

PPL-252A

Assessing Total and Regional Lung Deposition of Colistin Delivered Using a Dry Powder Inhaler and a Nebuliser Device in Volunteers with Cystic Fibrosis - A Pilot Study.

You are being invited to take part in a research study. Before you decide to participate 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 your 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.

What is the purpose of the study?

The purpose of the study is to determine the ability of a new dry powder inhaler to deliver a drug (colistin; Colomycin[®]) to your lungs. The effect of taking salbutamol (Ventolin[®]) before taking colistin by the dry powder inhaler will also be determined. The deposition of drug in your lungs from a nebuliser will be compared to deposition of drug from the dry powder device.

Why have I been chosen?

You have been referred to us by your hospital consultant because you appear to fulfill the entry requirements for the study.

Do I have to take part?

No - it is up to you whether or not to take part. You will have this Information Sheet for at least 24 hours. If you decide to take part, the study will be explained to you by either a nurse or a doctor. You will be given this information sheet to keep and will also be asked to sign a consent form. If you decide to take part you are still free to withdraw at any time without giving a reason. If you withdraw from the study after you have been dosed, you will be asked to attend a post-study medical.

The investigator is also free to withdraw you from the study at any time.

What will happen to me if I take part?

Pre-study Medical:

You will be required to attend a pre-study medical either at Pharmaceutical Profiles or at your CF centre. This will last for approximately one and a half hours.

- At the pre-study medical you will be asked about your medical history. You will also undergo the following: physical examination, lung function testing, sputum testing, blood and urine testing that will include tests for drugs of abuse, including cannabis. In addition, your heart will be monitored.
- If you are a female of child-bearing potential, you will be asked to provide a urine sample that will be used for a pregnancy test.



Acceptance into the study is not guaranteed and is subject to the results and tests carried out at this pre-study medical being approved by a physician.

APPROVED
NHL
17 FEB 2001**Study Days:**

If you are accepted into the study, you will be required to attend three study days to be held on dates that will be communicated to you in a separate letter. These study days will each be approximately five hours in length. Each study day will be within 44 hours to 7 days of the last study day. Travel to [REDACTED] will be organised and you will be reimbursed for any travel expenses incurred. Representatives from the company sponsoring the research study may be present on study days to witness routine study day procedures.

- Prior to attending each study day you will be required not to take any short acting short acting relievers within 6 hours of taking study medication and long acting relievers may not be taken within 12 hours of taking study medication. Three to four times daily theophylline should not be taken within 6 hours of dosing, twice daily theophylline should not be taken within 24 hours of taking study medication, and once daily theophylline should not be taken within 48 hours of taking study medication. At your pre-study medical you will be asked what medication you take and a nurse will inform you when you should stop taking it.
- You will be asked to bring your normal CF medication with you and inform staff when you take any medication.
- When you arrive for a study day, you will be asked some questions about your health since your last visit. Your urine will be tested for the presence of drugs of abuse.
- You will be asked to perform your normal physiotherapy before your lung function is tested.
- Lung function tests will be performed and recorded. If the lung function test results do not meet specific criteria, your study day will be re-arranged.
- If your study day is re-arranged, you will be required to return for an additional study day on a mutually agreed date.
- If you are a female of child bearing potential you will be pregnancy tested before receiving study drug on each study day.
- You will inhale colistin (Colomycin®) on each occasion. You will practice the inhalations beforehand using a placebo device. A placebo is a dummy treatment such as an inhaler that looks like the real thing but is not.
- does not contain active drug.
- On two occasions you will receive colistin (Colomycin®) from a dry powder device; on the other occasion you will receive colistin from a nebuliser, which produces a fine mist of drug.
- On one of the occasions that you receive colistin from the dry powder device you will first receive salbutamol (Ventolin®) from a metered dose inhaler.
- Immediately after you have received study drug, pictures of your lungs, the side of your head and, if necessary, your abdomen will be recorded.
- You will be instructed to collect all urine samples for 2 hours post-study medication. You must remain at the unit during this time.
- You will be asked to provide a sputum sample between 15 and 30 minutes after taking the study drug.
- The lung function test will be repeated before you go home. You must be assessed as being well before you are allowed to leave the premises.
- During the study you will be asked to inhale a radioactive gas (^{81m}Krypton) in order to record the shape of your lungs.
- You will be informed of any significant new findings that develop during the course of the study.



After the study:

Once you have completed the study, or if you withdraw from the study part-way through, you will be asked to attend a 30 minute post-study medical within 14 days of your last study day either at [REDACTED] or at your CF clinic.

What do I have to do?

- You must not drink any alcohol, in the 24 hours prior to each study day.
- You must not drink liquids or eat food containing caffeine or xanthine for 12 hours prior to receiving study drug and for the duration of the study period.

Please note: Drinks that contain caffeine and xanthines include coffee, tea and a number of soft drinks (eg cola drinks, Dr. Pepper, Mountain Dew, Lucozade and Red Bull. Chocolate also contains caffeine and xanthines)

- You must arrive at the Clinical Unit at a pre-determined time on each study day.
- You will undergo all the study day procedures as described in the 'What will happen to me if I take part' section of this information sheet.
- You must tell the investigators if you experience any symptoms of any type during the course of the study.
- You will be informed of any significant new findings that develop during the course of the study.

What is the drug or procedure that is being tested?

The drug being tested in this study, colistin (Colomycin®) is an antibiotic used for the treatment of bacterial infections in patients with cystic fibrosis. In this study the colistin will be labelled with a small amount of radioactivity called ^{99m}technetium so that we can see where the drug goes in your lungs.

What are the side effects of taking part?

At the dose of colistin (Colomycin®) given it is unlikely that you will have any side-effects, however, the side-effects that have been reported following colistin therapy include; coughing, tightness of the chest, minor throat irritation, and a mild unpleasant taste. There may also be some side-effects that are yet unknown.

The side-effects reported following salbutamol (Ventolin®) include; slight tremor (usually hands), nervous tension, headache, flushing, and palpitations

What are the possible disadvantages and risks of taking part?

By taking part in the study you will be exposed to ionising radiation. The Department of Health has authorised the administration of radioactive substances for this study. The maximum total radiation dose to you from taking part will be 0.46 mSv which is less than the dose received from 2 months natural background radiation.

What are the possible benefits of taking part?

You will not receive any medical benefit from taking part in this study, however new dry powder formulations of colistin may provide a more convenient delivery method of colistin (Colomycin®) over conventional nebuliser therapy for patients with CF.

What if something goes wrong?

Compensation for any injury caused by taking part in this study will be in accordance with the guidelines of the Association of the British Pharmaceutical Industry (ABPI). The ABPI guidelines recommend that the sponsor, without legal commitment, should compensate you without you having to prove that it is at fault. This applies in



cases where it is likely that such injury results from giving any new drug or any other procedure carried out in accordance with the protocol for the study. Your right under the law to claim compensation for injury where you can prove negligence is not affected. Copies of the guidelines are available on request.

In the event of a research related injury occurring you should contact [REDACTED]

Will my taking part in this study be kept confidential?

If you consent to take part in the research study, your privacy will be fully protected. Your medical records may be inspected by the company sponsoring the research for purposes of analysing the results. They will also be looked at by people from [REDACTED] and regulatory authorities to check that the study is being carried out correctly. Your name, however, will not be disclosed outside [REDACTED] with the exception that for your own safety, your GP will be told that you have taken part in this study, and will be notified if any of the results from your blood and urine tests are significantly abnormal or if any serious adverse events occur. For the same reason, brief details of your involvement in this trial may be revealed to other units, such as the [REDACTED] which carry out clinical trials.

What will happen to the results of the research study?

The results of the study will be analysed and given to the sponsor Pharmaceutical Company in the form of a research report that is usually prepared by [REDACTED]. The results will then be used in the further development of the treatment that is being tested. You will not be identified by name in this report.

Who is organising and funding the research?

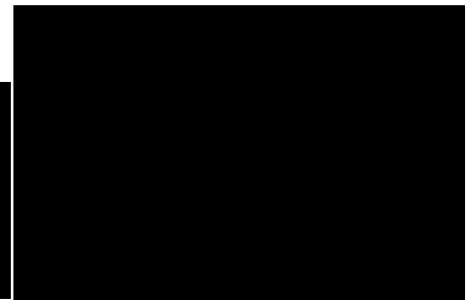
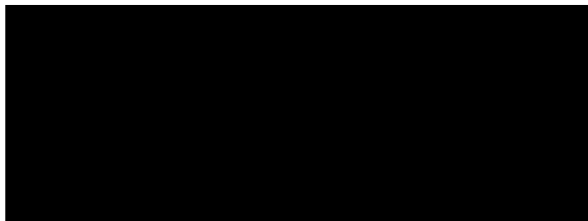
[REDACTED] are organising the research study that is being paid for by a sponsor Pharmaceutical Company.

Contact for further information:

If you would like any further information, or have any further questions please contact your referring consultant. Alternatively, you may also contact [REDACTED] at [REDACTED]

Thank you for considering to take part in this study.





When you attend for the pre-study medical examination, you will have the opportunity to discuss the study, and will then be asked to sign a consent form; the wording of the form is set out below:

CONSENT FORM

PPL-252A

Subject identification for this study:

Title of Project: Assessing Total and Regional Lung Deposition of Colistin Delivered Using a Dry Powder Inhaler and a Nebuliser Device in Volunteers with Cystic Fibrosis - A Pilot Study.

Investigator:



Please initial box

1. I confirm that I have read and understand the information sheet dated 08 February 2001 for the above study and have had the opportunity to ask questions.

☐

2. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care legal rights being affected.

☐

3. I understand that sections of any of my medical notes may be looked at by responsible individuals from [redacted] the sponsor Pharmaceutical Company or regulatory authorities where it is relevant to my taking part in research. I give my permission for these individuals to access my records.

☐

4. I agree to take part in the above study:

Name of Volunteer

Signature

Date

Name of Person taking consent

Signature

Date

Researcher

Signature

Date



CONFIDENTIAL

APPENDIX VII

**LETTER OF NOTIFICATION TO GENERAL PRACTITIONER OF VOLUNTEER
INFORMING OF INTENDED PARTICIPATION IN CLINICAL TRIAL - CYSTIC FIBROSIS
VOLUNTEERS**

Pharmaceutical Profiles
Mere Way
Ruddington Fields
Ruddington
Nottingham NG116JS UK

Tel 0115 974 9000
Fax 0115 974 8000

Protocol No. PPL-252A

Date

LREC Ref.:

Name of GP

Address of GP

Dear (Name of GP)

Re: (Name of Volunteer - Date of Birth of Volunteer)

Your patient, (name of volunteer), intends to participate in a non-therapeutic clinical trial to assess the deposition of an inhaled antibiotic (colistin) in volunteers with cystic fibrosis.

Each volunteer will attend [REDACTED] during the daytime on 5 separate occasions. At the first visit, the volunteer will undergo a full medical screen (including biochemical and haematological tests), a review of their personal medical history and a physical examination.

During the next 3 visits, each volunteer will receive a single dose of inhaled medicine. On two occasions each volunteer will receive colistin from a dry powder device (Turbospin) either with and without bronchodilating pre-medication. On a separate occasion each volunteer will receive nebulised colistin. This product has already been found to be safe in healthy volunteers. The antibiotic being evaluated is specifically intended for use in patients with cystic fibrosis. Prior to inhalation, the colistin will be radiolabelled with ^{99m}technetium to allow visualisation of the lung deposition. The estimated radiation dose that each volunteer will receive from participation in this study will be 0.46 mSV, which is less than the dose received from a single abdominal x-ray.

Volunteers for this phase of the project are expected to be:

- ☐ Free from any known sensitivity to colistin sulphomethate or salbutamol
- ☐ Free from any current CF related exacerbation
- ☐ Free from a history of alcoholism and drug abuse

If you should have any concerns regarding this volunteer's participation, please do not hesitate to contact

Yours Sincerely,

(Name of Pharmaceutical Profiles Contact)

(Department Title of Contact)



Protocol Number: PPL-252A

Amended 16 January 2001