EASi-KIDNEY
Aldosterone Synthase inhibition & Empagliflozin in CKD

Study Treatment Information Leaflet

This leaflet contains important information relating to your EASi-KIDNEY study treatment. Please read all the information contained in this leaflet very carefully. If you have any questions about your study treatment, please speak to your local study nurse or feel free to call a UK EASi-KIDNEY study nurse or doctor on: **Freephone 0808 164 4060.**

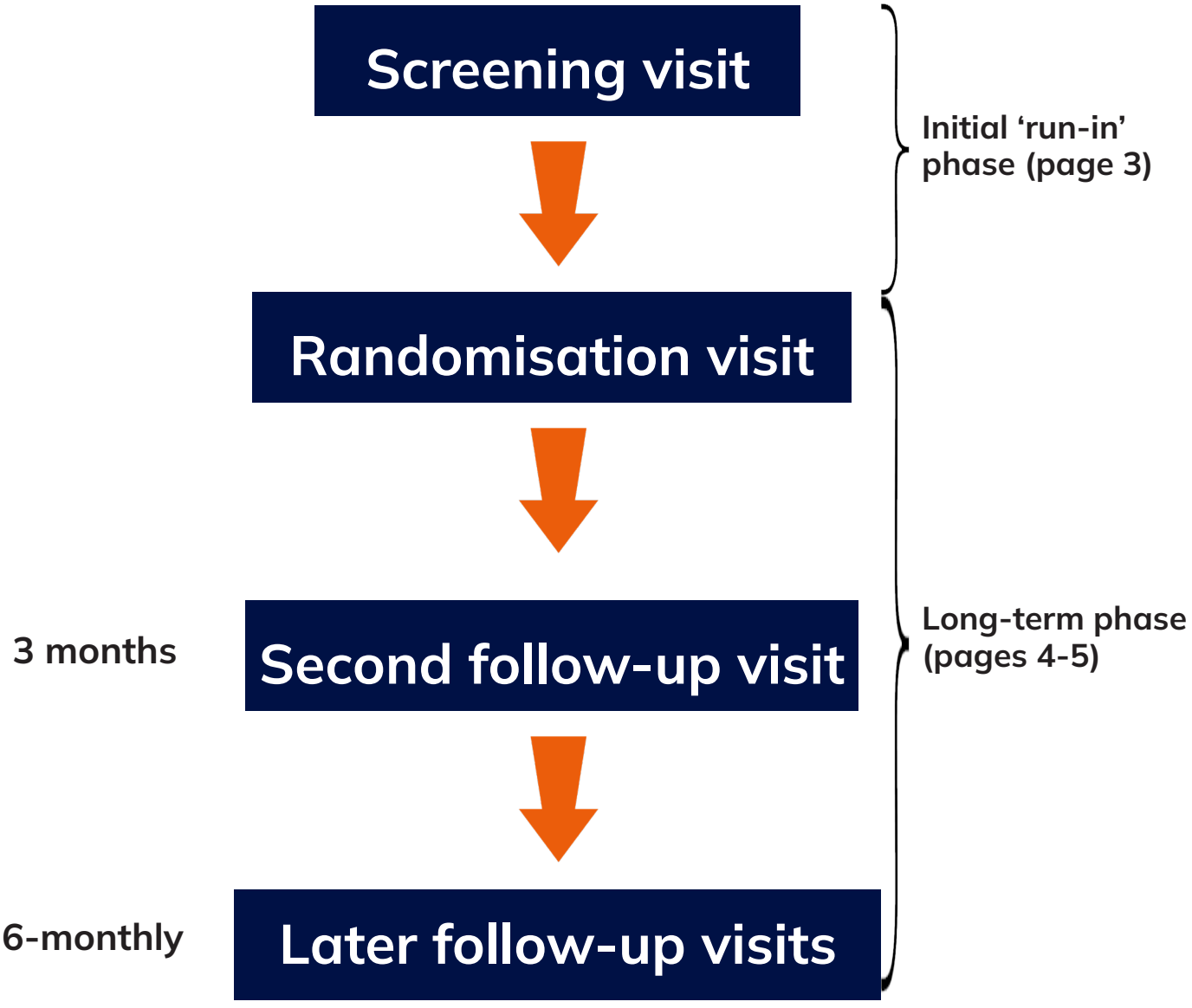
Please keep this information leaflet in a safe place for future reference.

EASi-KIDNEY visits when study pills are issued

Throughout the study you will be provided with study pills:

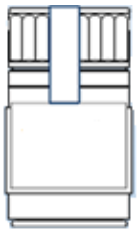
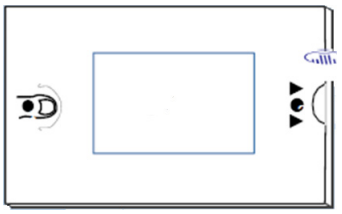
- **BI 690517 10mg or inactive dummy drug**
- **empagliflozin 10mg**

REMEMBER: On clinic visit days, please make a mental note of the exact time when you take your pills, as you will sometimes be asked for this information.



Initial ‘run-in’ phase

After your first study visit (the screening visit) you will enter the ‘run-in phase’. You will be issued with one pack of **Type F Run-in Treatment** consisting of one bottle (containing 112 pills) of BI 690517 10mg or matching placebo (“dummy pill”) and one pack of **Type E Treatment** consisting of one wallet (containing 112 pills) of empagliflozin 10mg.

Study treatment type	Number of pills	Information booklet colour
Type F Run-in BI 690517 10mg or matching placebo 	**1 pack** containing **1 bottle** of 112 pills	Pale Blue
Type E Empagliflozin 10 mg 	**1 pack** containing **1 wallet** of 112 pills	White

Start to take Type F treatment straight away, but do *not* start Type E treatment until instructed by one of the local team.

Opening the empagliflozin treatment wallets

To open a treatment wallet you need to press with your thumb on the left hand side (where marked) and pull the wallet from its sleeve from the right hand side.

Please retain and bring all your used and unused study treatment bottles and wallets to each study appointment.

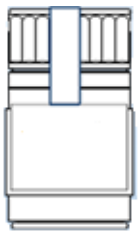
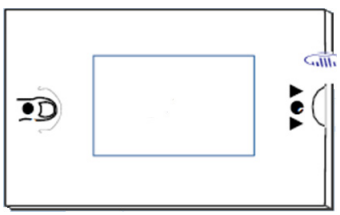
Long-term phase: Randomisation and first follow-up visits

At your second scheduled study visit (the randomisation visit), if you proceed into the long-term part of the study, you will be randomly allocated to receive pills containing either
BI 690517 10mg or matching placebo.

At the randomisation visit you will be issued one pack of **Type M Randomised Treatment** containing one bottle (112 pills) of study treatment and one pack of **Type E Treatment** containing one wallet (112 pills) of empagliflozin 10mg.

No study treatment will be issued at the bloods only (one to three weeks) and first follow-up visit (one-month).

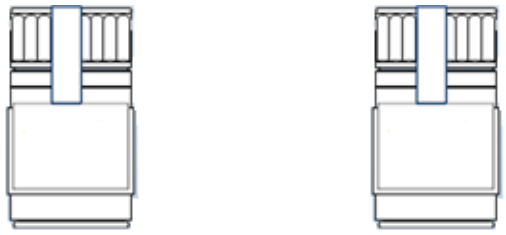
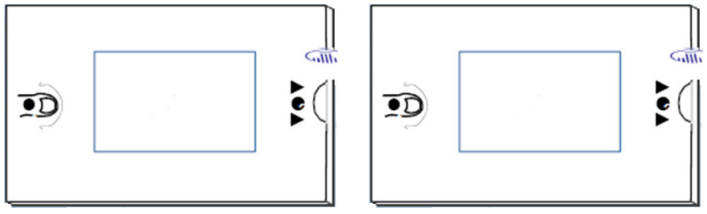
At the second follow-up visit (three months) you will also be issued one pack of **Type M Randomised Treatment** containing one bottle (112 pills) of study treatment and one pack of **Type E Treatment** containing one wallet (112 pills) of empagliflozin 10mg.

Study treatment type	Number of pills	Information booklet colour
Type M Randomised BI 690517 10mg or matching placebo 	**1 pack** containing **1 bottle** of 112 pills	Green
Type E Empagliflozin 10 mg 	**1 pack** containing **1 wallet** of 112 pills	White

Long-term phase:

Later follow-up visits (six-monthly)

At the later follow-up visits (six-monthly), you will be issued with **two** packs of **Type M Randomised Treatment** - each pack will contain one bottle of 112 pills (so a total of 224 pills) of study treatment - and two packs of **Type E Treatment** - each pack contains one wallet (containing 112 pills, so a total of 224 pills) of empagliflozin 10mg.

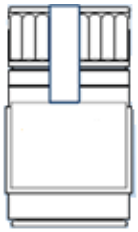
Study treatment type	Number of pills	Information booklet colour
Type M Randomised BI 690517 10mg or matching placebo 	**2 packs** each containing **1 bottle** of 112 tablets (each pack contains one bottle; total two bottles containing 224 pills provided)	Green
Type E Empagliflozin 10 mg 	**2 packs** each containing **1 wallet** (each pack contains one wallet of 112 pills; total two wallets containing total of 224 pills provided)	White

Please retain and bring all your used and unused study treatment bottles and wallets to each study appointment.

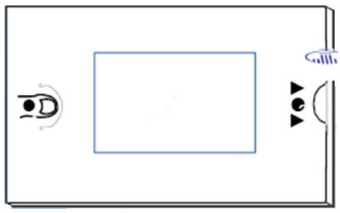
About your EASi-KIDNEY study pills

Study treatment (BI 690517 or matching placebo AND empagliflozin)

- Oral use only
- Storage conditions: keep the pills out of direct sunlight
- Keep out of the reach of children
- For clinical trial use only



BI 690517 or matching placebo



Empagliflozin

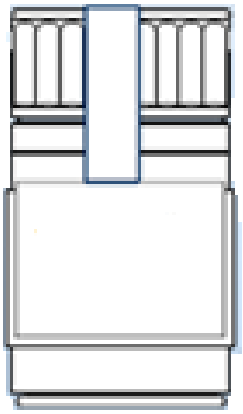
- Unless otherwise instructed, you should take **ONE pill of Type M Treatment** (BI 690517 10mg or matching placebo tablet from the bottle) and **ONE pill of Type E Treatment** (empagliflozin 10mg from the wallet) by mouth each day at about the same time (with or without food).
- If you forget to take one or both pills at your usual time, you may still take it later the same day. However, if you miss a whole day or more, do not make up for the missed pills on the day you restart.
- If you think you will reach the end of your pills before your next clinic visit or if you lose your pills, please contact your local study nurse or call the EASi-KIDNEY office and we will arrange for replacement pills.
- BI 690517 or matching placebo and empagliflozin should generally be temporarily stopped on days that you are unable to eat for prolonged periods, such as during an illness or in preparation for medical procedures. For scheduled major operations, you may be advised to stop treatment for three days before surgery. The study pills should be restarted on discharge,

unless you are instructed otherwise by your doctor. For advice regarding empagliflozin use when fasting for non-medical reasons, such as religious occasions, this should be discussed with your local study doctor who will advise you in accordance with local guidance.

- Note that if you permanently stop Type E treatment you will be required to stop Type M also. If, however, you permanently discontinue Type M treatment, Type E treatment should be continued (as it is indicated for use in adults with chronic kidney disease in many countries).
- Please remember to take a **mental note of what time you have taken your pills on clinic days** as you will sometimes be asked.
- For women: if you think you may be pregnant, become pregnant, or plan to get pregnant while taking the study pills, please stop them immediately and inform your local study nurse or call **Freephone 0808 164 4060** as soon as possible.

Possible side-effects:

BI 690517 or matching placebo



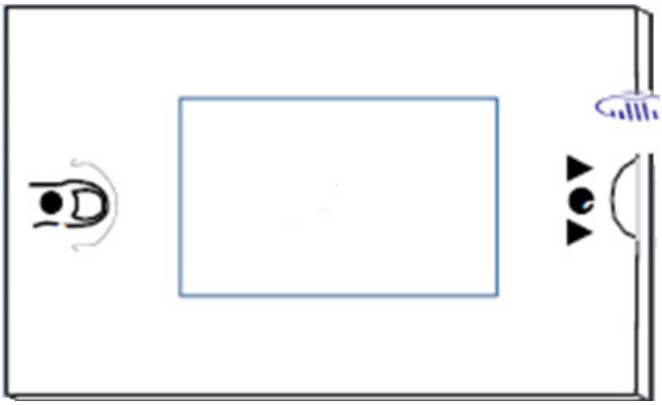
B1 690517 10mg or matching placebo pills may increase the levels of potassium (a mineral) and affect the level of the stress hormone, cortisol, in your blood.

Your potassium levels will be checked at each study appointment and participants with high potassium may be asked to modify their diet by their local team. Modifying amounts of
potassium in the diet is a common practice that patients with kidney disease are asked to follow. We have provided you with an additional **Dietary Potassium Leaflet**, in case you should ever be requested to modify the amount of potassium in your diet.

We will be **monitoring your stress hormone, cortisol, levels** because BI 690517 could affect your blood cortisol levels. Your blood cortisol levels normally fluctuate throughout the day so will need to be specifically measured in the **early morning** (ideally before 09:00) at two points in the trial: the one-month and three-month follow-up visits (and also if your local doctor requests it).

BI 690517 and the empagliflozin pills may lower your blood pressure. If you feel light-headed or dizzy on standing, please inform your local study nurse or the EASi-KIDNEY office. We can arrange for you to see your local study nurse in the next few days for a review where necessary.

Possible side-effects: Empagliflozin



You may be at risk of ketoacidosis (lack of insulin causing harmful substances called ketones to build up in the blood). This risk is higher if you have diabetes, particularly if you are taking insulin. Always stop your empagliflozin if you are unable to eat, if you are unwell or awaiting an operation. If you are fasting for non-medical reasons (such as for religious reasons) then please discuss this with your study team and follow their advice and guidance.

Empagliflozin might increase the chance of a fungal genital tract infection, like thrush. These infections are usually easily treated with a course of antifungal cream or pills. Occasionally it may also cause a urine infection, which may require antibiotics (but most urine infections are not caused by the drug). If such treatment is ever needed, your GP or local study team could help diagnose and treat you. If you develop groin pain, please seek medical advice urgently.

Allergies

In addition to the study medications (BI 690517/placebo and empagliflozin), the study tablets are manufactured from hypromellose, calcium carbonate, isomalt, triglycerides, hydroxypropylcellulose, croscarmellose, magnesium stearate, mannitol, iron oxide, lactose and cellulose. If you have any allergies to any of these components (or the study medications) please stop the pills and inform the study team.

Further information about side effects of study treatment (BI 690517) or matching placebo and empagliflozin) is given in the **EASi-KIDNEY Participant Information Leaflet** and on our **website: wwweasikidney.org.** If any new important information arises during the course of the study the study staff will discuss this with you.

If you develop any symptoms that you think are related to your study pills, please contact your **local study nurse** or call **Freephone 0808 164 4060** for further advice.

Other medications

BI 690517 is an aldosterone synthase inhibitor. This class of drug can be recognised by the following letters at the end of the name “drostat”. Examples include bax**drostat** and lorun**drostat**.

Empagliflozin is a sodium-glucose co-transporter-2 inhibitor. This class of drug can be recognised by the following letters at the end of the name “flozin”. Examples include empagli**flozin**, dapagli**flozin**, and canagli**flozin**. These treatments are recommended for the management of kidney disease in most patients.

You should not be taking study pills in addition to other medications of the same class (for example, do not take both study-provided empagliflozin and dapagliflozin together).

Empagliflozin is safe to take with other medication. BI 690517 clearance from the body can be affected by some other medications. These medications can still be taken together, but caution is recommended. We will send a letter about the study tablets to primary care doctors. The list of medications that might increase body levels of BI 690517 include: probenecid, valproic acid (valproate), fluconazole, amitriptyline, clomipramine. Those medications that could reduce BI 690517 levels are rifampicin and phenytoin. Methotrexate should also be used with caution. Your study team will update you if there is any new information about interactions of study treatments with other medications.

If your local doctor thinks you should definitely start treatments which work in a similar way to either of the study treatments (BI 690517 or empagliflozin) such as **finerenone**, you should stop your study pills first and inform your study team. You or they may call **Freephone 0808 164 4060** with any queries.

Study treatment delivery

You will normally receive study treatment at face-to-face study clinic visits. It may be necessary during the trial to conduct your follow-up appointments by telephone (as was the case during the COVID-19 pandemic). It may be possible to deliver study treatment to you by courier in this (or a similar) situation. If this is required, the research team will contact you to seek your verbal permission and explain further details.

Contact information

By telephone:

0808 164 4060 (UK 24-hour freephone number)

+44 1865 743868 (from outside the UK)

By post:

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Please contact the EASi-KIDNEY office if you would like to receive this document in another format

IRAS: 1009666

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