

**LOCAL
HOSPITAL
LETTERHEAD**

APPENDIX A

A randomised placebo controlled study of Ephedrine/Etilefrine for prevention of recurrent (stuttering) attacks of priapism in sickle cell disease.

PATIENT INFORMATION SHEET

Dear Patient

You are being asked to take part in a multi-centre randomised trial this is being conducted in many hospitals throughout the UK and two centres in Nigeria. It has been subjected to ethical review by your local hospital.

Before you decide whether or not to take part, it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with friends, relatives and your GP if you wish. Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.

RATIONALE FOR STUDY

Priapism is a persistent, painful erection of the penis. It can be caused by a variety of diseases but it is a well-recognised complication of sickle cell disease. Events that precipitate attacks are poorly understood, neither is there an agreed locally or internationally best way to treat this complication. We have some evidence that an acute major disabling attack is preceded by recurrent, short lasting (less than 4 hours) *stuttering* attacks. An acute attack can lead to severe pain, sexual dissatisfaction and impotence and may require major surgery.

We are conducting a clinical trial comparing two drugs Ephedrine and Etilefrine for preventing recurrent attacks of stuttering priapism and its other long-term problems such as impotence and sexual dissatisfaction. We do not know if by preventing such recurrent attacks medically, whether we can prevent a major attack thus reducing the number of people who may have to undergo a surgical operation to relieve it or be treated for impotence.

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Why have I been offered entry to the study? You have been offered to take part because you are a male patient with sickle cell disease who has stuttering priapism.

We would be grateful if you would consider participating in our trial, which consists of two stages. An initial stage 'A', which lasts 6 months, consists of filling in a diary on how frequently you experience these attacks. Your diary will be reviewed in your normal clinic every 6 weeks during a normal clinic appointment. At the end of six months, you will then be asked to submit the diary and to enter into stage 'B' to be randomised into one of four treatment arms these being; (1). Ephedrine 15 mg (2). Ephedrine 30 mg (3). Etilerfrine 50 mg and (4). Placebo (dummy drug). You will be reviewed initially after two weeks and then every six weeks for a period of 6 months. You will be asked to fill in the study diary.

Neither you nor your Doctor will know what tablets you are taking.

What do we know about the study drugs? Ephedrine is a common nasal decongestant present in most common cold preparations bought over the counter in the UK and in some developing countries. Ephedrine is also licensed for the treatment and prevention of asthma. We are testing two strengths, 15mg and 30 mg of the Ephedrine tablet to see which effective dose is associated with the least side effect(s). You will be asked to take one tablet of study medication at night.

We are also testing Etilerfrine (a drug with a similar action) at a trial dose of 50 mg. Etilerfrine is not licenced in the UK but has been used for treating priapism in the UK, though not in a clinical trial. This drug is licensed for the treatment of low blood pressure in other European countries such as Germany and Spain. The tablets to be used in the trial are identical in appearance. Neither drugs are licensed for this use but both have been used very occasionally in sickle cell disease.

What side effects can I expect? Both drugs have similar side effects. Side effects include; palpitations, tachycardia, anxiety, sweating. In abnormally susceptible patients; chest pain and a rise in blood pressure can rarely occur. The elderly are more susceptible to these effects on the heart. The side effects can be limited by taking the tablets just before going to bed at night. We are also using a low dose of both drugs, which should still be effective. Your local doctor will monitor you for any side effects you may be experiencing during that period and how often you are still getting the attacks and may advise you to stop if you are intolerant of the drugs. You will be asked to fill in your symptom diary.

What happens at the end of the study? At the end of your participation in the study you will receive standard clinical care as decided by your Doctor in discussion with you. All the results will be communicated back to your Doctor. He or she will then discuss subsequent treatment with you either based on the results of the analysis or his suggestion. Even if this drug is shown to be of benefit, it may be some time before it is licensed for use.

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What else would be involved in the study? We would take a drop of blood from your routine blood sample onto filter paper to re-confirm your exact sickle cell type. There are **no** other additional blood tests required for the purpose of the study. We will check your blood pressure at each clinic visit and review your diary.

What other treatments can I have? There are other treatments available for priapism but none of these have been universally accepted. These include drainage of blood in the erect penis by a needle and injection of a similar drug to cause flaccidity; or surgery. You could have a long period of blood transfusion.

What happens if anything goes wrong? You are free to participate or not and this will in no way affect your subsequent care in the hospital you attend. There is no payment for doctors or patients as this trial is not sponsored by any drug company. If you are harmed by taking part in this research project, there are no special compensation arrangements. If you are harmed due to someone's negligence, then you may have grounds for a legal action but you may have to pay for it. Regardless of this, if you wish to complain about any aspect of the way you have been approached or treated during the course of this study, the normal National Health Service complaints mechanism should be available to you. You may withdraw from the study at any time without explaining why.

Will the information be confidential? Yes. Only those involved will be able to look at your records. Your personal details will be available to your local doctor, the trial Medical Statistician and members of the study team.

What benefits may I get from the study? The study may not benefit you. We hope that the study will allow us to decide whether or not the drug works.

If further information is required, you can contact your local investigator or the Chief Investigator.

We hope you will agree to participate.

Many thanks for your anticipated co-operation

Chief Investigator

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