

## PARENT INFORMATION SHEET

### Study Title

**Short course daily prednisolone therapy at the time of upper respiratory tract infection in children with relapsing steroid sensitive nephrotic syndrome; the PREDNOS 2 study**

### Invitation to take part in this research study

We would like to invite your child to take part in our research study. Before you and your child decide we would like you to understand why the research is being done and what it would involve for your child. Please take time to read the following information carefully and discuss it with others, with your child, and your GP if you wish. Ask if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish your child to take part.

Part 1 tells you the purpose of this study and what will happen to you if your child takes part.

Part 2 gives you more detailed information about the conduct of the study.

### Part 1

#### What is the purpose of the study?

Children with nephrotic syndrome suffer from disease relapses, where the protein in the urine returns. When these occur, treatment with high dose prednisolone is commenced and this may be associated with a number of side-effects, such as a puffy face, high blood pressure or changes in mood. For this reason, every effort is made to prevent relapses from happening. This generally involves the use of either low dose every other day prednisolone, or other drugs such as levamisole, ciclosporin or mycophenolate mofetil.

It is well known that relapses may be caused by upper respiratory tract infection (URTI– the common cold). Three small studies performed in the developing world (India and Sri Lanka) have shown that if a short course of daily prednisolone treatment is commenced when children develop an URTI, this reduces the risk of a relapse developing. The purpose of this study is to see whether giving a six day course of daily prednisolone when children develop an URTI prevents relapses from developing: we will study this in a large population of UK children with relapsing nephrotic syndrome. The study is being conducted by the kidney specialists in every children's kidney unit in the UK and has been selected for funding by the National Institute for Health Research.

#### Why have has your child been chosen?

Your child has relapsing nephrotic syndrome and has had at least two relapses in the past 12 months. We are asking 360 patients from hospitals in the United Kingdom to take part.

#### Does my child have to take part?

No, taking part in the research is entirely voluntary. It is up to you and your child and your decision will not affect the standard of care your child receives. If you do decide your child should take part, you will be given this information sheet to keep and be asked to sign a consent form. If you decide your child should take part, you are still free to withdraw your child at any time and without giving a reason. This will not affect the standard of care your child receives. If your child does not take part or you withdraw your child from the study, your child will receive his or her consultant's usual treatment for nephrotic syndrome.

### **What will happen to my child if he or she takes part?**

Once you have agreed to your child participating in the study, you will receive a supply of study medicines – two pots of tablets which will be sent by Royal Mail Special Delivery to your family home. One half of children will receive pots of prednisolone and the other half will receive pots of identical placebo (a dummy medicine, with no activity or side effects). A computer will decide whether your child receives active prednisolone or the placebo – a bit like tossing a coin. Neither you, your child or your doctor will know whether your child has been given the prednisolone or the placebo, though this information can be found out in case of an emergency. This is to make the study the best possible test of which treatment is better.

Each time your child develops an URTI during the 12 month study we will ask you to commence them on a six day course of study medicine. For this to happen, your child must have had two of the following symptoms for at least 24 hours: sore throat, ear pain/discharge, runny nose, cough (dry or barking), hoarse voice or fever above 37°C. We will provide you with an electronic thermometer and clear written information about these symptoms. We will also provide you with clear written information about exactly how many tablets you should give – this will depend on your child's weight and height, as well as the dose of prednisolone that they may already be receiving.

We will monitor your child's progress in the usual way, through telephone calls with your local doctor and/or the nurse responsible for children with nephrotic syndrome.

All children will be followed up in clinic at 3, 6, 9, and 12 months to assess their progress.

At one of the study visits a single 10ml (two teaspoon) blood sample will be collected from your child to look at genetic changes associated with nephrotic syndrome. Where possible, we will collect this at a time when your child is having blood tests for routine clinical purposes. There is increasing information suggesting that nephrotic syndrome may be a genetic disease and the blood sample will be used to analyse the DNA from children in the study in order to see if there is a common genetic mutation (minor change) and also to see whether we can understand the cause of the disease. If you do not want your child to have a blood sample collected for the purposes of the study that is fine, your child can still take part in the study without giving a blood sample.

We will ask you to complete four short questionnaires about your child's behaviour and quality of life at the beginning of the study and at 3, 6, 9, 12 months. This should take a total of less than 20 minutes of your time on each occasion. These questionnaires will only be identified by your child's unique study number and date of birth in the month/year format to maintain confidentiality.

The rest of your child's treatment will be usual treatment for relapsing nephrotic syndrome. You will be asked to test your child's urine for protein in the usual way to see if the nephrotic syndrome is coming back. You will record the results in your child's patient diary and bring it with your child to regular check-ups with his or her doctor. In your child's patient diary we will also ask you to record whether your child has been unwell in any way, and record any visits

to your GP or hospital, along with any other medicines that you have given to your child. Study follow-up visits will be at baseline and months 3, 6, 9 and 12. See Table 1 below: Information from the diary that you complete will be recorded in your child's medical record and on the study assessment forms during the study follow-up visits.

Table 1

<b>Study Follow-up Visits</b>	<b>1</b>	<b>2</b>	<b>3</b>	<b>4</b>	<b>5</b>
Baseline/Months	Baseline	Month 3	Month 6	Month 9	Month 12
Regular checkups that are part of the usual treatment for nephrotic syndrome, including documentation of recent medical/drug history, any parental concerns, physical exam, height and weight, and blood pressure check	Yes	Yes	Yes	Yes	Yes
Blood sample for study	Yes (can be at any time in 12 month study period)				
Four short questionnaires about your child's behaviour and quality of life for study	Yes	Yes	Yes	Yes	Yes

### **What is the drug or procedure that is being tested?**

Prednisolone is a steroid drug which suppress the immune system. Prednisolone is the standard treatment for relapsing nephrotic syndrome.

### **What are the alternative treatments available?**

At present, the large majority of children are given no extra treatment when they develop an URTI. There is no agreed standard therapy, though it is hoped that if the results of this study show a benefit to giving a short course of prednisolone, then this will become standard therapy nationally.

### **What are the side effects of the treatment?**

Prednisolone treatment can cause side-effects, including a puffy face and body and mood changes. Other side effects include weight gain, skin problems, osteoporosis (thinning of the bones), sore throat or mouth and an increased risk of infection.

Patients taking prednisolone should avoid coming into contact with chicken pox, should not suddenly stop taking prednisolone and should carry a steroid card that explains they are taking prednisolone, a steroid drug. You should contact your child's consultant paediatrician straight away if your child has come into contact with chickenpox unless you have been told this is not necessary because your child is immune to chickenpox. This should be through contacting the consultant's secretary or nurse specialist during office hours or the hospital ward at other times.

Patients taking prednisolone should avoid all live vaccines. Therefore during the course of the study all live vaccines should be avoided. Routine live vaccines such as MMR can be given once immunosuppressive therapy has been stopped. Your GP will be informed of this.

### **What are the possible disadvantages and risks of taking part?**

The purpose of the study is to see whether giving a short course of prednisolone when children develop an URTI prevents them from developing a full relapse, which would need treatment with a long course of high dose prednisolone. If this is not the case, then those children who received prednisolone at the time of an URTI will have received this short course of prednisolone unnecessarily and there is a very small chance that this may be associated with minor side-effects. All children will be monitored for side-effects and if there

is any concern that these are in any way associated with the study then they can be withdrawn.

**What are the possible benefits of taking part?**

Children who participate in research studies such as this receive very close monitoring, which will be advantageous to your child's general health. The information we get from the study may help us to improve the treatment of all children in the UK with nephrotic syndrome in the future.

**What if new information becomes available?**

Sometimes during the course of a research study, new information becomes available about the treatment that is being studied. If this happens, your child's research doctor will tell you about it and discuss with you whether you want your child to continue in the study. If you decide to withdraw your child, your research doctor will make arrangements for his or her care to continue. If you decide your child should continue in the study you will be asked to sign an updated consent form. Your child's research doctor may also discontinue your child from the study if your child's safety is compromised at any time.

**What happens when the research study stops?**

When the research study stops the results of the study will be published and the information we get from the study may help us to improve the treatment of children presenting with relapsing nephrotic syndrome in the future. If we discover that daily prednisolone treatment at the time of URTI does reduce relapse then it will be used in future as standard care. When the research study stops and the study results have been published you can request to be told which arm of the study your child was in.

**What if there is a problem?**

Any complaint about the way you/your child may have been dealt with during this study or any possible harm your child might suffer will be addressed. The detailed information is given in Part 2.

**Will my child taking part in the study be kept confidential?**

Yes. We will follow ethical and legal practice and all information about your child will be handled in confidence. The detailed information is given in Part 2.

**Thank you for reading so far – if you are still interested, please go to Part 2**

**Part 2**

**What if relevant new information becomes available?**

Sometimes, during the course of a research project, new information becomes available about the treatment(s) being studied. If this happens, your study doctor will discuss how this affects your child's care and participation in the PREDNOS 2 study. Your study doctor might consider that your child should continue in the study or withdraw. Either way, he/she will explain the reasons and arrange for your child's care to continue. If you decide for your child to continue in the study he/she may ask you to sign an updated consent form. If the study is

stopped for any other reason, your doctor would, again, tell you and arrange your child's continuing care.

### **What will happen if I do not want to carry on with the study?**

You and your child can decide not to continue with study at any time but, if you do, we would still like to follow-up your child's progress and your child's data would remain on file and be included in the final study analysis unless you request that they should not be.

### **What if there is a problem?**

If your child is harmed due to someone's negligence, then you may have grounds for a legal action but may have to pay for it. Regardless of this, if you wish to complain, or have any concerns about any aspect of the way your child has been approached or treated during the course of this study, the normal National Health Service complaints mechanisms should be available to you. Taking part in this study would not affect your child's legal rights.

If you have a concern about any aspect of this study, you should ask to speak to the researchers who will do their best to answer your questions. The contact details for the PREDNOS 2 Chief Investigator are: Dr Martin Christian, Telephone 0115 924 9924 x63832. If you remain unhappy and wish to complain formally, you can do this through the NHS Complaints Procedure. Details can be obtained from the hospital.

### **Will my child taking part in the study be kept confidential?**

If you decide for your child to take part in the PREDNOS 2 study all information which is collected about your child during the course of the research will be kept strictly confidential in the same way as their medical records. Information about your child's disease and progress will be sent by your doctors to the PREDNOS 2 study office at the University of Birmingham Clinical Trials Unit, on paper and electronically, where it will be securely stored under the provisions of the General Data Protection Regulation and Data Protection Act 2018. If you consent to your child taking part in this study, your child's GP and the other doctors involved in your child's clinical care will be notified of your child's participation in the PREDNOS 2 study and kept informed of your child's progress. With your permission, your child's relevant medical records may be inspected by authorised individuals from the Birmingham Clinical Trials Unit or your hospital. They may also be looked at by the study team and regulatory authorities. The purpose of this is to check that the study is being carried out correctly. All will have a duty of confidentiality to your child as a research participant and will do their best to meet this duty. If you consent to your child taking part in this study a copy of the consent form will be faxed to the Birmingham Children's Hospital Pharmacy Department who will distribute the study medication direct to your home.

In line with clinical trial guidelines, at the end of the study, the data will need to be securely archived for 25 years. Arrangements for confidential destruction will then be made. Should you withdraw consent for your child's data to be used, it will be confidentially destroyed.

### **What will happen to the blood sample my child gives?**

The blood sample will, where possible, be collected at a time when your child is having a blood test performed for routine clinical purposes. (If you do not want your child to have a blood sample collected for the purposes of the study that is fine, your child can still take part in the study without giving a blood sample). Following collection, the sample will be sent to the Institute of Child Health, London (Prof Detlef Bockenhauer's laboratory), where DNA will be isolated. Half will be used in experiments to see if there is a genetic cause for nephrotic

syndrome (by Prof Detlef Bockenhauer and Prof Robert Kleita at Great Ormond Street Hospital) and the other half will be used by Dr Ania Koziell at Kings College, London and Professor Moin Saleem at Bristol University in other experiments using different techniques to look at genetic changes in relapsing nephrotic syndrome. Following completion of this work, any remaining DNA samples will be retained in the laboratories of Prof Bockenhauer/Prof Kleita in London and/or Dr Koziell/Professor Saleem in London and Bristol for use in future research projects investigating genetic factors and disease mechanisms in steroid sensitive nephrotic syndrome which may arise as a result of this work. Any such studies on these samples would require Research Ethics Committee approval. Your child's DNA sample will be identified only by their study number and their date of birth in the month/year format; the sample will not be labelled with any personal information.

### **What will happen to the results of the research study?**

Once the study has finished the results from all patients who took part in the study will be published in a scientific journal. The publication will appear when all the patients have completed the study and the results have been analysed. Your child's doctor can provide you with a copy of this publication if you are interested. We will also publicise the results on the study's website. Only anonymous data will be published and your child's name will not appear in any report, presentation or publication.

### **Who is organising and funding the research?**

The PREDNOS 2 study is being co-ordinated by the Birmingham Clinical Trials Unit at the University of Birmingham and is sponsored by the University of Birmingham and Manchester University NHS Foundation Trust. The study Chief Investigator is Dr Martin Christian at Nottingham Children's Hospital. The study is supported by the British Association for Paediatric Nephrology and the Clinical Research Network for Children. The study is being funded by National Institute for Health Research Health Technology Assessment Programme. The research has been reviewed and approved by all these organisations. Your child's doctor will not be paid for including your child in this study.

### **Who has reviewed the study?**

All research in the NHS is looked at by an independent group of people called a Research Committee to protect your safety, rights, wellbeing and dignity. This study has been reviewed and given favourable opinion by North West – GM Central Research Ethics Committee. Research Ethics Committees include healthcare professionals as well as non-medical people, and are completely independent from anyone organising the study.

### **Where can I get further information?**

For queries about the study or for further information please contact:

Dr Martin Christian, Telephone 0115 924 9924 x63832, PREDNOS 2 Chief Investigator

<Insert Local PI Name>, Telephone <Insert Local PI Tel. No.>, PREDNOS 2 Principal Local Investigator

The PREDNOS 2 study co-ordinating centre is located at the Birmingham Clinical Trials Unit, Institute of Applied Health Research, Public Health Building, , University of Birmingham, Edgbaston, Birmingham B15 2TT. Tel 0121 415 9131, Fax: 0121 415 9135, Web address: [www.birmingham.ac.uk/PREDNOS2](http://www.birmingham.ac.uk/PREDNOS2).

**Thank you for considering your child's participation in this study**

**You will be given a copy of this information sheet and a signed consent form to keep if you decide that your child wishes to take part in the study.**