PARTICIPANT INFORMATION SHEET

PART 1

We would like to invite you to take part in a research study. Before you decide, you need to understand why the research is being done and what it would involve for you. Please take time to read the following information carefully. Talk to others about the study if you wish.

Part 1 tells you the purpose of this study and what will happen to you if you take part. Part 2 gives you more detailed information about the conduct of the study.

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.

What is the purpose of the study?
We are conducting a large study to try and find out the best treatment for pyoderma gangrenosum. This condition causes painful ulcers on the skin and these can take many months to heal.

The study is comparing the two most commonly used medicines for the treatment of pyoderma gangrenosum. We want to do this as these treatments have never been properly studied before and doctors are confused about the best treatment to give.

Why have I been chosen?
We are asking you to participate because you have pyoderma gangrenosum (or your doctor feels that it is possible that you may
have pyoderma gangrenosum). We are looking for 140 people with pyoderma gangrenosum to take part in this study.

**Do I have to take part?**

It is up to you to decide. We will describe the study to you and go through this information sheet. We will then ask you to sign a consent form to show you have agreed to take part. You are free to withdraw at any time, without giving a reason. This would not affect the standard of care you receive.

If you and your doctor feel that your pyoderma gangrenosum can be treated with a cream rather than medications taken by mouth, you can still help the study by allowing us to record you well your treatment is working.

**What will happen to me if I take part?**

We are asking you to take part in a randomised trial. Sometimes we don’t know which way of treating patients is best. To find out, we need to compare different treatments. We put people into groups and give each group a different treatment. The results are compared to see if one is better. To try to make sure the groups are the same to start with, each patient is put into a group by chance (randomly, like the toss of a dice). You will have a 50% chance of receiving either treatment.
The table below shows what will happen throughout the study:

<table>
<thead>
<tr>
<th></th>
<th>Week 0</th>
<th>Week 2</th>
<th>Week 6</th>
<th>Month 6</th>
</tr>
</thead>
<tbody>
<tr>
<td>Give consent to take part in the research</td>
<td>✓</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Blood tests undertaken</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Give basic details about yourself, including medical history</td>
<td>✓</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Blood pressure checked</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Weight checked</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Assessment of your ulcer undertaken</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Measurement of your ulcer undertaken</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Digital photograph of ulcer undertaken</td>
<td>✓</td>
<td></td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Complete a diary</td>
<td></td>
<td></td>
<td></td>
<td>To be completed as instructed</td>
</tr>
</tbody>
</table>

In addition to the visits described above, your doctor will continue to see you as he/she normally would.

We are asking you to take part in this study for 6 months, or until your ulcer has healed (depending which happens first). We would also like to stay in touch with you after this period, just in case your ulcer comes back.

As pyoderma gangrenosum is very rare, we will be looking for patients in at least 50 hospitals, and the whole study will take five years to complete.

The researchers may wish to contact you occasionally in order to assess how your ulcer is healing. This will either be by telephone or letter.

We will inform your GP that you are taking part in the study. We may also contact your GP after you have finished in the study to check on how well you have been since.

In some cases, it may be possible to treat the ulcers with a cream or an ointment instead of tablets. If this is a suitable treatment for you, then your doctor may advise you to try a cream or an ointment first rather than joining the randomised study. **This is a decision that**
you and your doctor should make together. If you decide to have an alternative treatment, we would still like to collect information on how well your ulcers responds, as this is still useful information for doctors to know.

Expenses and payments
If you choose to take part, you will receive an inconvenience allowance of £45. This will be in the form of three £15 vouchers sent to you on separate occasions during the study. The vouchers will be general ‘high street’ vouchers which can be used in a variety of shops. The vouchers are intended to cover any additional costs (e.g. travel, prescription charges) that you may have as a result of taking part in the study, although the majority of your visits will be for your normal care with your skin doctor.

If you are normally able to claim your expenses back through the hospital, you should still be able to do this.

What will I have to do?
This study has been designed so that it reflects how these treatments are normally used for pyoderma gangrenosum. Because of this, we do not want to change anything about your normal care. Once your treatment has been decided, then your doctor will treat you as he normally would. You will be asked to return to clinic at regular intervals so that your doctor can check how your ulcer is healing up, and to check that the drugs are not causing other health problems.

You should take the study medication regularly as directed. You should not take part if you are taking part in any other drug study. You will not be able to take part in the study if you are already taking one or both of the study drugs.

- You will be given a treatment card which you should carry with you at all times.
- It is very important that you DO NOT stop taking the medication suddenly. The dose needs to be reduced very gradually over several weeks or months and your study doctor will advise you on this.
- We recommend you avoid contact with anyone who has (or they suspect they may have) chicken pox, measles or shingles. If you do come into contact with anyone you must see your doctor urgently.
• We recommend that if you drink grapefruit juice or take the herbal remedy, St John’s Wort, you discuss this with your skin doctor, since they may alter how the study drug works.

• Before having any kind of medical treatment or surgery, including dental or emergency treatment, vaccinations or any medical tests, tell the doctor, dentist or surgeon you are taking this study medication and show them your treatment card.

You will be asked to complete some short questionnaires and to keep a diary about your treatment and symptoms.

Your doctor will take a digital photograph of your ulcer when he sees you, and this will help us to assess how quickly the ulcer is healing. We are also interested in knowing how long it takes for your ulcer to completely heal. In order to do this we will ask you to contact us as soon as you stop using dressings for your ulcer.

**What are the drugs that are being tested?**

If you choose to enter the main study, you will receive one of the following medications. As the treatments are allocated by chance, it will not be possible to choose which treatment you receive.

• **prednisolone** (0.75 mg/kg of bodyweight/day) – this is a corticosteroid and one of the most commonly used treatment for pyoderma gangrenosum.

• **ciclosporin** (4 mg/kg of body weight) – this is a drug that reduces the body’s immune system (ability to fight off infections).

Prednisolone and ciclosporin are the two most commonly used drugs for the treatment of pyoderma gangrenosum, but they have never been properly assessed in a clinical trial because the condition is so rare. This means that the drugs are not “licensed” for use in this condition but clinicians feel that they may have beneficial effects.

These are both treatments that you take by mouth. If you have difficulty swallowing tablets, it may be possible for the medication to be given to you as a liquid. You will need to discuss this with the doctor who sees you. They are strong drugs and have known side-effects. Your doctor will talk to you about these and will explain the possible effects of each.
Both treatments can be taken in combination with other drugs. However, some drugs should not be taken at the same time as the study drugs. You should always tell any doctor treating you that you are taking these medicines. You should not take over-the-counter preparations without discussing this first with your doctor or pharmacist. You will be given further information about which drugs to avoid once you receive your medication.

**If the treatment that you have been given does not seem to be working, or you experience bad side-effects, then your doctor will withdraw you from the study and try another treatment.**

If you choose NOT to enter the main (randomised) study, then your doctor will recommend a treatment that he thinks is best for you. If your doctor prescribes a cream or ointment, we would still like to stay in touch with you, and to collect details of how well your pyoderma gangrenosum is responding. You will be asked to sign a consent form agreeing to this.

**What are the alternatives for diagnosis or treatment?**
Because pyoderma gangrenosum is such a rare condition, very little is known about the best treatments to use. The ones included in this study are the ones that are most commonly used, but the effects of these have never been properly studied in a randomised trial.

**What are the possible risks and benefits of taking part?**
Because this study is comparing two commonly used treatments and the study is designed to mimic normal care, there are no additional risks or benefits to you personally in taking part in this study.

The care that you will receive will be very similar to the care that you would receive if you were not taking part in the study. The main benefit will be for future pyoderma gangrenosum patients, as this study will help doctors to understand which treatments work best.

**What are the side effects of any treatment received when taking part?**
Pyoderma gangrenosum is a serious condition that needs medical treatment. Both prednisolone and ciclosporin have been in use for many years for a wide range of medical conditions and their side-effects are well known. One of the things that we hope to look at as part of the study is whether one treatment has worse side-effects than the other for patients with pyoderma gangrenosum.
The most common side-effects of *prednisolone* are:
- feeling sick, indigestion, stomach pain
- mood changes, feeling tired
- increased appetite / weight gain
- dizziness / difficulty sleeping
- thrush in the mouth
- a round face

Less common side effects of *prednisolone* are:
- rise in blood pressure
- osteoporosis (brittle bones)
- more likely to develop infections
- diabetes

The most common side-effects of *cyclosporin* are:
- rise in cholesterol
- mild tremor
- headache
- rise in blood pressure
- abnormalities of kidney tests

Less common side-effects of *cyclosporin* are:
- more likely to develop infections
- feeling sick and vomiting
- diarrhoea
- changes to your gums
- excessive hair growth
- feeling tired
- muscle cramps
- abnormalities of liver tests
- tingling/numbness sensation, like ‘pins and needles’
- non-melanoma skin cancer (pre-cursor)
- increased risk of lymph gland tumours

The side effects of both of these drugs tend to get better if the dose is reduced. In order to adjust the dose of the drug to suit you, your doctor will conduct regular tests of your blood and urine, and check your blood pressure at every visit.

**Harm to the unborn child:**
If you are pregnant or trying to have a baby, you will not be able to enter this study. If you are of child-bearing age, then a pregnancy test will be carried out before you receive any treatment and you will be asked to use contraceptives throughout the treatment period.
The doctor may want to repeat the pregnancy test again. If you do get pregnant whilst you are involved in the study, you should tell your doctor straight away and you will be withdrawn from the study immediately.

**What happens when the research study stops?**
Because both the study drugs are in everyday use, if you still need treatment after the study has ended, this will be available. Your normal care will continue after your involvement in the study has ended.

We will inform all participants of the results of the trial after it has ended.

**What if there is a problem?**
Any complaint about the way you have been dealt with during the study or any possible harm you might suffer will be addressed. The details are included in part 2.

**Will my taking part in the study be kept confidential?**
Yes. We will follow ethical and legal practice and all information will be handled in confidence. The details are included in part 2.

This is the end of Part 1. If you are interested in taking part, please read the additional information in part 2 before making any decision.
PART 2

What if relevant new information becomes available?
Sometimes during a study, we get new information about the treatment being studied. If this happens, your doctor will tell you and discuss whether you should continue in the study. If you or your doctor should decide that it is not in your best interest to carry on, your normal treatment will continue instead. If you do carry on, you may need to sign another consent form.

What will happen if I don’t want to carry on with the study?
If you find that you want to stop taking the study medication, a member of the study team or your doctor will ask you if you would be prepared to keep in touch so that we can keep a record of how well you are after finishing the study. This information would be very useful to us. Alternatively, you may wish to withdraw altogether from the study and this will not affect your future care at all. However, we will need to use the information we have collected so far.
If you have started taking the study medication you should not stop taking them suddenly – the dose needs to be reduced very gradually over several weeks or months. Your doctor will advise you on this. But please remember, **DO NOT** stop taking your medication suddenly.

What if I have a complaint?
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 help. You can telephone 0115 8230489, or email stopgap@nottingham.ac.uk or contact the STOP GAP Trial Manager, Eleanor Mitchell, Office B39, Medical School, Queen’s Medical Centre, Nottingham, NG7 2UH. If you are still unhappy and you wish to complain formally, then you can do this through the NHS complaints procedure. Details of how to lodge a complaint can be obtained from your local hospital.

What if there is a problem?
There are no special compensation arrangements for this study. However, if you are harmed as a result of someone’s negligence, then you may have grounds for a legal action for compensation, but you may have to pay your legal costs.
**Will my taking part in the study be kept confidential?**
All information which is collected about you during the course of the research will be kept confidential. Some parts of your medical records and the data collected for the study will be looked at by authorised members of the study team. They may also be looked at by representatives of regulatory authorities and by authorised people to check that the study is being carried out correctly. All will have a duty of confidentiality to you as a research participant.

With your agreement, the co-ordinating centre will be sent your personal details (e.g. name, address, telephone number) in order for them to keep in touch with you throughout the study. Health information that is sent to the co-ordinating centre will be identified by a number, rather than your name and address.

All information will be stored in accordance with regulatory requirements and will be destroyed after a period of five to seven years from the end of the study (depending on local policy).

**Who else will be told of my involvement in the study?**
We will inform your GP, and possibly doctors that are treating you for other conditions, that you are taking part in the study and what study tablets you are taking.

**What will happen to my blood samples?**
Any routine blood samples or biopsies that are taken will be sent to your normal hospital laboratory for analysis. They will be treated in exactly the same way as if you were not in the study.

**What will happen to the results of the study?**
We will submit the results for publication in a respected journal and make sure that the results are available to all doctors who treat pyoderma gangrenosum patients. We will send all participants a summary of the results at the end of the study. The results will also be available on the study website: [www.stopgaptrial.co.uk](http://www.stopgaptrial.co.uk)

**Who is organising and funding the research?**
The Department of Health is funding this study via the National Institute for Health Research (NIHR). The study doctor will not get paid for including you in this study. However, his/her hospital department may get a small fee to cover administrative time spent on the study.
The study will be carried out in hospitals in the UK. It will be run through the UK Dermatology Clinical Trials Network, which is a registered charity that supports independent clinical trials in the UK. The study is also being Clinical Trials Units at the University of Nottingham and University of Glasgow. Nottingham University Hospitals NHS Trust is sponsoring this study in the UK.

**Who has reviewed the study?**
All research in the NHS is looked at by an independent group of people, called a Research Ethics Committee to protect your safety, rights, wellbeing and dignity. This study has been reviewed and given a favourable opinion by the Northern and Yorkshire Research Ethics Committee.

**Further information and contact details**
If you would like more information about the study, please talk to your study doctor or contact the study team on:

<Study doctor contact details to be inserted>

Email: stopgap@nottingham.ac.uk  
Website: www.stopgaptrial.co.uk  
Telephone: 0115 8230489 / 0115 8230486

If you would like to know more about the work of the UK Dermatology Clinical Trials Network, you can visit www.ukdctn.org or telephone the Network Manager on 0115 8468625 or write to UK DCTN, Centre of Evidence Based Dermatology, University of Nottingham, King’s Meadow Campus, Lenton Lane, Nottingham, NG7 2NR.