NHS LOGO

PARTICIPANT INFORMATION SHEET

SOPHIST Trial

Sotagliflozin in **P**atients with **H**eart Fa**i**lure **S**ymptoms and **T**ype 1 Diabetes

A Trial of the Effect of Sotaglifozin for Treating Patients with Type 1 Diabetes and Heart Failure Symptoms

Chief Investigator

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We are inviting you to take part in a research trial.

Before you choose whether to take part, we want you to understand why we're doing this trial. We also want you to know what will be involved if you agree to take part. Please take time to read this information carefully. You can ask us any questions you have and talk to other people if you want. We'll do our best to answer your questions and give you any more information you ask for. You don't have to decide straight away.

If you decide that you'd like to take part in this trial, then please return the attached reply slip (in-person, by post or email) so that we can discuss the trial with you and answer any questions that you have.

Why have I been contacted?

We're inviting you to take part in this trial either because you have type 1 diabetes and have been diagnosed with heart failure or you have changes on your heart scan or you have other heart conditions such as high blood pressure or have had a previous heart attack, that can sometimes lead to changes in your heart function. In this case, heart failure is used to describe changes in your heart structure and/or function.

If you take Sotagliflozin already, or other similar drugs, you'll not be able to take part. The research doctor will check this with you and if there are any other reasons why the trial wouldn't be suitable for you.

To be in the trial you will need to be using a continuous glucose monitor and be willing to share glucose and ketone monitoring data.

Female participants: you'll not be able to take part if you are pregnant, breastfeeding or planning a

pregnancy.

Male participants: you'll not be able to take part if you are planning a pregnancy with your partner.

Why are we doing this research?

We are doing this trial to see if a tablet called sotagliflozin, a Sodium-glucose Cotransporter (SGLT) inhibitor, can improve quality of life in people with type 1 diabetes and heart failure. Sotagliflozin has been shown to improve blood sugar control in people with type 1 diabetes, but SGLT inhibitors are more often used in people with type 2 diabetes and at present are not used in people with type 1 diabetes. SGLT inhibitors also help heart and kidney function in people with type 2 diabetes or without diabetes, but we have no evidence yet as to whether they have the same benefits in people with type 1 diabetes. If we find that sotagliflozin improves quality of life in people with type 1 diabetes and heart failure, then we might use sotagliflozin to treat people like you in future.

This trial is being carried out in hospitals across the UK. We will study 320 patients with type 1 diabetes and heart failure.

Approximately 3 out of 100 people with diabetes will develop heart failure. People with heart failure can

have symptoms like breathlessness, tiredness or ankle swelling. These symptoms can reduce quality of life and lead to being admitted to hospital, or in the worst-case scenario dying.

Trials have shown that SGLT inhibitors can reduce the chances of people developing heart failure. They can also improve patients' quality of life and reduce the chance of people with heart failure being admitted to hospital or dying. But people with type 1 diabetes and heart failure were not in any of the trials carried out with SGLT inhibitors. This means that most guidelines recommend that we don't give SGLT inhibitors to people with type 1 diabetes and heart failure. We believe that SGLT inhibitors would work just as effectively in people with type 1 diabetes and heart failure as they do in people with type 2 diabetes or those without diabetes.

In this trial we hope to find out if sotagliflozin is effective in improving heart failure symptoms in people with type 1 diabetes.

What is being tested?

We will compare the health and quality of life of participants given Sotagliflozin with participants given a placebo. A placebo is a tablet that looks the same

as Sotagliflozin but is not an active medicine (dummy medicine). You won't be able to choose whether you receive the Sotagliflozin tablets or the placebo tablets, this will be decided in a random way (a bit like tossing a coin but done by a computer). Neither you, your nurse nor your doctor will be told if you'll receive the Sotagliflozin or placebo. You'll not be able to ask to find this out, but we'll tell you once the trial is finished and the results of the trial are published. In an emergency, if a doctor looking after you needs to know what treatment you are receiving, for your safety, they'll be able to ask for this information. To take part in the trial you'll have to be happy to receive either the Sotagliflozin tablets or the placebo tablets.

You will be given the Sotagliflozin 200 mg or placebo tablets to take once per day for 4 months.

You should continue to take your usual medications as directed. Taking the trial tablets may mean that you need to adjust your regular insulin dose, your trial doctor or nurse will discuss this with you.

Do I have to take part?

No. Taking part in this trial is entirely up to you. If you choose to take part, you can stop the trial at any time. You don't have to give a reason for not taking part.

The medical care you get and your relationship with the medical or nursing staff looking after you won't be affected if you decide not to take part. If you are happy to tell us, we would find it useful to know the reason for not taking part so that we can look at ways of improving this trial and future trials.

What will happen to me if I take part?

You'll be in the trial for approximately 6 months which will involve you attending hospital for 5 visits and having 3 telephone or video calls with the research team.

During the trial we will ask you to record your blood sugar (using your continuous glucose monitor (CGM)) and ketone levels at the following times and keep a record of these readings to discuss with the trial staff at your next visit.

- 4 times per day and 2 hours after changing each insulin giving set (for those on insulin pump therapy) for 3 days before and 3 days after you start your tablets.
- At least once per week for the rest of the trial.

Ketones should also be measured if:

- Sugar level is more than 11.1 mmol/L for more than 2 hours.

- Feeling unwell, even if your blood sugar level is normal.

We'll also ask you to record any hypos (blood sugar less than 3.9mmol/L):

- For 2 weeks at the beginning of the trial
- For 2 weeks before the end of the trial
- At all times during the trial if you have a severe hypo and you need help from someone else.

Visit 1

The first appointment is a screening visit where we'll carry out assessments to confirm whether the trial is suitable for you. This visit will take up to 3 hours. We'll ask you to complete a consent form to confirm that you wish to take part in the trial. At all visits and calls we'll ask about your medicines and illnesses and check your medical notes. We'll then carry out several assessments:

- Height, weight, hip and waist circumference.
- Pulse and blood pressure
- Physical examination - checking your breathing, heart, abdomen, and nervous system.
- ECG (electrocardiogram) – a tracing of your heart rate

- Echo heart scan (echocardiogram, an ultrasound test) – We'll do this if you haven't had one in the last 2 years. This measures the function and size of your heart muscles and lasts around 30 minutes. This is usually a painless procedure although occasionally there may be a little discomfort. During the echo gel is put on your chest and an ultrasound scanner will take pictures of your heart.
- Provide you with a ketone monitor (if you don't already have one)
- Questionnaire – you'll be asked to complete a questionnaire about how troublesome your heart failure and diabetes are and how it impacts your quality of life.
- Pregnancy test (urine) – for women of childbearing age
- Blood samples - one of the tests will check if you have a marker for heart failure called N-terminal pro-B-type natriuretic peptide (NT-pro BNP).

If your blood sample shows you have the marker for heart failure (NT-pro BNP) and the other assessments confirm that the trial is suitable for you, you'll be invited to join the trial and will be asked to come for your next visit.

Visit 2 – 3 weeks after visit 1
This visit will take about half an hour. The main reason for this visit is to review your blood sugar and

ketone recordings and to adjust your diabetes medication including insulin if required. If you do not use a CGM app, we can help you sign up/create your own account if you want.

Treatment phase

Visit 3 – 1 week after visit 2

This visit will last about 2 hours and you'll have the following assessments:

- Weight, pulse and blood pressure
- Documentation of CGM data from previous 2 weeks
- Review of your blood glucose and ketone levels
- Questionnaires
- 6-minute walk test
- Pregnancy test (urine), if required.
- Blood samples
- Urine sample
- Trial medication – we will supply the tablets which you will take for the next 4 months.

Phone or video call

This call will be 1 week after you start your trial medication. If a video call is offered by your research team, this will use a service approved by your local NHS Trust e.g. Attend Anywhere. Your research team will give you guidance on how to join the video call. You can let

your research team know if you would rather have a phone call instead.

Your glucose and ketone readings will be reviewed with you and recommendations on managing your insulin and other diabetes medication will be given.

Visit 4

This visit will be 4 weeks after you start your trial medication and will take about 45 minutes. The following assessments will be carried out:

- Blood samples
- Urine sample
- Documentation of CGM data from previous 2 weeks
- Review of your blood glucose and ketone levels and insulin requirements.
- Questionnaire

Phone or video call

This will be 10 weeks after you started the trial medication and will be the same as the previous call.

Visit 5

This visit is at the end of your trial medication period, 4 months after you started your trial treatment. This visit assessments will be the same as visit 3, except for the urine pregnancy test that is not undertaken, and the inclusion of a physical examination as done in visit 1.

Phone or video call

This is your last call and will be 1 month after you have finished your trial medication. This will be the same as the previous calls.

What will my blood and urine samples be used for?

During the trial blood and urine samples will be collected at your visits. The maximum amount of blood taken at any visit will be 60ml (4 tablespoons), These will be collected for the following reasons.

- Safety blood samples: to check that your liver, kidney and other organs are working well and to check your glucose and HbA1c levels.
- Biomarker blood samples: for the research lab to check markers of heart failure including NT-pro BNP and C-peptide.
- Urine samples: used to check your kidney function and pregnancy test, if appropriate.
- Optional blood and urine samples: If you agree, we will also take additional blood and urine samples at visits 3 and 5 and store them so researchers can use them in the future for clinical research biomarker and/or genetic tests. Biomarkers are substances in blood and urine which can measure a disease process. Genetic blood tests allow researchers to learn about differences and changes in an individual's genetic makeup, which may help to discover the role that genetics play in disease and treatment. The genetic tests are done only for

research and will not be useful for your clinical care. You and your family will not get the results of any of these tests, including if there are any inherited factors discovered in the tests.

- You do not have to agree to giving these additional samples and you can still take part in the trial if you don't want to.

Trial visits	Visit 1	Visit 2	Visit 3	Phone call	Visit 4	Phone call	Visit 5	Phone call
	Screening	Review	Start	Week 1	Week 4	Week 10	Week 16	Week 20
Consent form	✓							
Health & medication check	✓	✓	✓	✓	✓	✓	✓	✓
Weight	✓		✓				✓	
Height, waist and hip circumference	✓							
Blood pressure & pulse	✓		✓				✓	
Physical examination	✓						✓	
ECG & echo heart scan	✓							
Review of glucose management		✓	✓	✓	✓	✓	✓	✓
Questionnaires	✓		✓		✓		✓	
6-minute walk test			✓				✓	
Pregnancy test	(✓)		(✓)					
Blood samples	✓		✓		✓		✓	
Urine sample			✓		✓		✓	
Start trial medication			✓					
Stop trial medication							✓	

Will taking part in the trial affect my usual care?

No, you'll continue to receive your usual care including taking any medications which you normally take.

What will happen when the trial finishes?

The trial medication won't be available after the end of the trial, so you won't receive the trial medication when the trial finishes. If the trial shows a possible benefit from the sotagliflozin it is possible that sotagliflozin may become available for people like you with type 1 diabetes and heart failure.

We hope to finish the trial in early 2026 but it may take up to a year before we can publish the results. If you want to be informed of the results and whether you received Sotagliflozin or the placebo, we'll send you a letter with this once we have the results. Let us know when you finish the trial if you do not want to receive this.

What are the possible benefits of taking part in the trial?

By taking part you are contributing to medical science. The results may help other people in the future.

If we find that sotagliflozin does make people with type 1 diabetes and heart failure feel better, then we might use sotagliflozin to treat people like you in future.

You'll be monitored closely during the trial by the trial team. If any of the investigations and assessments reveal any new clinically significant abnormality, we'll tell you and either discuss this with your GP (with your consent) or refer you to a specialist clinic at the hospital. We'll also be reviewing your current treatment for diabetes and heart failure and may be able to help improve this.

If sotagliflozin has the same effect as SGLT inhibitors have in people with type 2 diabetes or people without diabetes, and you are allocated to take sotagliflozin in this trial you might notice that your heart failure symptoms improve. You may also find that your glucose levels improve.

What are the possible disadvantages and risks of taking part?

We know that there is a small chance that people with type 1 diabetes are more likely to have episodes of diabetic ketoacidosis (DKA) when they take sotagliflozin. The risk of DKA is about 1 in 50.

Symptoms of diabetic ketoacidosis (DKA) include feeling thirsty, needing to pee more often, stomach pain, feeling sick or being sick, diarrhoea, breathing more deeply than usual, breath that smells fruity (like

pear drop sweets or nail polish remover), feeling tired, sleepy or confused, blurred vision. We can reduce the chance of people developing DKA by carefully choosing the patients who we include in the trial. We'll ask you to check your glucose and ketone levels regularly and will give you information about how to reduce your chance of developing DKA and how to treat it. We'll review your glucose and ketone levels with you at every visit and phone call. If you are found to be suitable for this trial, it is because the risk of DKA occurring is judged to be lower and you meet the national criteria for receiving sotagliflozin.

Because sotagliflozin also helps to lower blood glucose there is a small risk (about 1 in 50) of having a hypo. Very rarely (less than 1 in 1000) hypos can cause you to have a seizure or become unconscious. We will ask you to check your blood glucose regularly to make sure they are not going too low, and you might need to take less insulin to make sure that this does not happen.

Sotagliflozin can make people more prone to thrush, urine or bladder infections. The risk of this is about 1 in 20. This is because sotagliflozin makes you pass more sugar in your urine. These infections are usually minor but might require a course of antibiotics or

treatment for thrush. If this was to happen, you should let your research team know and contact your GP to discuss it.

Sotagliflozin can make you pass more urine. This is normally a good thing in people with heart failure and can help symptoms such as breathlessness or ankle swelling, however sometimes people can lose more fluid than expected and become dehydrated. This happens in about 1 in 50 people. Usually this just needs monitoring and resolves on its own but sometimes other measures may be required. The local trial team will be able to monitor and discuss these with you. For example, if you are taking water tablets (diuretics) the dose of these may need adjusted. But if you are unable to drink enough fluid for a certain reason (such as a stomach bug) this could make you too dehydrated. If this happened you might feel lightheaded or faint, and if very severe it could affect your kidneys. If it was very severe you might need to be admitted to hospital to treat your dehydration. If this was to happen we would stop the trial medication for a period of time. You may well be taking other medications that have a similar caution, such as ACE inhibitors (drug name ends in -pril) or angiotensin receptor blockers (drug name ends -

sartan).

What COVID-19 precautions will be in place when I come for my visits?

The current local COVID-19 guidelines will be in place when you come for your visits. This may include wearing facemasks, handwashing, social distancing when appropriate, checking your temperature and asking about any recent COVID-19 symptoms.

Contraceptive advice

If you are a woman and could get pregnant you must have a pregnancy test at the visits 1 and 3. If you are sexually active with a man you must be willing to use a birth control method which is medically approved during this trial.

If you are a man and are sexually active with a woman who could get pregnant, you must be willing to use a birth control method which is medically approved during this trial.

If you or your partner does get pregnant during the trial, please tell us and we'll follow your health and the health of the baby during pregnancy and at birth.

Medically approved birth control:

- Combined or progesterone only hormonal contraception e.g. pill, injection, implant or patch
- Intrauterine device – ‘coil’
- Female sterilisation
- Male partner vasectomy – sterilisation
- Male condom

What will happen if I want to stop the trial medication or don't want to carry on with the trial?

If you develop any concerns about taking part in the trial, please talk to us and we will discuss the different options available to you.

It is important for us to get as much data as possible for the results of the trial to be reliable. If either you, or the trial doctor, stops the trial medication, continuing to attend the trial visits and phone calls and completing the assessments will help make sure the results of the trial are as useful as possible.

You are free to withdraw from the trial at any time without providing a reason. However, we’d find it useful to know the reason for withdrawal, this may help us improve this trial and future trials. If you want to stop the trial, all medical care you get and your relationship with the medical or nursing staff looking after you won’t be

affected. We'll keep the trial information about you that we have already collected. All personal identifiable data can be withdrawn, should you request it.

Will I receive any payment for taking part?

You won't receive any payment for taking part, but you'll receive taxi transport or reasonable travel expenses to attend the research visits.

Who is organising and funding this research?

This trial is being sponsored by the University of Dundee and NHS Tayside. It is being funded by the JDRF (Juvenile Diabetes Research Foundation Ltd) charity. The sotagliflozin and placebo tablets are being provided free of charge by Lexicon Pharmaceuticals. The trial is being organised by Dr Ify Mordi.

The researchers and your doctor won't receive any personal payment for your participation in the trial. Your hospital will only receive payment to cover the costs of your taking part.

How have patients and the public been involved in the trial?

Many of the assessments being carried out, such as the questionnaires, have been developed with feedback from people with type 1 diabetes and/or heart disease. Patients

like you have also helped to design documents for trial participants such as this information sheet and consent forms.

Who has reviewed this trial?

This trial has been reviewed and approved by Leeds West Research Ethics Committee who are responsible for reviewing research which is conducted in humans.

What will happen with the information collected about me?

Identifiable information about you and the information collected about you during the trial will be stored by your local NHS research team either on paper or on their local NHS computers. Only certain members of the research team can access this information.

People who don't need to know who you are won't be able to access your name or contact details. Your data will have a code number instead. Only certain members of your local research team will have the link between your code number and your personal information.

Information collected about you during the trial is called "trial information". Your electronic trial information will be anonymised and securely stored on password protected databases in the University of Dundee. All paper-based

trial information will be kept in a locked filing cabinet in a locked room.

Your trial information will be kept securely for 25 years after the end of the trial. This is a legal requirement for trials using medication. After 25 years your identifiable information will be removed, and the rest of the information will be kept for research purposes. If you'd like to be informed about future trials that you might be interested in, we'll ask you to sign a consent to allow your local research team to hold your contact details.

We'll ask your permission to tell your GP that you are taking part in this trial.

Information which identifies you will not be published or shared.

Your de-identified (anonymised) trial information may be shared with JDRF and Lexicon Pharmaceuticals to allow them to continue their research into treatments for type 1 diabetes and heart failure. This anonymous data may also be shared with others for ethically approved future research, possibly including research with commercial organisations.

What if something goes wrong?

If you are concerned about taking part in the trial, you have the right to discuss your concern with a researcher involved in carrying out the trial or a doctor involved in your care.

If you have a complaint about your participation in the trial, please first talk to a researcher involved in the trial. You can also make a formal complaint. You can make a complaint to a senior member of the research team or to the Complaints Officer:
[LOCAL CONTACT DETAILS]

If you think you've come to harm due to taking part in the trial, there aren't any automatic arrangements to get financial compensation, but you might have the right to make a claim for compensation. If you wish to make a claim, you should consider getting independent legal advice, although you might have to pay for your legal costs.

Insurance

The University of Dundee holds Clinical Trials indemnity cover which covers the University's legal liability for harm caused to patients/participants. The Scottish Health Boards which are participating as trial sites, are members of the NHS Scotland Clinical Negligence and Other Risks

Insurance Scheme (CNORIS) which gives legal liability cover of Scottish Health Boards for this trial. This will cover their liability for carrying out the trial.

NHS Health Trusts in England have membership of an insurance scheme from the NHS Litigation Authority (NLA).

NHS Health Trusts in Wales have membership of an insurance scheme from the Welsh Risk Pool.

NHS Health Trusts in Northern Ireland have membership of an insurance scheme from the Clinical Negligence Fund.

If you apply for health, life, travel or income protection insurance you may be asked questions about your health. These questions might include questions about any medical conditions you have or have had in the past. You might also be asked if you have had any genetic tests or about taking part in this trial. We don't expect that taking part in the trial will adversely affect your ability to buy insurance. Some insurers may use this information to limit the amount of cover, apply exclusions or increase the cost of insurance. Your insurer may take into account any medical conditions you have, including any which are diagnosed as part of a research trial, when deciding whether to offer insurance to you.

Data Protection Privacy Notice

How will we use information about you?

We'll need to use information from you and from your medical records for this trial.

This information will include your:

- Initials
- NHS/CHI number
- Name
- Contact details
- Age
- Gender
- Ethnicity
- Date of birth

Staff will use this information to do the research or to check your records to make sure that the research is being done properly.

People who don't need to know who you are won't be able to access your name or contact details. Your data will have a code number instead.

We'll keep all information about you safe and secure.

- All records, electronic or paper, will be kept in a secure storage area with access limited to appropriate trial staff only.

Computers used to collate data will have limited access measures via usernames and passwords.We may share data about you outside the UK for research related purposes to:

- continue investigating treatments for type 1 diabetes and heart failure.

If this happens, we will only share the data that is needed. We will also make sure you can't be identified from the data that is shared where possible. This may not be possible under certain circumstances – for instance, if you have a rare illness, it may still be possible to identify you. If your data is shared outside the UK, it will be with the following sorts of organisations:

- Funder (i.e. JDRF).
- Pharmaceutical company providing the trial drug (i.e. Lexicon Pharmaceutical).

We will make sure your data is protected. Anyone who accesses your data outside the UK must do what we tell them so that your data has a similar level of protection as it does under UK law. We will make sure your data is safe outside the UK by doing the following:

- (some of) the countries your data will be shared with have an adequacy decision in place. This means

that we know their laws offer a similar level of protection to data protection laws in the UK.

- we use specific contracts approved for use in the UK which give personal data the same level of protection it has in the UK. For further details visit the Information Commissioner's Office (ICO) website.
- we do not allow those who access your data outside the UK to use it for anything other than what our written contract with them says.
- we need other organisations to have appropriate security measures to protect your data which are consistent with the data security and confidentiality obligations we have. This includes having appropriate measures to protect your data against accidental loss and unauthorised access, use, changes or sharing.
- we have procedures in place to deal with any suspected personal data breach. We will tell you and applicable regulators when there has been a breach of your personal data when we legally have to. For further details about UK breach reporting rules visit the Information Commissioner's Office (ICO) website.

Once we've finished the trial, we'll keep some of the data

so we can check the results. We'll write our reports in a way that no-one can work out that you took part in the trial.

We will keep your study data for the minimum period of time required by regulatory authorities and Good Clinical Practice (i.e. 25 years). The study data will then be fully anonymised and securely archived or destroyed.

What are your choices about how your information is used?

- You can stop being part of the trial at any time, without giving a reason, but we'll keep the trial information about you that we have already collected.
- you have the right to ask us to remove, change or delete data we hold about you for the purposes of the study. We might not always be able to do this if it means we cannot use your data to do the research. If so, we will tell you why we cannot do this.
- If you agree to take part in this study, you will have the option to take part in future research using your data saved from this study. Specimens will be registered with NHS Tayside Biorepository and access for future use of those specimens will be via the CI. Not allowing blood samples to be used

for future research will not affect your participation in the trial.

Where can you find out more about how your information is used?

You can find out more about how we use your information at, including the specific mechanism used by us when transferring your personal data out of the UK.

- **www.hra.nhs.uk/patientdataandresearch**
- by asking one of the research team
- by sending an email to SOPHIST-trial@dundee.ac.uk, or
- by ringing us on +44 (0)7386657801
- https://www.dundee.ac.uk/information-governance/dataprotection/
- http://www.nhstayside.scot.nhs.uk/YourRights/PROD_298457/index.htm

Contact details for further information

Thank you for taking time to read this information and for considering taking part in this trial.

If you'd like more information or want to ask questions about the trial, please contact the trial team using the contact details below.

Principal Investigator: [TBC]

Researcher Nurse: [TBC]

You can contact us Monday – Friday between 09:00 - 17:00.

Outside of those hours, if you need advice, you can contact your out of hours GP service/NHS24 via 111.