During the HPS2-THRIVE study you will take two types of tablets: a statin (to lower the ‘bad’ cholesterol; this tablet replaces the statin prescribed by your doctor) and ER niacin/laropiprant (the medication being studied, to raise ‘good’ cholesterol). In this first part of the study you will be taking ‘active’ ER Niacin/laropiprant. If you later enter the full study you may be allocated to a ‘placebo’ or ‘dummy’ version of this tablet or you may be allocated to continue the ‘active’ version. The statin will always be ‘active’ medication.

Depending on your initial cholesterol level the statin you will be given will be either simvastatin (Type A) or a tablet combining ezetimibe/simvastatin (Type B). The study nurse will tick the box below to indicate which type you are given.

Simvastatin (2 cards supplied)  
Ezetimibe/simvastatin (2 cards supplied)

and everyone takes type C

ER niacin/laropiprant (Type C) (1 box with 1 blue and 3 white cards)

Large white tablet. Use blue card for first 4 weeks (1 tablet a day), then white card (2 tablets a day, see next page)
How to take your tablets

Both types of tablets (the statin and the ER niacin/laropiprant) should be taken at the same time, ideally in the evening or at bedtime with food.

IMPORTANT INSTRUCTIONS

Every evening take one tablet from the statin pack (A or B) out of the blister corresponding to the day of week (see picture on front page to make certain you know which tablet this is). You will always take only one statin tablet each evening.

and at the same time

Also take your ER niacin/laropiprant (again see the front page to make certain you know which tablet this is). When you open the box you will see a blue coloured blister card (Type C). For the first four weeks, you need to take one tablet each day from this blue blister card.

After four weeks you should have finished this blue card and need to increase your dose to two tablets daily of the large tablets from the white blister card (Type C). There are three Type C white blister cards provided, each with sufficient tablets for two weeks. The blisters are labelled with the day of the week.

• Do not crush or break niacin tablets - they must be swallowed whole to allow the anti-flushing medicine (laropiprant) to be released first.

• If you forget either type of tablet at your usual time, you may still take it later the same day. However, if you miss a whole day or more, do not make up for the missed tablets. Leave them in the blister card and continue from the day you restart.

• If you think you will reach the end of your last blister-card before your next clinic visit or if you lose your study treatment, please contact the HPS2-THRIVE office on Freephone 0800 585323 and we will arrange for replacement treatment to be provided.

• Please return surplus tablets at each clinic visit.

• Keep the tablets out of the reach of children.

• Store in the original packaging in a dry place, away from excessive heat, cold or moisture. Protect from light.
Possible side-effects

If you develop **unexplained muscle aches, pains or weakness**, please keep taking your study tablets, and contact your study nurse or call Freefone 0800 585323 as soon as possible. We will arrange for you to see your study nurse in the next few days for a blood test and review.

Some people may experience side effects when taking ER niacin/laropiprant tablets:

- **Flushing** sometimes occurs soon after taking the tablet. This is an uncomfortable feeling of warmth or heat, which may be associated with a ‘prickling’ sensation and reddening of the skin. Although people find it unpleasant it is not dangerous and if you can persist with taking the tablets the flushing effect usually diminishes with time. Some people find that the flushing is worse if they drink either a hot drink or an alcoholic drink at the same time as taking the tablet(s). If the flushing does settle, it may return if you forget to take your ER niacin/laropiprant for a few days and then restart, so try to remember to take it every day.

- **Rashes or itching** sometimes develop, usually this is mild but if it persists please contact your study nurse or call Freefone 0800 585323 for advice.

- **A mild stomach upset** (nausea and/or diarrhoea most commonly) may occur, which tends to settle after taking the medication for a few weeks.

- **Raised blood sugar levels** may occur, particularly in people with diabetes. It is often transient and usually easily controlled with changes to diabetes medication.

- **Other side-effects** which have been reported include: allergic reactions, headaches, dizziness, gout, visual disturbance, palpitations, discomfort when passing urine or increased frequency of urination. Many of these settle after taking the tablets for a short time, whereas others may require the ER niacin/laropiprant to be stopped.

Both simvastatin and niacin occasionally affect the **liver blood tests**. This does not usually make people unwell, but hepatitis has been reported rarely. As part of HPS2-THRIVE you will have a blood test to check your liver function at every study clinic visit. If the test is abnormal you might be asked to come back for an extra visit.

If any of these or other symptoms occur that you think are related to your study medication, please contact your study nurse or call **Freefone 0800 585323** for further advice.

Should any side-effect of the study treatment become intolerable for you, you would, of course, be free to stop either type of study tablet at any time.

If you have been randomized into the study, and you have to stop one type of study tablet, you may still be able to continue on the other type of study tablet. Once randomized, even if you have stopped all study treatment, we would still like to follow you up if possible.
**Other medications**

At each visit the study nurse will check that any other medications you are taking are compatible with the statin (either simvastatin or the combined ezetimibe/simvastatin) that you will be given throughout the study and also compatible with ER niacin/laropiprant. However, it is important that any doctor treating you, knows you are in HPS2-THRIVE so any prescription they give you will also be compatible. They may call 0800 585323 if they have any queries.

If you are taking warfarin, it is important that you have a blood test (INR) within 5 - 10 days of starting the study tablets, as simvastatin, ezetimibe/simvastatin and ER niacin/laropiprant may change the dose of warfarin that you require. Similarly, if at any point you stop either simvastatin or ezetimibe/simvastatin and/or ER niacin/laropiprant, you should have a blood test soon afterwards as again your warfarin requirement may change.

Certain medications may increase the risk of muscle problems when taken with simvastatin or ezetimibe/simvastatin and ER niacin/laropiprant, and it would be important for you to stop your study tablets whilst you are taking them.

These include:
- erythromycin or clarithromycin (antibiotics);
- fluconazole, ketoconazole, itraconazole or prosaconazole (antifungals) tablets (not creams);
- verapamil or amiodarone (drugs for stabilizing heart rhythm).

If you are prescribed any of these medications, or if you have any further questions please either contact your study nurse or call: **Freefone 0800 585323** for advice.

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**Thank you for taking part in HPS2-THRIVE**