PATIENT INFORMATION LEAFLET

SCHEDULING STATUS

Schedule 3

EVRA® (Transdermal Patch)

Norelgestromin 6 mg and Ethinyloestradiol 600 micrograms

Read all of this leaflet carefully before you start using EVRA.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- EVRA has been prescribed for you personally and you should not share your medicine with other people. It may harm them even if their symptoms are the same as yours.

What is in this leaflet:

1. What EVRA is and what it is used for:

EVRA is a combination transdermal contraceptive patch used to prevent pregnancy.

2. What you need to know before you use EVRA

Do not use EVRA if:

EVRA should not be used if you suffer or have ever suffered from any of the conditions listed below.

- You are allergic (hypersensitive) to norelgestromin, ethinyloestradiol or any of the other ingredients in EVRA (See “WHAT EVRA CONTAINS”)
- You have ever had a heart attack or a type of chest pain called “angina”
- You have ever had a stroke or signs which may lead to stroke. This includes a slight, temporary stroke, without any after effects
- You have high blood pressure (160/100 mm Hg or above)
- You have diabetes with damaged blood vessels
- You have bad headaches with neurological symptoms such as changes in vision or numbness in any part of your body (migraine with focal aura)
- You have ever a blood clot (thrombosis) in your legs (deep vein thrombosis or DVT) or lungs (pulmonary embolism) or another part of your body
- You have an illness which runs in your family which affects the clotting of your blood (such as “protein C deficiency” or “protein S deficiency”)
- You have very high fat levels in your blood (cholesterol or triglycerides)
- You have an illness which runs in your family which affects fat levels in your blood (called dyslipoproteinaemia)
- You have ever had liver tumours or any problem with your liver

- You have ever been told you might have breast cancer or cancer of the womb, cervix or vagina
- You have unexplained vaginal bleeding
- You have a blood problem called porphyria
- You are pregnant or think you might be pregnant
- You have certain types of jaundice (yellowing of the skin and whites of the eye)
- You have had pemphigus gestationis (a rare skin blistering disorder that occurs in women of childbearing age. It usually presents in pregnancy but can also recur in women who subsequently use oral contraceptive therapy or with menstruation. It usually starts with an itchy rash that develops into blisters. It is commonest during mid to late pregnancy (the second and third trimesters)).
- You take any medicines with paritaprevir/ritonavir, ombitasvir, and/or dasabuvir

Warnings and special precautions:

Take special care with EVRA:

Tell your doctor or health care provider before using EVRA:

- That you are on treatment for depression
- That you have had depression with previous use of hormonal contraceptives
- That you have a substance abuse problem
- You have underlying psychiatric disorder such as post-traumatic stress disorder or bipolar disorder
- That you have a family history of mental disorders
- That you have a history of physical or sexual abuse

Hormonal contraceptives including EVRA, may cause mood changes and depression, which may be severe. Severe depression is associated with a higher risk of suicidal thoughts/behavior (eg.

talking about suicide, withdrawing from social contact, having mood swings, being preoccupied with death or violence, feeling hopeless about a situation, increasing use of alcohol/drugs, doing self-destructive things, personality changes) and suicide. If you experience mood changes and depression contact your doctor for advice.

Medical-check-ups

Before using EVRA you will need to see your doctor for a medical check-up.

Check with your doctor or pharmacist before using EVRA if you have any of the following or they happen to get worse while using EVRA:

- You weigh 90 kg or more
- You, or any of your family, have high fat levels in the blood (triglycerides or cholesterol)
- You have high blood pressure or your blood pressure gets higher
- You have an immune system problem called “SLE” (systemic lupus erythematosus)
- You have a blood problem which causes kidney damage called “HUS” (haemolytic uraemic syndrome)
- You have a hearing loss
- You have epilepsy or any other problem that can cause fits (convulsions)
- You have a problem of the nervous system involving sudden movements of the body called “Sydenham’s chorea”
- You have diabetes
- You have depression of a history of this condition
- You have gallstones
- You have liver problems, including yellowing of the skin and whites of the eyes (jaundice)
- You have an inflammatory illness of your gut (Crohn’s disease or ulcerative colitis)

- You have “pregnancy spots”. These are yellowish-brown patches or spots, especially on your face (called “chloasma”)
- Smoking and age: Cigarette smoking increases the risk of serious cardiovascular events from EVRA use. This risk increases with age, particularly in women over 35 years of age, and with the number of cigarettes smoked. For this reason, EVRA should not be used by women who are over 35 years of age and smoke.

If you are not sure if any of the above applies to you, talk to your doctor or pharmacist before using EVRA.

Potentially serious conditions:

The following information is based on information about combined birth control pills. As the EVRA transdermal patch contains similar hormones to those used in combined birth control pills, it is likely to have the same risks. All combined birth control pills have risks, which potentially could lead to disability or death.

Thrombosis (Blood Clots)

Using combined hormonal contraceptives, including EVRA, increases the chances of getting a thrombosis (blood clots). It is possible that the risk of blood clots in the legs and/or lungs with EVRA is more than the risk with combined birth control pills. The risk of developing blood clots is not affected by how long you use EVRA. The risk may also be higher if you restart taking a combined hormonal contraceptive (the same product or a different product) after a break of 4 weeks or more. The risk returns to normal, a few months after you stop using EVRA.

Blood clots can cause blockage in a vein or artery and this may make you permanently disabled or even cause death.

- Blood clots can form in a vein in your leg (deep vein thrombosis or DVT) and travel to the lungs. This can cause chest pain and make you breathless or collapse. This is called a “pulmonary embolism” or PE
- Blood clots can form in the blood vessels of the heart (causing a heart attack) or the brain (causing a stroke)
- Blood clots can happen in other places such as the liver, gut, kidney or eye. Blood clots in the eye may cause loss of eyesight or double vision.

Tell your doctor immediately if you notice any possible signs of a blood clot, such as:

- Pain or swelling in either leg
- Pain in the chest, which may spread to the arm
- Sudden shortness of breath or sudden coughing
- Unusual, severe or long-lasting headache
- Vision problems
- Difficulty speaking
- Feeling dizzy or fainting spells
- Feeling weak or numb on one side or one part of the body
- Difficulty walking or holding things
- Sudden stomach pain

If you think you might have any of these, talk to your doctor immediately.

Your chances of getting a blood clot increases:

- As you get older
- If blood clots in blood vessels (veins or arteries) runs in the family
- If you smoke, especially if you are over 35 years of age
- If you stay in bed for many days
- If you are very overweight
- If you have just had a baby, miscarriage or abortion
- If you have had a serious injury, particularly of the leg or hip
- If you have had or are going to have a major operation or need to have bed rest for a long time.

Normally you should not use EVRA for two weeks before or two weeks after surgery

- If you have ever had blood clots before
- If you have problems with your blood fats (cholesterol or triglycerides)
- If you have high blood pressure
- If you have heart problems (problems with heart valves, abnormal heart rhythm).

Cancer

Breast cancer

Breast cancer has been found more often in women who use combined hormonal contraceptives, such as EVRA. The increased risk gradually goes down after stopping the combined hormonal contraceptives, such as EVRA. After ten years, the risk is the same as for people who have never used the combined hormonal contraceptive.

Cervical cancer

Cervical cancer also has been found more often in women taking combined hormonal contraceptives, such as EVRA.

Liver cancer

Liver tumours have been found in women taking combined hormonal contraceptives, such as EVRA. This can cause bleeding inside the body with severe pain in the stomach area. **If this happens, talk to your doctor immediately.**

Pregnancy and breastfeeding

- Do not use EVRA if you are pregnant or if you think you are pregnant
- Do not use EVRA if you are breastfeeding or planning to breastfeed your baby.

EVRA should not be taken together with any medicines with paritaprevir/ritonavir, ombitasvir, and/or dasabuvir. This may increase levels of the liver enzyme 'alanine aminotransferase' (ALT) in the blood.

Driving or using machines:

You can drive or operate machinery while wearing EVRA.

Children and adolescents

EVRA has not been studied in children and adolescents under 18 years of age. EVRA must not be used in children and adolescents who have not yet had their first menstrual period.

Taking other medicines with EVRA

Always tell your healthcare professional if you are taking any other medicine. (This includes complementary or traditional medicine).

Certain medicines and herbal remedies may stop EVRA from working properly. If this happens you could get pregnant.

Tell your doctor if you are taking:

- Medicines for HIV infection (such as ritonavir, nevirapine, nelfinavir), or medicines given in combination with HIV/AIDS medicines (e.g. cobicistat)
- Medicines for infection (such as rifampicin, rifabutin and griseofulvin)
- Medicines for epilepsy (such as topiramate, barbiturates, phenytoin sodium, carbamazepine, primidone, oxcarbamazepine, eslicarbazine acetate, rufinamide and felbamate)
- (fos)aprepitant (a medicine to treat nausea)
- Medicines for high blood pressure in the blood vessels in the lung (bosentan)
- St. John's Wort – an herbal remedy used for depression
- A mood enhancing substance called modafinil.

If you use any of these medicines, you may need to use another method of birth control (such as a condom, diaphragm or foam). The interfering effect of some of these medicines can last for up to 28 days after you have stopped taking them.

Blood levels of oestrogen from EVRA may be increased if you use certain medicines (see below) or drink grapefruit juice

- Paracetamol

- Ascorbic acid (Vitamin C)
- Certain anti-fungal medicines, such as itraconazole, ketoconazole, voriconazole and fluconazole
- Etoricoxib (an anti-inflammatory medicine)
- Certain cholesterol lowering medicines, such as atorvastatin and rosuvastatin
- Some HIV medicines such as etravirine, atazanavir and indinavir are some examples.

EVRA may make other medicines less effective, such as:

- Medicines containing:
  - Ciclosporin, omeprazole, prednisolone, prednisone, selegiline, tizanidine, voriconazole and theophylline (the levels of these medicines may be increased)
  - Paracetamol, clofibric acid, morphine, salicylic acid and temazepam (the levels of these medicines may be decreased)
- The anti-epileptic lamotrigine. This can increase the risk of fits (seizures).

Ask your doctor or pharmacist for advice before taking any medicine. Healthcare providers are advised to consult the package inserts of concurrently-used medicines to obtain further information about interactions with hormonal contraceptives or the potential for enzyme alterations and the possible need to adjust dosages.

Laboratory tests:

If you are having any blood or urinary test, tell your health care professional that you are using EVRA as it may affect the results of some tests.

3. How to use EVRA:

Always use EVRA exactly as described in this leaflet otherwise you may increase your risk of becoming pregnant. You should keep non-hormonal contraceptives (such as condoms, foam or sponge) as a back-up in case of errors when using EVRA. You should check with your doctor or pharmacist if you are unsure.

Talk to your doctor about using EVRA after having a baby or after an abortion or miscarriage.

How to use the EVRA patch:

- Weeks 1, 2 and 3: Put on one EVRA patch and leave it on for exactly seven days
- Week 4: Do **not** put on an EVRA patch this week.

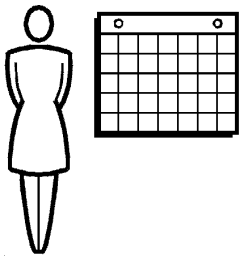
IMPORTANT INFORMATION TO FOLLOW WHEN USING THE EVRA PATCH

- Change EVRA on the same day of each week. This is because it is designed to work over 7 days.
- Never go without wearing EVRA for more than 7 days in a row.
- Only wear one patch at a time.
- Do not put the patch on skin that is red, irritated or cut.
- To work properly the patch must stick firmly to your skin.
    - Press the patch down firmly until the edges stick well
    - Do not use creams, oils, lotions, powder or makeup on the skin where you are placing a patch or near a patch you are wearing. This may cause the patch to become loose.
- Do not put a new patch on the same area of skin as the old patch. If you do you are more likely to cause irritation.
- Check each day to make sure the patch has not fallen off

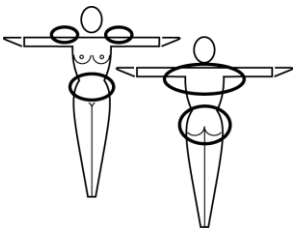
- Keep using the patches even if you do not have sex very often.

HOW TO USE EVRA

If this is the first time you are using EVRA, wait until the day you get your menstrual period.



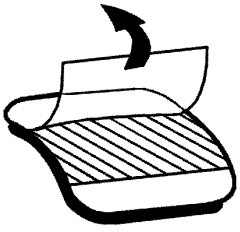
- Apply your first patch during the first 24 hours of your period
- If the patch is put on after the first day of your period, use a non-hormonal contraceptive until Day 8, when you change your patch
- **The day you apply your first patch will be Day 1. Your 'Patch Change Day' will be on this day of the week every week.**



Choose a place on your body to put the patch.

- Always put your patch on clean, dry, hairless skin
- Put it on the buttock, abdomen, upper outer arm or upper back – places where it won't be rubbed by tight clothing.
- **Never put the patch on your breasts.**

Using your fingers, open the foil sachet



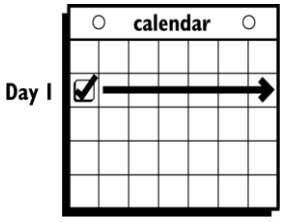
- Open it by tearing it along the edge (do not use scissors).
- Firmly grasp a corner of the patch and gently use it from the foil sachet
- There is a clear protective covering on the patch

- **Sometimes patches can stick to the inside of the sachet – be careful not to accidentally remove the clear covering as you remove the patch**
- Then peel away half of the clear protective covering (see picture).

Try not to touch the sticky surface.

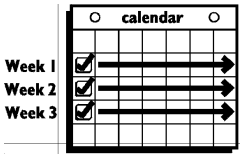
Put the patch on your skin

- Now use off the other half of the covering
- Press down firmly on the patch with the palm of your hand for 10 seconds
- Make sure that the edges stick well.



Wear the patch for 7 days (one week).

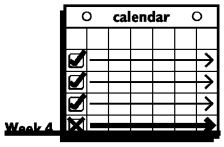
- On the first 'Patch Change Day', Day 8, use off the used patch
- Put on a new patch immediately
- On Day 15 (Week 3), use off the used patch
- Put on another new one.



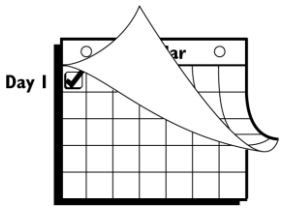
This makes a total of three weeks with the patches

To help stop irritation, do not put the new patch on the same area of your skin as your last patch

Do not wear a patch on Week 4 (Day 22 through Day 28)



- **You should have your period during this time.**
- During this week you are protected from getting pregnant only if you start your next patch on time.



For your next four week cycle

- Put on a new patch on your normal ‘Patch Change Day’, the day after Day 28
- **Do this no matter when your period begins or ends.**

If you want to change your “Patch Change Day” to a different day of the week talk to your doctor.

Everyday activities while using EVRA

- Normal activities such as having a bath or shower, using a sauna and exercising should not affect how well the EVRA patch works.
- The patch is designed to stay in place during these types of activities.
- However, you should check that the patch has not fallen off after doing these activities.

If you need to place the EVRA patch on a new area on your body on a day other than your “Patch Change day”

If the patch causes irritation or you become uncomfortable wearing it:

- You can use it off and replace it with a new patch in a different place on your body until your next ‘Patch Change Day”
- You may only use one patch at a time.

If you have trouble remembering to change your EVRA patch:

- Talk to your doctor or another healthcare professional at the clinic. He/she may be able to make patch changing easier for you. He/she may also talk about whether you need to use another method of contraception.

If your patch becomes loose, lifts at the edges or falls off:

For less than one day (up to 24 hours)

- Try to put it on again or put on a new patch immediately
- Back-up contraception is not needed
- **Your 'Patch Change Day' should remain the same**
- Do not try to put a patch on if:
    - it is no longer sticky
    - it has become stuck to itself or another surface
    - it has other material stuck to it
    - it is the second time it has become loose or has fallen off
- Do not use tapes or wrapping to keep the patch in place
- If you cannot get a patch back on, put on a new patch immediately.

For more than one day (24 hours or more) or if you are not sure for how long:

- **Start a new four week cycle immediately** by putting on a new patch.
- You now have a new Day 1 and a new 'Patch Change Day'.
- You must use non-hormonal contraception as back up for the first week of your new cycle.

You may get pregnant if you do not follow these instructions.

If you forget to change your EVRA patch:

At the start of any patch cycle (Week 1 (Day 1)),

If you forget to put on your patch, **you may be at particularly high risk of becoming pregnant**.

- You must use non-hormonal contraception as back up for one week
- Put on the first patch of your new cycle as soon as you remember
- You now have a new 'Patch Change Day' and new Day 1.

In the middle of your patch cycle (Week 2 or 3):

If you forget to change your patch for **one or two days** (up to 48 hours):

- You must put on a new patch as soon as you remember.
- Put on your next patch on your normal 'Patch Change Day'

No back-up contraception is needed.

For more than 2 days (48 hours or more):

- If you forget to change your patch for **more than 2 days, you may become pregnant**
- You must stop the current contraceptive cycle and start a new four week cycle as soon as you remember by putting on a new patch
- You now have a different 'Patch Change Day' and a new Day 1
- You must use back-up contraception for the first week of your new cycle.

At the end of your patch cycle (Week 4):

If you forget to use off your patch:

- Use it off as soon as you remember
- Start your next cycle on your normal 'Patch Change Day', the day after Day 28

No back-up contraception is needed.

If you switch from the oral contraceptive pill to EVRA:

If you are switching from an oral contraceptive pill to EVRA

- Wait until you get your menstrual period.
- Put on your first patch during the first 24 hours of your period.

If the patch is applied after Day 1 of your period, you should:

- Use a non-hormonal contraceptive until Day 8 when you change your patch

If you do not get your period within 5 days of taking the last contraceptive pill, check with your

doctor or clinic before starting EVRA.

Changing from the mini-pill to EVRA:

- You may start EVRA any day after stopping the mini-pill.
- The first day after stopping the mini-pill, put on a patch.
- Use a non-hormonal contraceptive until Day 8, when you change your patch.

If you have absent or irregular bleeding with EVRA

EVRA may cause unexpected vaginal bleeding or spotting during the weeks when you are wearing the patch.

- This usually stops after the first few cycles
- Misuses in using your patches can also cause spotting and light bleeding
- Continue using EVRA and if the bleeding lasts more than the first three cycles, talk to your doctor or pharmacist.

If you do not get your period during the EVRA patch free week (Week 4), you should still us a new patch on your usual “Patch Change Day”.

- If you have been using EVRA correctly and you do not have a period, this does not necessarily mean that you are pregnant
- However, if you miss two periods in a row, talk to your doctor or pharmacist as you maybe pregnant.

If you use more than one EVRA patch at any one time

Use the patches off and talk to a doctor or pharmacist immediately. If neither is available, contact the nearest hospital or poison control centre.

Using too many patches may cause you to have the following:

- Feeling sick (nausea) and being sick (vomiting)
- Bleeding from the vagina

If you stop using EVRA

You may get irregular, little or no bleeding. This usually happens in the first 3 months and especially if your periods were not regular before you started using EVRA.

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

4. Possible side effects:

EVRA can have side effects.

Tell your doctor if you notice any side effects. If you think that you have a serious side effect when using EVRA, use off the patch and speak to your doctor or pharmacist immediately. In the meantime, you should use another method of contraception.

Serious side effects associated with the use of combined hormonal contraceptives are described in the sections above, on Potentially serious conditions: Blood Clots and Cancer (breast cancer; cervical cancer and liver cancer). Please read these sections for additional information.

Frequent side effects:

- headache
- feeling sick (nausea)
- breast tenderness

- vaginal yeast infection, sometimes called thrush
- mood problems such as depression, change in mood or mood swings
- feeling dizzy
- migraine
- stomach pain or bloating
- being sick (vomiting) or diarrhoea
- acne, skin itching or skin irritation
- muscle spasms
- breast pain or enlargement
- uterine cramps, painful or heavy periods, bleeding between periods or vaginal discharge
- problems where the patch has been on the skin (such as redness, irritation, itching or rash)
- feeling tired or generally unwell
- weight gain.

Less frequent side effects:

- swelling due to water retention in the body
- high levels of fats in the blood (such as cholesterol and triglycerides)
- uncontrollable emotions
- anxiety
- problems sleeping (insomnia)
- less interest in sex or increased interest in sex
- skin rash, redness of the skin
- swelling of the breast, lumps in the breast or abnormal breast milk production
- premenstrual syndrome

- vaginal bleeding or dryness
- problems where the patch has been on the skin (such as swelling, discoloured skin, pain, spots, blisters or the skin feeling oversensitive)
- swelling
- rise in blood pressure
- increased appetite
- abnormal crying
- blood clot in the lung
- inflammation of the gall bladder
- yellow-brown pigment spots on the face
- irregular periods
- a bumpy rash (hives) where the patch has been on the skin
- rise in cholesterol levels
- aggression
- having more periods than normal

Other side effects include:

- other problems where the patch has been on the skin, skin reactions or allergic reactions
- A severe allergic reaction that may include swelling of the face, lips, mouth, tongue or throat which may cause difficulty in swallowing or breathing
- non-cancerous (benign) tumours in your breast or liver
- breast, cervical or liver cancer
- fibroids in the womb (uterus)
- Abnormal blood sugar, cholesterol or insulin levels
- blood clots, blocked arteries, heart attack or stroke

- problems when wearing contact lenses
- high blood pressure
- inflammation of the colon
- gallstones or blockage of the bile duct
- abnormal taste
- yellowing of the skin and whites of the eyes
- hair loss
- sensitivity to sunlight
- less frequent, light or no periods
- anger, feeling irritable or frustrated
- suicidal thoughts/behavior and suicide

If you have an upset stomach

- The amount of hormones you get from EVRA should not be affected by being sick (vomiting) or diarrhoea
- You do not need to use extra contraception if you have an upset stomach.

You may have spotting or light bleeding or breast tenderness or may feel sick during the first three cycles. The problem will usually go away but if it does not, check with your doctor or pharmacist.

Not all side effects reported for EVRA are included in this leaflet. Should your general health worsen or if you experience any untoward effects while taking EVRA, please consult your doctor, pharmacist or other healthcare professional for advice.

Reporting of side effects

If you get side effects, talk to your doctor, or, pharmacist, or nurse. You can also report side effects to SAHPRA via the "**6.04 Adverse Drug Reaction Reporting Form**", found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8. By reporting side effects, you can help provide more information on the safety of EVRA.

Alternatively, suspected adverse reactions may be reported directly to Acino Pharma (Pty) Ltd:
E-mail: drugsafety_za@acino.swiss Tel: 060 998 7896

5. How to store EVRA:

Store all medicines out of reach of children.

Store at or below 30 ^{0}C. Do not refrigerate or freeze. Store in the original container to protect from light and moisture. Do not store in bathroom.

Do not use after the expiry date printed on the label.

Used patches still contain the active hormones. To protect the environment, the patches should be disposed of with care. To discard the used patch, you should:

- Peel back the disposal label on the outside of the sachet
- Place the used patch within the open disposal label so that the sticky surface covers the shaded area
- Close the label sealing the used patch within and discard, keeping out of reach of children

Used patches should not be flushed down the toilet or placed in liquid disposal systems. Ask your pharmacist how to dispose of any patches no longer required. These measures will help protect the environment.

Return all unused medicine to your pharmacist.

6. Contents of the pack and other information

What EVRA contains:

EVRA contains two types of hormones:

- Norelgestromin: 6 mg per patch; and
- Ethinyloestradiol: 600 micrograms per patch

Because it contains two hormones, EVRA is called a “combination hormonal contraceptive”.

The other inactive ingredients are polyisobutylene, polybutene, crospovidone, non-woven polyester fabric and lauryl lactate.

What EVRA looks like and contents of the pack

Each container has 3, 9 or 18 EVRA transdermal patches in individual foil-lined sachets

20 cm^2 transdermal patch with radius corners consisting of:

i. A beige flexible backing
ii. Colourless adhesive containing the active components
iii. A clear, peel-cut release liner

Holder of certificate of registration

Acino Pharma (Pty) Ltd

106 16th Road

Midrand,

1686

This leaflet was revised in:

23 May 2022

Registration number:

36/18.7/0491

Access to the corresponding Professional Information:

Included in the carton, accompanying this patient information leaflet.