assess risk factors that may predispose the patient to DKA**
- ☐ **Educate eligible patients on how and when to monitor blood 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
- ☐ **Ensure the patient is able and willing to monitor ketones (blood preferred to urine)**
- ☐ **Ensure that ketone levels are normal**
- ☐ **Advise patients to monitor ketones regularly for 1-2 weeks and individualise frequency thereafter**
- ☐ **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**

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.

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 (section 5)**
- ☐ **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 Health Care 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:

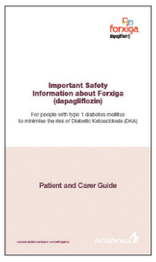
- **this booklet in full AND**
- **the Summary of Product Characteristics (SmPC).**

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:

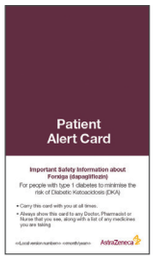


A) A Patient and Carer Guide: use the guide to help you discuss DKA with patients and carers, including:

- 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: Measurement of blood ketones is preferred to urine

AND



B) A 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.

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.

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, 43 events of DKA were reported in 42 patients (3.8%) in the Forxiga group, and 6 events in 6 patients (1.1%) in the placebo group. There were corresponding incidence rates per 100 patient years of 4.23 for Forxiga and 1.27 for placebo.

Inadequate insulin doses, as a result of missed insulin dose or insulin pump failure, were the most common reason for DKA. Of the DKA events in the Forxiga group, 13 out of 43 events occurred in patients with blood glucose in the euglycaemic range (under 14 mmol/L or under 250 mg/dL). Patients with DKA events responded to conventional treatment for DKA. See 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

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.

Reminder that insulin infusion pump users:

- have a higher risk of DKA.
- should only take Forxiga if they are experienced in pump 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 and how to treat it

If DKA is suspected:

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

Treatment of DKA should be treated as per standard of care and may require:

- insulin
- fluid
- extra carbohydrate - especially if blood glucose levels are not markedly raised.

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.

Suspected Adverse Drug Reactions (side effects) or medication errors may be reported using the Medicines Authority ADR reporting form available online at www.medicinesauthority.gov.mt/adrportal and sent to Pharmacovigilance Section at Post-Licensing Directorate, Medicines Authority, Sir Temi Żammit Buildings, Malta Life Sciences Park, San Ġwann SĠN or sent by email to postlicensing.medicinesauthority@gov.mt.

Adverse Events should also be reported to Associated Drug Company Limited on: 00356 2277 8115.

More information on Forxiga and this material are available online at www.associateddrug.com/frx.hcp.mt

The Patient and Carer Guide and Patient Alert Card are available online at www.associateddrug.com/frx.pat.mt