Theophylline with Inhaled Corticosteroids

Theophylline With Inhaled CorticoSteroids (TWICS) study

Patient Information Leaflet

We would like to invite you to take part in a research study into COPD treatment. COPD is the term now used instead of chronic bronchitis and emphysema. In this study we are trying to find out if flare-ups of COPD can be prevented by low doses of the established COPD drug theophylline. We believe that you might be eligible to take part in this study because you may have had two or more flare ups of your COPD in the last year. Before you decide whether you would like 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 short information sheet carefully and discuss it with others if you wish. Ask us if there is anything that is not clear.

If you are interested in learning more about the study or taking part please let us know by telephone, or email, or use the reply slip and freepost envelope, (see below) and we will contact you. Thank you for reading this.

Thank you for reading this.

What is the purpose of the study? COPD is a common lung condition that can suddenly get worse. These 'flare ups' are known as exacerbations and can result in people being admitted to hospital.

This research study is trying to find out if low doses of the established COPD drug theophylline reduces the number of COPD exacerbations. Theophylline has been used at 'high dose' for about 70 years, but it has fallen out of favour because of new steroid inhalers. Recent laboratory work has shown that low doses of theophylline make steroid inhalers work better in people with COPD. In our study, we want to show that low-dose theophylline used alongside inhaled steroids works in people with COPD. Theophylline will not reduce how well your existing medication works.

Why have I been chosen? We are approaching you because we understand that you have COPD. We are aiming to recruit 1424 people with COPD who have had 2 or more exacerbations in the last year. In order to get 1424 people with COPD, the study is taking place in and around major cities in the UK.

Do I have to take part? No. It is up to you to decide whether to take part. If you decide to take part, you are still free to withdraw at any time, without giving a reason, and this will not affect the standard of care you receive.

What will happen to me if I take part? To find out if low dose theophylline reduces the number of exacerbations we are comparing the effects of low dose theophylline against the effects of a placebo 'dummy treatment', which looks like the genuine medicine but contains no active ingredient.

To try to make sure the low dose theophylline and placebo groups are the same to start with, each person is put into a

group selected randomly by a computer. Half of the 1424 people will take low dose theophylline and half will take the placebo for a year. To make sure that the true effects of low dose theophylline are being studied neither you nor your doctor will know which treatment group you are in (although, if your doctor needs to find out he/she can do so).

If you are interested in taking part we will send you more information and make plans to see you in a local study centre at a time convenient to you.

At the first visit, we will ask you to sign a consent form, fill in a short questionnaire on how COPD affects your life and we will measure your lung function by asking you to do some blowing tests (spirometry).

We will ask you to take one study tablet once or twice a day for a year depending on your weight and whether you currently smoke. There is a 50:50 chance that you will be taking low dose theophylline or placebo 'dummy treatment.' We will either hand you supplies of the study tablets or arrange for them to be delivered to your house by courier.

We will ask you to continue taking all of your normal medicines. If you need to go to your GP for treatment you should go, any flare ups/exacerbations of your COPD can be treated as they normally would.

We will see you again at 6 and 12 months to repeat the questionnaire, to find out how many exacerbations you have had, and to measure your lung function again.

What are the possible benefits of taking part? We cannot promise the study will help you but we expect the information we get from this study will help improve the treatment of people with COPD.

Will my taking part in the study be kept confidential? All information which is collected about you during the research will be kept strictly confidential and will be held securely.

Who is organising and funding the research? This study is being organised by the University of Aberdeen and chest doctors in Aberdeen, Birmingham, Glasgow, Hull, Liverpool, Newcastle, and Norwich. The research is being funded by the National Institute for Health Research, Health Technology Assessment programme: NIHR-HTA.

Contact for further information

If you have any questions or are interested in taking part in this research please let us know and we will send you more information. You can telephone us, email us, or use the reply slip and freepost envelope. Our contact details are:

Local contact details

Thank you for taking the time to read this information leaflet. We hope that you have found it useful in deciding whether or not to take part in the TWICS study.

TWICS

Theophylline with Inhaled Corticosteroids

Patient information leaflet

A study of low dose theophylline in Chronic Obstructive Pulmonary Disease (COPD)

Theophylline With Inhaled CorticoSteroids (TWICS) study.

We would like to invite you to take part in a research study into COPD treatment. COPD is the term now used instead of chronic bronchitis and emphysema. In this study we are trying to find out if flare-ups of COPD can be prevented by low doses of the established COPD drug theophylline. We believe that you might be eligible to take part in this study because you may have had 2 or more flare ups of your COPD in the last year. Before you decide whether you would like 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 others 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 you wish to take part. If you are interested in taking part you can make contact with us (our contact details are at the end of this leaflet).

Thank you for reading this.

What is the purpose of the study?

COPD is a common lung condition and one of the features of COPD is that it can suddenly get worse. These 'flare ups' are known as exacerbations and are usually treated with antibiotics and steroids. Often exacerbations result in people being admitted to hospital.

One of the aims of our research into COPD is to prevent exacerbations occurring. Our study is trying to find out if low doses of the established COPD drug theophylline reduces the number of COPD exacerbations. Theophylline has been used at 'high dose' for about 70 years, but it has fallen out of favour because of new inhalers containing steroids. Recent laboratory work has shown that low doses of theophylline make inhaled steroids work better in COPD. In our study, we want to show that low-dose theophylline used alongside inhaled steroids works in people with COPD. Theophylline will not reduce how well your existing medication works.

Why have I been chosen?

We are approaching you because we understand that you have COPD. We are approaching people with COPD who attend certain General Practices, or who have been admitted to hospital with COPD, or who attend chest clinics, or who have been cared for in the community or have attended pulmonary rehabilitation classes.

We are aiming to recruit 1424 people with COPD who have had two or more exacerbations in the last year. In order to get 1424 people with COPD, the study is taking place in and around major cities in the UK.

Do I have to take part?

No. It is up to you to decide whether to take part. If you decide to take part, you are still free to withdraw at any time and without giving a reason. A decision to withdraw at any time, or

a decision not to take part, will not affect the standard of care you receive.

What will happen to me if I take part?

To find out if low dose theophylline reduces the number of exacerbations we are comparing the effects of low dose theophylline against the effects of a placebo 'dummy treatment', which looks like the genuine medicine but contains no active ingredient.

To try to make sure the low dose theophylline and placebo groups are the same to start with, each person is put into a group selected by chance (randomly by a computer). Half of the 1424 people will take low dose theophylline and half will take the placebo for a year (as well as your usual medicines). To make sure that the true effects of 'low dose theophylline are being studied neither you nor your doctor will know which treatment group you are in (although, if your doctor needs to find out he/she can do so).

If you are interested in taking part we will make plans to see you in a local study centre at a time convenient to you.

At the first visit, we will ask you:

- To sign a consent form saying that you are willing to take part in the study.
- To fill in a short questionnaire to find out how COPD is affecting your life.
- To let us know what medicines and inhalers you are taking.
- To let us measure your height and weight.
- To do some blowing tests (spirometry) to measure your lung function.

We will ask you to take one study tablet once a day or one study tablet twice a day for a year depending on your weight and whether you currently smoke. There is a 50:50 chance

that you will be taking low dose theophylline or placebo 'dummy treatment.'

At this visit, we will provide you with a months supply of study tablets. After about two weeks, we will telephone you to see how you are getting on. We will then arrange a further supply of study tablets to be delivered to your house by courier. We will telephone you again to make sure you received the further supply of tablets.

We will ask you to continue taking all of your normal medicines and tablets and if you do have a flare up/exacerbation of your COPD needing treatment that you make a note of the dates and treatment. You will be able to write these details down on the tablet box.

After 6 months of treatment we will invite you to come along to the local study centre at a time convenient to you and ask you to:

- Let us know how you are getting on with the tablets.
- Let us know if you have had any flare ups of your COPD.
- To fill in a short questionnaire to find out how COPD is affecting your life.
- To let us know what medicines and inhalers you are taking.
- To let us measure your weight.
- To do some blowing tests (spirometry) to measure your lung function.

A further supply of study tablets will be delivered to your house by courier approximately two weeks later. We will telephone you to make sure you received the further supply of tablets.

After 12 months of treatment we will invite you to come along again to the local study centre at a time convenient to you and ask you to:

- Let us know how you are getting on with the tablets.

- Let us know if you have had any flare ups of your COPD.
- To fill in a short questionnaire to find out how COPD is affecting your life.
- To let us know what medicines and inhalers you are taking.
- To do some blowing tests to see how well your lungs are working.

If you are not able to come along to the local study centre after 6 or 12 months of treatment, we may be able to arrange a home visit for you, or telephone you to collect your information, or send you a questionnaire to fill in at home.

Expenses and payments

You can receive travel expenses to attend your local study centre. Please ask your research nurse for information about how to claim travel expenses.

What will I have to do?

We ask that you:

- Take the study tablet once or twice a day as directed, for a year,
- That you attend three study visits (first visit, at 6 months, at 12 months).
- That you make a record of any flare ups of your COPD whilst on the study tablets.
- That you carry a card explaining you are in the study.

Otherwise you should continue on your normal medicines and inhalers and carry on as normal. If you need to go to your GP for treatment you should go, any flare ups/exacerbations of your COPD can be treated as they normally would.

What is the drug that is being tested?

The drug being tested is low dose theophylline (Uniphyllin MR) 200mg one tablet once a day or twice a day depending on your weight and whether you smoke. Theophylline has been

used at a higher dose to treat COPD and asthma for about 70 years.

In order to prevent exacerbations of COPD the laboratory studies show that theophylline must be at low dose levels in the blood. Doctors have known for many years that a number of drugs increase the level of theophylline in the blood above low dose levels and that these drugs should be avoided if a patient is taking theophylline.

We will let your GP know that you are in the study, which drugs to avoid and what to do if (s)he wants to put you on one of these drugs. The study card will also let doctors know where to find a list of these drugs. If your doctor wants to start you on one of these drugs then they will tell you to stop taking the study tablets whilst on these drugs.

For reference, the list of drugs to avoid is:

antibiotics: aciclovir, clarithromycin, ciprofloxacin, erythromycin, fluconazole, ketoconazole, levofloxacin, norfloxacin;

heart drugs: diltiazem, mexiletine, pentoxphylline, verapamil;

neurological: bupropion, disulfiram, fluvoxamine, lithium;

hormones: medroxyprogesterone, oestrogens;

immunological drugs: methotrexate, peginterferon alpha, tacrolimus;

others: cimetidine, deferasirox, febuxostat, roflumilast, thiabendazole.

These drugs are not frequently used in patients with COPD. But if you have any questions about any of these drugs, please get in touch with us, or ask your GP.

If you stop smoking or lose or gain weight during the study, please tell us. Our contact details are at the end of this leaflet.

What are the side effects of any treatment received when taking part?

It has long been known that some people can develop side effects when taking high dose theophylline and this is one of the reasons why high dose theophylline is rarely used nowadays.

By using low dose theophylline at levels well below high dose we anticipate that very few people will have any side effects, (less than 1 person in 20). If side effects do develop then they should stop when the study tablets are stopped. The possible side effects include nausea, vomiting, diarrhoea, headache, anxiety and a fast heart rate. If you decide to participate in our study, we will give you another information leaflet with your medicine that will tell you more about the study tablets, how to take them, and the possible side effects. Please read all the information contained in this leaflet.

If you feel unwell at any point, please seek medical help as you would do usually. If you are concerned that you may have developed side effects, you should contact your local study centre or your GP and they will provide help and advice.

What are the possible benefits of taking part?

We cannot promise the study will help you but we expect the information we get from this study will help improve the treatment of people with COPD, reduce the need for antibiotics and steroids and reduce hospital admissions for COPD. The lung function measurements we make during the study will be useful to your GP.

We hope to show that low dose theophylline reduces the number of exacerbations in people with COPD.

What happens when the research study stops?

When you have attended for the 12 month follow-up, we will not give you any more study tablets. Stopping the tablets is

safe. If, at the end of the study, you feel that the study tablets have improved your COPD we can let your GP know and (s)he will be able to prescribe low dose theophylline. You would need to discuss this with your GP though.

Involvement of the General Practitioner (GP)

We will ask your permission to let your GP know that you are taking part in the study. We will also ask your permission to send your GP copies of the lung function readings we take during the study. At the end of the study, again with your permission we will ask your GP if we can look at your GP records to count up the number of times you have visited your GP and the number of exacerbations you have had whilst on the year of study treatment.

What if relevant new information becomes available?

Sometimes we get new information about the study treatment. If this happens, your local study team will tell you and discuss with you whether you should continue in the study. If you decide not to carry on, arrangements will be made for your usual care to continue. This may be with your GP, or may be with the chest clinic at the hospital. If you decide to continue in the study you may be asked to sign an updated consent form.

What will happen if I don't want to carry on with the study?

You are still free to withdraw at any time and without giving a reason and this will not affect the standard of care you receive. You can stop the study treatment but keep in contact with us to let us know your progress. Information collected may still be used.

What if there is a problem?

If you believe that you have been harmed in any way by taking part in this study, you have the right to pursue a complaint and seek compensation through the research sponsors of the study - the University of Aberdeen and NHS Grampian.

Contact details for both research sponsors are available through the research team.

As a patient of the NHS 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, or have any concerns about any aspect of the way you have been approached or treated during the course of this study, the normal National Health Service complaints mechanisms would be available to you.

If you have a concern about any aspect of this study you should ask to speak to the study doctors who will answer your questions (contact details are at the end of this information leaflet). If you remain unhappy and wish to complain formally, you can do this through the NHS Complaints mechanisms (or Private Institution). Contact details can be obtained from your local hospital. In addition to this, you may contact the chairman of the TWICS Trial Steering Committee (who is independent from the study) through the TWICS study office.

Will my taking part in the study be kept confidential?

Yes. We will follow ethical and legal practice and all information about you will be handled in confidence. All information which is collected about you during the research will be kept strictly confidential and will be held securely in accordance with the Data Protection Act. Only certain members of the research team will have access to your information.

We will ask you to give us the name and address of someone that you know who we can contact if we cannot get in touch with you. This might be a family member, friend or neighbour. Again, with your permission, we will tell this person that you are taking part in the study.

With your permission we will need to pass on your name and address to the company who will package the study tablets for you and the courier company who will deliver the study tablets to your home. These details will be kept strictly confidential, and be used only to send you the tablets

The statistical analysis of the study is being conducted at the University of Aberdeen, and to maintain confidentiality, the statistical team will only analyse completely anonymous data. (Anonymous data does not include names or addresses, and it is not possible to identify individual participants from anonymous data). Any reports or publications arising from the study will contain totally anonymous data so that you cannot be recognised from it.

Other researchers may wish to access anonymous data from this study in the future . If this is the case, the Chief Investigator will ensure that the other researchers comply with legal, data protection and ethical guidelines.

If you join the study, the data collected for the study, together with any relevant medical records, may be looked at by authorised persons from the University of Aberdeen, the Research and Development Department of your local NHS Organisation and the Regulatory Authorities to check that the study is being carried out correctly. All will have a duty of confidentiality to you as a research participant.

What will happen to the results of the research study?

The results of the study will be published in scientific journals and presented at scientific meetings. In addition with the help of the British Lung Foundation and Chest Heart Stroke Scotland we will pass on the results to other people with chest disease. We will also send you a summary of the findings.

Who is organising and funding the research?

This study is being organised by the University of Aberdeen and chest doctors in Aberdeen, Birmingham, Glasgow, Hull, Liverpool, Newcastle, and Norwich. The research is being funded by the National Institute for Health Research, Health Technology Assessment programme: NIHR-HTA.

The study is being co-ordinated by the Centre for Healthcare Randomised Trials (CHaRT), a registered clinical trials unit at the University of Aberdeen.

Who has reviewed the study?

The study has been reviewed by an NHS Research Ethics Committee, which has responsibility for scrutinising proposals for medical research on humans. In this case, the reviewing committee was Scotland A Research Ethics Committee, who have raised no objections to the study.

In addition, the study has also been reviewed and approved by the Medicines and Healthcare Products Regulatory Agency. The Research and Development Department of your local hospital and/or local primary care organisation has also reviewed and approved the study.

Contact for further information

If you have any questions or would like more information, please contact us. Our contact details are on the back of this leaflet.

If you are interested in taking part in this research please let us know. You can telephone us, email us, or use the reply slip and freepost envelope. Our contact details are on the back of this leaflet.

Local contact details:

Thank you for taking the time to read this information leaflet. We hope that you have found it useful in deciding whether or not to take part in the TWICS study.

TWICS

Theophylline with Inhaled Corticosteroids

TWICS Study Medication
Patient Information Leaflet

Please read this leaflet carefully before you start taking this medicine. If you have any questions please ask a member of the TWICS research team or your doctor or pharmacist. This medicine has been prescribed for you – do not pass it on to others.

Please return any unused medicine and the empty bottles when you come back for your next appointment with the TWICS study team. If you do not attend your follow up appointment, please take unused medicine to a pharmacy for appropriate disposal.

Thank you.

In this study we are testing whether taking theophylline reduces the risk of exacerbations or "flare-ups" in patients with COPD. The medicine you receive as part of the TWICS study may contain theophylline, or a non-active 'dummy' capsule (placebo). We believe that theophylline may reduce your risk of exacerbations.

Please contact your local TWICS study team if any of the symptoms on the attached information sheet become troublesome or last longer than a few days, or if you notice any side effects not listed in this leaflet. Alternatively, you should tell your doctor or pharmacist.

If you give up, or start smoking, please let us or your local study team know.

If you have any queries please contact the trial office and we can put you in contact with your local study team. Details are below.

TWICS Study Office
Centre for Healthcare Randomised Trials (CHaRT)
Health Services Research Unit
University of Aberdeen
3rd Floor, Health Sciences Building
Foresterhill
Aberdeen AB25 2ZD
Telephone: +44 (0)1224 438178 or 438193
Email: twics@abdn.ac.uk
Website: https://w3.abdn.ac.uk/hsru/twics/

This leaflet is based on the manufacturer's packaging information leaflet which was last revised in October 2010.

Package Leaflet: Information for the user

***Uniphyllin*® *Continus*® 200 mg prolonged-release tablets**
Theophylline

Read all of this leaflet carefully because it contains important information for you.
This medicine is available without prescription. However you still need to take ***Uniphyllin Continus*** tablets carefully to get the best results from them.

- Keep this leaflet. You may need to read it again.
- Ask your pharmacist if you need more information or advice.
- You must contact a doctor if your symptoms worsen or do not improve.
- If any of the side effects become serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

In this leaflet:

1. What *Uniphyllin Continus* tablets are and what they are used for

These tablets are used to treat asthma, long-term breathing difficulties such as chronic obstructive pulmonary disease and chronic bronchitis, and are sometimes used to treat heart failure.

They contain the active ingredient theophylline which belongs to a group of medicines called bronchodilators.
Bronchodilators help stop you wheezing and being breathless. Theophylline also reduces swelling in the lungs of asthma patients and relieves the feeling of ‘tightness’ in their chest.

2. Before you take *Uniphyllin Continus* tablets

Do not take *Uniphyllin Continus* tablets if you:

- are allergic (hypersensitive) to theophylline, aminophylline or any of the other ingredients of the tablets (see section 6 ‘Further Information’);
- have porphyria (a rare disease of the blood pigments).

Take special care with *Uniphyllin Continus* tablets

Before treatment with these tablets tell your doctor or pharmacist if you:

- have high blood pressure or any other heart problems;
- have an over-active thyroid gland (hyperthyroidism);
- have a stomach ulcer;
- have liver problems;
- suffer from seizures, fits or convulsions;
- are unwell with a high temperature or fever;
- have a viral infection;
- are addicted to alcohol;
- are male and have difficulty in passing urine (for instance due to an enlarged prostate gland);
- smoke, as smoking may alter the way your tablets work.

Children under seven years of age should not take these tablets.

Taking other medicines

Tell your doctor or pharmacist if you are taking:

- certain other medicines to treat asthma or breathing conditions that contain theophylline, aminophylline, salbutamol, terbutaline or salmeterol, as you may need additional monitoring;
- steroids;
- diuretics to increase urine production;
- oral contraceptives;
- a herbal remedy called St John's Wort (also known as Hypericum perforatum);
- aminoglutethimide, methotrexate or lomustine to treat cancer;
- carbamazepine or phenytoin to treat seizures, fits or convulsions;
- medicines known as barbiturates to help you sleep;
- adenosine, moracizine, diltiazem, isoprenaline, mexiletine, propafenone, propranolol, verapamil or beta blockers to treat high blood pressure and other heart problems;
- oxpentifylline to treat diseased blood vessels;
- medicines known as benzodiazepines, which are used as a sedative or to treat anxiety;
- sulphinpyrazone or allopurinol to treat gout;
- carbimazole to treat problems with your thyroid gland;
- cimetidine or nizatidine to treat stomach ulcers, indigestion or heartburn;
- certain antibiotics such as ciprofloxacin, clarithromycin, erythromycin, norfloxacin, ofloxacin;
- fluconazole to treat fungal infections;
- rifampicin or isoniazid to treat tuberculosis;
- ritonavir to treat HIV;
- medicines known as interferons, which you may be taking to treat conditions such as herpes, cancer, leukaemia or hepatitis;
- thiabendazole to treat worms such as threadworms;

- viloxazine, fluvoxamine or lithium to treat depression;
- doxapram to stimulate breathing;
- disulfiram to treat alcoholism.

Also tell your doctor or pharmacist if:
- you are going to have an operation, as these tablets may interact with certain anaesthetics such as halothane and ketamine;
- you have recently had, or are going to have a flu injection;
- these tablets have been prescribed for your child and they are also taking a cough medicine or decongestant containing ephedrine.

Please tell your doctor or pharmacist if you are taking or have recently taken any other medicines, including medicines obtained without a prescription. If you take these tablets with some other medicines, the effect of these tablets or the other medicine may be changed.

Taking *Uniphyllin Continus* tablets with alcohol
Alcohol can alter the way these tablets work. Please consult your doctor if you intend to drink alcohol whilst taking these tablets.

Pregnancy and breastfeeding
If you are pregnant or breastfeeding do not take these tablets until you have talked to your doctor or pharmacist.

Ask your doctor or pharmacist for advice before taking any medicine.

3. How to take *Uniphyllin Continus* tablets

Always take these tablets exactly as your doctor or pharmacist has told you.

Swallow your tablets whole with a glass of water. **Do not crush or chew them.**

Uniphyllin Continus **tablets are designed to work properly over 12 hours. If a tablet is crushed or chewed the entire 12-hour dose may be absorbed rapidly into your body. This can be dangerous, causing serious problems such as an overdose.**

Do not exceed the dose recommended by your doctor. You should check with your doctor or pharmacist if you are not sure.

If you take more *Uniphyllin Continus* tablets than you should or if someone accidentally swallows your tablets
Call your doctor or hospital straight away. People who have taken an overdose may have stomach pains and feel or be sick. They may also have a fast or irregular heartbeat, feel very restless or have a fit. These symptoms may appear up to 12 hours after the overdose. When seeking medical attention make sure that you take this leaflet and any remaining tablets with you to show the doctor.

If you forget to take *Uniphyllin Continus* tablets
If you remember within 4 hours of the time your tablet was due, take your tablet straight away. Take your next tablet at your normal time. If you are more than 4 hours late, please call your doctor or pharmacist for advice. Do not take a double dose to make up for a forgotten tablet.

If you stop taking *Uniphyllin Continus* tablets
You will probably take these tablets for a long time. Do not stop taking them unless your doctor tells you to, even if you feel better.

If you have any further questions on the use of these tablets, ask your doctor or pharmacist.

4. Possible side effects

Like all medicines, these tablets can cause side effects, although not everybody gets them.

All medicines can cause allergic reactions, although serious allergic reactions are rare. Tell your doctor immediately if you get any sudden wheeziness, difficulties in breathing, swelling of the eyelids, face or lips, rash or itching especially those covering your whole body.

The following side effects have been reported in patients treated with these tablets:

- Feeling sick.
- Headache.
- Vomiting (being sick), abdominal pain, diarrhoea, heartburn or gastrointestinal disorders (e.g. upset stomach).
- Difficulty in sleeping, agitation, anxiety or shaking.
- A fast heart beat or palpitations.
- Dizziness.
- Difficulty in passing urine (especially in men) or passing increased amounts of urine.
- Increased uric acid level in the blood, which could cause painful, swollen joints.
- Seizures, fits or convulsions.
- Rash or itchy skin.

If any of the side effects become serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

5. How to store *Uniphyllin Continus* tablets

Keep out of the reach and sight of children.

Do not use any tablets after the expiry date stated on the packaging.

Do not store your tablets above 25^{o}C.

Do not take your tablets if they are broken or crushed as this can be dangerous and can lead to serious problems such as overdose.

Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

6. Further information

What *Uniphyllin Continus* tablets contain
The active ingredient is theophylline. Each tablet contains 200 mg of theophylline.

The other ingredients are:

- Hydroxyethylcellulose
- Povidone
- Magnesium stearate
- Cetostearyl alcohol
- Macrogol
- Talc

What *Uniphyllin Continus* tablets look like and the contents of the pack

The tablets are white and capsule shaped.
The 200 mg tablets are plain on one side and marked with "U200"on the other.

Each bottle will contain 28 or 56 tablets.

Marketing Authorisation Holder and Manufacturer

The tablets are made by Bard Pharmaceuticals Limited for the marketing authorisation holder Napp Pharmaceuticals Limited, both at Cambridge Science Park, Milton Road, Cambridge CB4 0GW, UK.

This leaflet was last revised in October 2010.

Patient card

A credit card sized card:-

FRONT

TWICS Theophylline with Inhaled Corticosteroids	A randomised, double-blind placebo controlled trial of the effectiveness of low dose oral theophylline as an adjunct to inhaled corticosteroids in preventing exacerbations of COPD

Please show this card to any doctor if they are prescribing you medication.

More info: https://w3.abdn.ac.uk/hsru/twics/

Local contact details: <<insert number>>

Out of hours contact for emergency unblinding:

Version 2, 23 August 2013

BACK

Participant ID:		Drug pack ID:	

Entry into trial: D D / M M / Y Y

IMP details: Theophylline (Uniphyllin® Continus®) 200mg or Placebo. Taken orally, once or twice daily for 12 months.

- Assume on low-dose theophylline, serum level 1-5mg/l.
- Try to avoid drugs that increase serum theophylline*
- Safe to give IV aminophylline 250mg bolus (5mg/kg if <50kg) with maintenance 0.5mg/kg/h with level check at 24h*.

* (more info: https://w3.abdn.ac.uk/hsru/twics/ or BNF).

Version 2, 23 August 2013