EMPA-KIDNEY

MRC Population Health Research Unit

UNIVERSITY OF OXFORD

Additional information for EMPA-KIDNEY participants with diabetes

You have been provided with this extra information as you have diabetes. As explained in the study's participant information leaflet people with diabetes are at risk of a condition called ketoacidosis. If you have had ketoacidosis in the last 5 years you cannot join the trial. If have *not* had ketoacidosis for the last 5 years, you may still be eligible to join the trial, but we want to give you more information about ketones and ketoacidosis.

What are ketones?

Ketones build up if there is too little insulin in the body. Ketones are common in everyone when they fast as the body starts to burn fat rather than sugar. Ketones are also increased when there is too little insulin in the body. If the levels of ketones stay high for sufficiently long, they can cause the blood to become acidic and a person to become ill. This is called ketoacidosis.

What are the causes of ketoacidosis?

The chances of getting ketoacidosis are increased by prolonged starvation (including low carbohydrate diets), insulin dose reduction (including missed doses and insulin pump failure) and acute illness. Therefore, particular caution is required when doses of insulin are reduced or when you become unwell. When taking empagliflozin, the chances of developing ketoacidosis may be increased, especially if you have type 1 diabetes. In previous studies with medications like empagliflozin, this risk was particularly increased in women and in people using an insulin pump.

What are the symptoms of ketoacidosis?

The symptoms of ketoacidosis are non-specific, and can include feeling or being sick (i.e. vomiting), tummy ache and shortness of breath. Others may notice a sweet smell (like pear drops or nail varnish) on your breath. As the ketoacidosis worsens you may become increasingly tired, confused and later you may become unconscious. If you have had ketoacidosis before, you may recognize other symptoms which are particular to you. When taking empagliflozin, the chances of developing ketoacidosis may be increased. Importantly, it can develop without blood sugars being particularly high. This is unusual, as blood sugar is normally high when you develop ketoacidosis. We have provided you with an EMPA-KIDNEY participation card. Please show this to the doctors who treat you so they are aware of this potential side-effect.

How is ketoacidosis prevented?

The following may help reduce the chances of getting ketoacidosis:

- Avoiding triggers such as dehydration, excess alcohol intake or low-carbohydrate diets
- If you are on insulin, monitor your blood sugar regularly (usually a few times a day) and increase your insulin dose if your blood sugars become high (as per advice from your local diabetes nurse or your local doctors)
- If you become unwell, continue to take your insulin (unless you have low blood sugar) and increase monitoring of your blood sugar.

How is ketoacidosis treated?

Ketoacidosis is treated with intravenous insulin and fluid drips. If you think that you are becoming unwell with ketoacidosis, you should immediately seek medical care (e.g. go to the nearest hospital), as treatment with a drip and insulin may be needed. *Take your EMPA-KIDNEY card!*

If you have any more questions please ask your study doctor or call our 24-hour Freefone service: **0808 1644060.** If you have type 1 diabetes, please also read the next page.

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Additional information just for participants with type 1 diabetes

I have type 1 diabetes, do I need a ketone meter?

Yes, participants with type 1 diabetes should have a monitor which can measure blood ketones available to them at home.

If you already have a blood sugar monitor which can measure ketones, you can continue to use it during the study, but please make sure you have the strips needed to use it.

If your blood sugar monitor is not able to measure ketones, then your local study nurse will ask your local doctors to supply you with a ketone meter and strips. Please note that in order to proceed into the study, you will need to have a ketone meter and strips by the time of your Randomization Visit. This is usually your second visit to the study clinic about 8-12 weeks after starting your first study pills.

When do I need to measure ketones?

Unlike blood sugar monitoring, you do *not* need to measure your blood ketones levels on a regular basis (although you may wish to). You should measure blood ketone levels when the chances of getting ketoacidosis are increased. This includes whenever:

- You have any of the ketoacidosis symptoms described on page 1
- Your blood sugar levels become high and stay high (i.e. above about 11 mmol/L)
- You have problems giving your insulin (e.g. insulin pump failure or missed doses)
- You are fasting, unable to eat or are on a very low carbohydrate diet.

Your local doctors may also give you advice on other times to measure your ketone levels.

What are the normal levels of blood ketones?

A blood ketone level of less than 0.6 mmol/L is normal. *If you are testing your ketones because you are feeling unwell and your blood ketone levels are normal, please do not delay seeking medical advice about your symptoms as they may be related to another important medical condition.*

What should I do if my blood ketone levels are high?

Any blood ketone measurement of 0.6 mmol/L or higher means ketones are building up in your blood and your blood is at risk of becoming too acidic.

If you feel well and your blood ketone levels are above 0.6 mmol/L, you should increase how often you monitor your blood sugar and blood ketone levels and do the following:

- Increase your fluid intake
- If your blood sugar is high, ensure you have given yourself enough insulin
- If you are unsure, seek advice (e.g. from your local diabetes nurse or your local doctors).

If you think that you are becoming <u>unwell</u> with ketoacidosis, you should temporarily stop study treatment and immediately seek medical attention (e.g. go to the nearest hospital)

A blood ketone level of 1.5 mmol/L or above (or if your ketone meter reads "HI") means you should temporarily stop study treatment & seek prompt medical attention

A study doctor from the co-ordinating centre on **0808 1644060** may also be able to advise.