

Package leaflet: Information for the user

Synphase® 500 microgram / 35 microgram tablets and 1 milligram / 35 microgram tablets
norethisterone / ethinylestradiol

Important things that you SHOULD know about your medicine:

- Synphase is an oral contraceptive medicine for use by women.
- You should take Synphase regularly as instructed by your doctor or nurse, in order for it to be effective. When taken as instructed, it is a very effective contraceptive. See section 3, ‘If you forget to take Synphase’.
- Taking some other medicines may stop Synphase from working properly. See section 2 for details. Check with your doctor, nurse or pharmacist before taking any other medicines while you are taking Synphase.

Read all of this leaflet carefully before you start taking this medicine because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Synphase is and what it is used for
2. What you need to know before you take Synphase
3. How to take Synphase
4. Possible side effects
5. How to store Synphase
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1. What Synphase is and what it is used for

Synphase is one of a group of medicines called combined oral contraceptives or “the Pill” for short.

Synphase contains two hormones, a progestogen hormone called norethisterone and an oestrogen hormone called ethinylestradiol. These two hormones act together to prevent a pregnancy from occurring.

2. What you need to know before you take Synphase

Do not take Synphase:

- If you are allergic to norethisterone or ethinylestradiol, or any of the other ingredients of this medicine (listed in section 6)
- If you have a family history of clotting problems
- If you have had blood clots in the legs, blood clots in veins, the lungs, the brain or elsewhere (coronary and cerebral thrombotic disorders)
- If you have had a heart attack or stroke, or have had angina
- If you have or have had high levels of fats in your blood (hyperlipidaemia) or other disorders of body fats

- If you have or have had cancer of the breast, cervix, vagina or womb
- If you have had any of the following during a previous pregnancy: pruritus (itching of the whole body) or jaundice (yellowing of the skin or eyes), for which your doctor could not find the cause; or pemphigoid gestationis (a rash previously known as herpes gestationis typically with blistering of the palms of the hands and the soles of the feet)
- If you have or have had severe chronic liver disease (liver tumours, Dubin-Johnson or Rotor syndrome)
- If you have or have had vaginal bleeding (not a period), for which your doctor could not find the cause
- If you have or have had bad migraines
- If you are pregnant or think you could be pregnant
- If you have hepatitis C and are taking the medicinal products containing ombitasvir/paritaprevir/ritonavir and/or dasabuvir (see also in section ‘Other medicines and Synphase’).

Warnings and precautions

Talk to your doctor, pharmacist or nurse before taking Synphase if you have or have had any of the following conditions:

- Migraine
- Headaches
- Slow or sudden development of visual disturbances such as complete or partial loss of vision
- Asthma
- Epilepsy (a condition where you suffer from fits)
- Diseases of the heart and blood vessels (cardiovascular disease)
- High blood pressure (hypertension)
- Kidney disease
- Diabetes
- Multiple sclerosis (a problem of the nervous system)
- Tetany (muscle twitches)
- Breast problems of any sort
- Varicose veins (widened or twisted vein usually in the leg)
- Liver dysfunction
- Severe depression
- Fibroids in your uterus
- Irregular periods
- Sharp pain in your abdomen
- Gallstones
- Sickle-cell anaemia
- Otosclerosis (an inherited form of deafness)
- Porphyria (a metabolic disease)
- Chloasma (brown patches on your skin which can happen during pregnancy but may not fade completely)
- Any disease that is likely to get worse during pregnancy

Possible risk of thrombosis (blood clot)

- Some evidence suggests that women who take the pill are more likely to develop various blood circulation disorders than women who don't take the pill.
- A thrombosis is a blood clot. A thrombosis can develop in veins or in arteries and can cause a blockage. The chance of a thrombosis forming in women taking the pill and women not taking the pill is rare. When blood clots form in the arteries they can cause chest pain (angina), strokes (blood clots in or bleeding from the blood vessels in the brain) and heart attacks.
- If blood clots form in veins they can often be treated, with no long-term danger. On rare occasions a piece of thrombosis may break off. It can travel to the lungs to cause a condition called pulmonary embolism. Therefore in rare cases a thrombosis can cause serious permanent

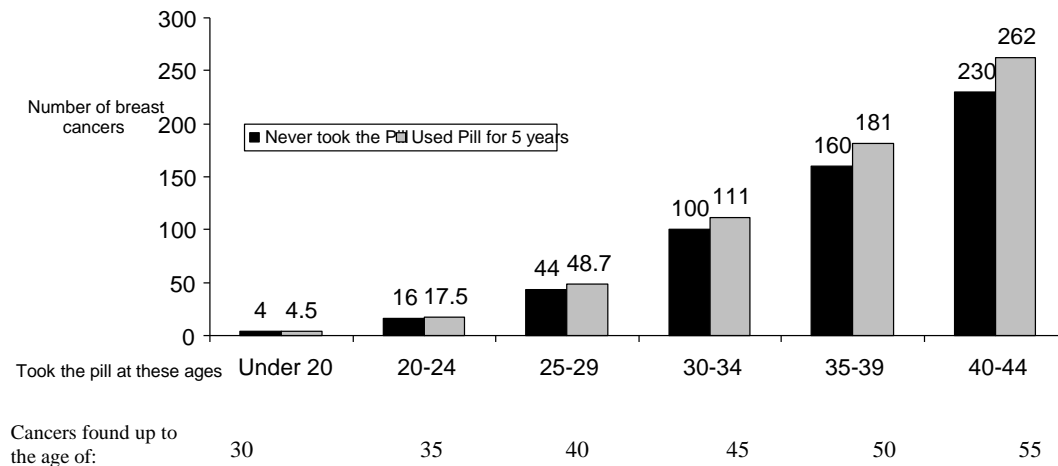
disability or could even be fatal.

- It is important to note that a thrombosis can form in people who are not taking the pill as well as those who are taking it. The risk is higher in women who take the pill than in women who don't take the pill, but is not as high as the risk during pregnancy. The extra risk of thrombosis is highest during the first year that a woman ever uses a combined oral contraceptive pill.
- For healthy non-pregnant women: the chance of having a blood clot is about 5 in 100,000 each year.
- For women taking the Pill containing either levonorgestrel or norethisterone (a second generation Pill): the chance of having a blood clot is about 15 in 100,000 each year.
- For women taking the Pill containing desogestrel or gestodene (a third generation pill): the chance of having a blood clot is about 25 in 100,000 each year.
- For women who are pregnant: the chance of having a blood clot is about 60 in 100,000 pregnancies.
- The risk of heart attacks and strokes for women who use the combined Pill increases with age and smoking. Other conditions also increase the risk of blood clots in the arteries. These include being greatly overweight, having diseased arteries (atherosclerosis), high blood pressure during pregnancy (pre-eclamptic toxæmia), high blood levels of cholesterol, and diabetes. If you have any of these conditions, you should check with your doctor, pharmacist or nurse to see if the pill is suitable for you. Smokers over 35 are usually told to stop taking these pills.

Possible risk of breast cancer

- Every woman is at risk of breast cancer whether or not she takes the pill. Breast cancer is rare under the age of 40 years, but the risk increases as a woman gets older.
- Breast cancer has been found slightly more often in women who take the pill than in women of the same age who do not take the pill. If women stop taking the pill, this reduces the risk so that 10 years after stopping the pill, the risk of finding breast cancer is the same as for women who have never taken the pill. Breast cancer seems less likely to have spread when found in women who take the pill than in women who do not take the pill.
- It is not certain whether the pill causes the increased risk of breast cancer. It may be that women taking the pill are examined more often, so that breast cancer is noticed earlier. The risk of finding breast cancer is not affected by how long a woman takes the pill but by the age at which she stops. This is because the risk of breast cancer strongly increases as a woman gets older.
- The chart below shows the background chances of breast cancer at various ages for 10,000 women who have never taken the pill (black bars) and for 10,000 women whilst taking the pill and during the 10 years after stopping it (grey bars). The small extra risk of finding breast cancer can be seen for each age group. This small possible additional risk in women who take the pill has to be balanced against the fact that the pill is a very effective contraceptive and it helps prevent cancer of the womb or ovary.

Estimated number of breast cancers found in 10,000 women who took the pill for 5 years then stopped, or who never took the pill



- There have been some reports on the risk of liver tumors and cervical cancer associated with the use of oral contraceptives.
- There is evidence to suggest that the use of combined oral contraceptives offer protection against both ovarian and endometrial cancer.

Cervical cancer

Some research suggests an increased risk of getting cancer of the cervix (neck of the uterus or womb) in women who take combined oral contraceptives for a long time. However, this may be due to other causes, such as sexual behaviour.

Liver cancer

- Very rarely, tumours of the liver have been seen in women taking combined oral contraceptives, especially if they have been taken for a long time.
- If you are worried about any of these things or if you have had cancer in the past, talk to your doctor, pharmacist or nurse to see if you should take the combined oral contraceptive pill.

Endometrial and ovarian cancer

Research shows that combined oral contraceptives protect against cancer of the ovary and cancer of the endometrium (lining of the womb).

If you are going to have a major operation

Make sure your doctor knows about it. You may need to stop taking Synphase about 4 weeks before the operation until at least 2 weeks after the operation and until you are fully mobile. Alternatively, your doctor may prescribe an oestrogen-free hormonal contraceptive.

Patients undergoing injection treatment for varicose veins should not resume taking Synphase until 3 months after the last injection.

Your doctor, pharmacist or nurse will advise you whether you can still take Synphase.

Medical check-ups while taking Synphase

Your doctor or nurse will give you regular check-ups while you are taking Synphase. Your blood pressure will be checked before you start Synphase and then at regular intervals whilst you are on Synphase. You may be required to have an examination of your breasts, abdomen and pelvis including taking a cervical smear test at regular intervals, if this is considered necessary by the doctor.

Other medicines and Synphase

Tell your doctor, pharmacist or nurse if you are taking, have recently taken or might take any other medicines.

The following medicines may stop Synphase from working properly (the condition they treat being shown in brackets):

- The herbal remedy St John's wort – Latin name *Hypericum perforatum* (depression)
- Carbamazepine (epilepsy)
- Oxacarbazepine (epilepsy)
- Phenytoin (epilepsy)
- Phenobarbital (sleeplessness, anxiety, epilepsy)
- Primidone (epilepsy)
- Topiramate (epilepsy)
- Nelfinavir (HIV – Human Immunodeficiency Virus - infection)
- Nevirapine (HIV infection and AIDS)
- Ritonavir (HIV infection and AIDS)
- Rifabutin (bacterial infection)
- Rifampicin (bacterial infection)
- Griseofulvin (fungal infection)
- Modafinil (narcolepsy i.e. daytime sleepiness)

Do not use Synphase if you have Hepatitis C and are taking the medicinal products containing ombitasvir/paritaprevir/ritonavir and/or dasabuvir as this may cause increases in liver function blood test results (increase in ALT liver enzyme).

Your doctor will prescribe another type of contraceptive prior to start of the treatment with these medicinal products.

Synphase can be restarted approximately 2 weeks after completion of this treatment. See section 'Do not take Synphase'.

If you do need to take any of the medicines listed above, Synphase may not be suitable for you. Your doctor, pharmacist or nurse will advise you whether to stop taking these medicines or to use another contraceptive method, such as a condom while you are taking these medicines.

Tell your doctor, pharmacist or nurse if you are taking or have recently taken any other medicines, including those bought without a prescription, because they might interact with Synphase.

Laboratory tests

Synphase may interfere with some tests, tell your doctor, pharmacist or nurse if you need to give samples for laboratory assessment.

Synphase with food and drink

Please refer to section 3.

Pregnancy and breast-feeding

Do not take Synphase if you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby.

If you miss a period while you are taking Synphase, tell your doctor, pharmacist or nurse. Your doctor, pharmacist or nurse will inform you about the increased risk to the foetus if you have become pregnant while taking Synphase. You will need to have a pregnancy test before you continue to take Synphase.

Sexually transmitted diseases

Synphase helps to prevent pregnancy. It will not protect against sexually transmitted diseases including AIDS. For safer sex, use a condom as well as your usual contraceptive.

Driving and using machines

No effects on the ability to drive or use machines have been seen with Synphase.

Synphase contains lactose

Lactose is a type of sugar. If you have diabetes or you have been told by your doctor that you have an intolerance to some sugars, contact your doctor or pharmacist before taking this medicine.

3. How to take Synphase

Always take this medicine exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.

A pack of Synphase contains different coloured tablets.

- Seven blue ones.
- Nine white ones.
- Five more blue ones.

The different coloured tablets contain different amounts of hormones. When you take them in the correct order they imitate the natural rise and fall of your body's hormone levels during your monthly cycle.

Take one tablet every day, in the right order. Synphase can be taken with or without food.

Each blister strip has a row of bubbles marked with the days of the week. When you take your first tablet, press the bubble for the day of the week you have started taking the tablets, for example, if you take your first tablet on a Tuesday, press the bubble marked 'Tue'. This will help you to remember the day of the week you started the pack. Each new pack after this will also start on the same day of the week.

How to start the treatment

Starting your first blister strip:

- Take tablet number one, marked 'start here' on your first day of bleeding. This is the day when your period starts. If you are not having periods, ask your doctor, pharmacist or nurse when you should start taking your tablets.
- You will be protected at once as long as you take a tablet every day.
- You can take the tablet at a time that suits you, **but you must take it at about the same time every day.**
- Take a tablet every day until you finish a blister strip.
- If you cannot start taking the tablets on the first day of your period you may start to take it on any day up to the fifth day. However, if you do this, you may not be protected for the first seven days, so you should use another method of contraception such as a condom during those days.

Starting the next blister strip:

- Once you have finished all 21 tablets, **stop for seven days**. You will probably bleed during some or all of these seven days.
- Then, start the next blister strip. Do this whether or not you are still bleeding. You will always start the next blister strip on the same day of the week.
- You are protected during the seven day break, but only if you start the next blister strip on time. The first tablet in your next blister strip is the worst pill of all to miss or take late.

If you notice a change in your periods

It is normal that your periods may become irregular and you may notice some bleeding between periods. Your periods may become lighter and you may occasionally have no bleeding during the tablet free days. Make a note of what happens so that you can tell your doctor or nurse at your next check-up.

If you forget to take Synphase

- If you forget to take a tablet take it as soon as you remember and take the next one at your normal time. This may mean taking two tablets on the same day.
- If you are 12 or more hours late in taking one or more tablets, it may not work. As soon as you remember, take your last missed tablet and carry on taking them normally. However, you may not be protected for the next seven days, so either avoid sexual intercourse or use an extra contraceptive method, such as a condom.
- If you have fewer than seven tablets in your blister strip after you have missed taking a dose, you should complete the blister strip and start the next blister strip without a break. This will give you protection from when you took the last missed tablet. You may not have a period until the end of two blister strips, but this will not harm you. You may also have some bleeding on days when you take the tablets.

If you take more Synphase than you should

Taking too many tablets at once may make you sick, cause vaginal bleeding or breast swelling. Contact your doctor or go to your nearest hospital casualty department immediately.

If you want to stop taking Synphase or want to have a baby

- If you stop taking Synphase, this will result in the loss of contraceptive protection and the risk of pregnancy.
- If you wish to become pregnant, you should contact your doctor or nurse about stopping the tablets. It is advisable to stop taking Synphase three (3) months before you want to start trying to have a baby.
- If you have any further questions on the use of this product, ask your doctor, pharmacist or nurse.

If you are changing brands of oral contraceptive (pill)

Take the first tablet of your new blister strip on the day immediately after you have finished your old blister strip. Your period will usually be delayed until the new blister strip is finished, but you may have some breakthrough bleeding during the first few days of the new blister strip. This is quite normal and you will still be protected against pregnancy.

If you have a stomach upset or you are sick

- Synphase may not work if you are sick or have severe diarrhoea. You should carry on taking the tablets as normal, but use a condom while you are ill and for the next seven days. If these seven days run beyond the end of the blister strip, start the next pack without a break.
- If you do have a break, ask your doctor, pharmacist or nurse whether you need an extra contraceptive method, such as a condom.

If you have just had a baby

- If you are breast-feeding, you should not take the combined oral contraceptive. This is because the oestrogen in the tablets may reduce the amount of milk you produce. You should be able to take another type of contraceptive instead. Ask your doctor, pharmacist or nurse for advice.
- If you are not breast-feeding, you may start taking Synphase twenty one (21) days after your baby is born. This will protect you immediately. If you start later than this, you may not be protected until you have taken the tablets for seven days.

If you have just had a miscarriage or abortion

You may be able to start taking Synphase immediately. If you can, you will be protected straight away. Ask your doctor, pharmacist or nurse if you should do so.

If you have any further questions on the use of this medicine, ask your doctor, pharmacist or nurse.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Tell your doctor or call an ambulance immediately if you experience any of the following symptoms of an allergic reaction after taking this medicine. Although they are rare, the symptoms can be severe and you may need urgent medical attention or hospitalisation.

- Sudden wheeziness, difficulty in breathing, chest pain, fever, sudden swellings, rash or itching (especially affecting the whole body).

Stop taking Synphase and contact your doctor straight away if you notice any of the following serious side effects. These may be signs of thrombosis (a blood clot):

- You are coughing up blood
- You have swelling or tenderness in your stomach
- You have a sudden sharp or severe pain in your chest
- You suddenly become short of breath or find breathing is painful
- You have painful or inflamed veins in your legs
- You have a first attack of migraine (a bad headache with sickness)
- You have migraines which get worse, especially if your sight is affected, you see flashing lights, your limbs feel weak, you lose the sensation or feel a different sensation in your limbs, or you have a fit
- You have sudden and unusual severe headaches
- You experience dizziness or you faint
- You develop a problem with your sight or speech

For more information on this possible side effect, see also ‘Possible risk of thrombosis (blood clot)’ section further below.

Other side effects that you might have include:

- Feeling sick
- Stomach upsets
- Weight gain
- Changes in appetite
- Changes in the way your body breaks down sugars, fats or vitamins
- Headaches
- High blood pressure
- Depression
- Swollen or sore breasts
- Change in sex drive

- Worsening of womb disorders
- Irregular vaginal bleeding.

Taking any medicine carries some risk. You can use the information in this leaflet, and the advice your doctor, pharmacist or nurse has given you to weigh up the risks and benefits of taking the pill. Don't be embarrassed, and ask as many questions as you need to.

Reporting of side effects

If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via Yellow Card Scheme, website: www.mhra.gov.uk/yellowcard. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Synphase

- Keep this medicine out of the sight and reach of children.
- Do not use this medicine after the expiry date which is stated on the carton or blister strip after EXP. The expiry date refers to the last day of that month.
- Do not store above 25°C.
- Store in the original package to protect from light and moisture.
- Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away any medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Synphase contains

- The active substances are norethisterone and ethinylestradiol.
- The other ingredients in each tablet are maize starch, polyvidone, lactose, magnesium stearate and colouring E132 (in the blue pills only). Please also refer to section 2, 'Synphase contains lactose'.

What Synphase looks like and contents of the pack

Synphase tablets are blue or white, and are marked 'SEARLE' on one side and 'BX' on the other side. They are packed in blister strips containing 21 tablets and come in cartons containing either 21 or 63 tablets. Not all pack sizes may be marketed.

Each foil strip contains:

- Seven blue tablets containing 500 micrograms of norethisterone and 35 micrograms ethinylestradiol
- Nine white tablets containing 1 milligram of norethisterone and 35 micrograms ethinylestradiol
- Five blue tablets containing 500 micrograms of norethisterone and 35 micrograms ethinylestradiol

Marketing Authorisation Holder and Manufacturer

Marketing Authorisation Holder

Pfizer Limited
 Ramsgate Road
 Sandwich
 Kent, CT13 9NJ.

Manufacturer

Piramal Healthcare UK Limited
Whalton Road
Morpeth
Northumberland
NE61 3YA
United Kingdom.

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