

PATIENT INFORMATION LEAFLET

SCHEDULING STATUS: S3

CLOPIWIN PLUS® 75/75 film-coated tablets

clopidogrel and acetylsalicylic acid (aspirin)

Contains sugar (7,0 mg lactose and 68,925 mg mannitol)

Read all of this leaflet carefully before you start taking CLOPIWIN PLUS

- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor, pharmacist, nurse or other health care provider.
- CLOPIWIN PLUS 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 CLOPIWIN PLUS is and what it is used for
2. What you need to know before you take CLOPIWIN PLUS
3. How to take CLOPIWIN PLUS
4. Possible side effects
5. How to store CLOPIWIN PLUS
6. Contents of the pack and other information

1. What CLOPIWIN PLUS is and what it is used for

CLOPIWIN PLUS contains the active substances clopidogrel and acetylsalicylic acid (aspirin), which belongs to a group of medicines called antiplatelet medicines.

CLOPIWIN PLUS is used to treat people who have suffered a severe type of chest pain called angina, or who have had a heart attack.

CLOPIWIN PLUS helps to prevent platelets from sticking together and forming a clot that can block an artery. Platelets are normal blood components involved in the clotting of blood.

CLOPIWIN PLUS is used to lower your chance of having another serious problem with your heart or blood vessels.

2. What you need to know before you take CLOPIWIN PLUS

Do not take CLOPIWIN PLUS:

- If you are hypersensitive (allergic) to clopidogrel, aspirin or any of the other ingredients of CLOPIWIN PLUS, listed in section 6.
- If you develop a skin rash while taking CLOPIWIN PLUS.
- If you are allergic to other products called non-steroidal anti-inflammatory products usually used to treat painful and/or inflammatory conditions of muscles and joints.
- If you have a history of gastrointestinal bleeding, gastrointestinal ulcer or gastrointestinal perforation related to previous use of a medicine called a non-steroidal anti-inflammatory drug (NSAID).
- If you have a medical condition that include the combination of asthma, nasal discharge (runny nose) and polyps (a type of growth in the nose).
- If you have a medical condition that is currently causing bleeding such as a stomach ulcer, haemophilia or bleeding within the brain or bowel or a history of such a condition.
- If you have heart problems which can cause shortness of breath or ankle swelling (heart failure).
- If you suffer from severe liver disease.
- If you suffer from severe kidney disease.
- If you suffer from a dysfunction of, or reduction in, blood platelets which increases risk of bleeding and bruising.

- If you are pregnant and/or breastfeeding.
- If you have a medical condition called mastocytosis. The use of CLOPIWIN PLUS may cause a severe hypersensitivity (allergic) reaction.

Do not take CLOPIWIN PLUS if any of the above applies to you. If you are not sure, talk to your doctor before taking CLOPIWIN PLUS.

Warnings and Precautions

Tell your doctor or health care provider before taking CLOPIWIN PLUS:

- If you have a risk of bleeding such as:
 - a medical condition that puts you at risk of internal bleeding (such as a stomach ulcer).
 - a blood disorder that makes you prone to internal bleeding (bleeding inside any tissues, organs or joints of your body).
 - a recent serious injury.
 - a recent surgery (including dental).
 - a planned surgery (including dental) in the next seven days.
 - a planned spinal, epidural anaesthetic or lumbar puncture in the next seven days.
- If you have had a clot in an artery of your brain (ischaemic stroke) which occurred in the last seven days.
- If you have kidney or liver disease.
- If you have a history of asthma or allergic reactions.
- If you have gout.
- If you have a history of heart problems which can cause shortness of breath or ankle swelling (heart failure) or high blood pressure.
- If you are elderly.
- If you have a history of inflammation of the colon which causes abdominal pain or diarrhoea.
- If you are taking any other type of medication (see Other medicines with CLOPIWIN

PLUS).

- If you have a condition known as glucose-6-phosphate dehydrogenase (G6PD) deficiency (a condition where your red blood cells are broken down prematurely), because of the risk of a particular form of anaemia.
- If you are a CYP2C19 poor metaboliser (you have very little or no function of the CYP2C19 enzyme, used to break down medicines, in your body).
- If you are hypersensitive (allergic) to other antiplatelet medicines used to prevent clots (such as ticlopidine or prasugrel),
- If you consume alcohol, because of the increased risk of bleeding or gastrointestinal injury.

Take special care while taking CLOPIWIN PLUS:

- You should tell your doctor and anaesthetist that you take CLOPIWIN PLUS:
 - if surgery (including dental) is planned.
 - if you have any stomach or abdominal pain or bleeding in the stomach or bowels (red stools or black stools).
- You should also tell your doctor immediately if you develop a medical condition (also known as Thrombotic Thrombocytopenic Purpura or TTP) that includes fever and bruising under the skin that may appear as red pinpoint dots, with or without unexplained extreme tiredness, confusion, yellowing of the skin or eyes (jaundice) (see section 4).
- If you cut or injure yourself, it may take longer than usual for bleeding to stop. This is linked to the way your medicine works as it prevents the ability of blood clots to form. For minor cuts and injuries e.g., cutting yourself or shaving, this is usually of no concern. However, if you are concerned by your bleeding, you should contact your doctor straightaway (see section 4).

Your doctor may order blood tests.

Children and adolescents

CLOPIWIN PLUS is not intended for use in children or adolescents less than 18 years of age. There is an association between aspirin and Reye's Syndrome when products containing aspirin are given to children or adolescents with a viral infection. Reye's Syndrome is a very rare disease which can be fatal.

Other medicines with CLOPIWIN PLUS

Always tell your health care provider if you are taking any other medicine. (This includes all complementary or traditional medicines).

Some other medicines may influence the use of CLOPIWIN PLUS or vice versa

You should tell your doctor if you take:

- Medicine that may increase your risk of bleeding such as:
 - oral anticoagulants, medicines used to reduce blood clotting.
 - aspirin or another non-steroidal anti-inflammatory medicine usually used to treat painful and/or inflammatory conditions of muscle or joints.
 - heparin or any other injectable medicine used to reduce blood clotting.
 - ticlopidine or prasugrel or other antiplatelet medicines used to reduce blood clotting.
 - a selective serotonin re-uptake inhibitor (SSRI) (e.g. fluoxetine or fluvoxamine), medicines usually used to treat depression,
 - rifampicin (used to treat severe infections)
- omeprazole, esomeprazole or cimetidine, medicines to treat upset stomach or to prevent gastric reflux (heartburn).
- methotrexate, a medicine used to treat severe joint disease (rheumatoid arthritis) or skin disease (psoriasis).
- probenecid, benzbromarone, or sulfinpyrazone, medicines used to treat gout.
- fluconazole, voriconazole, ciprofloxacin or chloramphenicol, medicines to treat bacterial and fungal infections.

- moclobemide, a medicine to treat depression.
- valproic acid, valproate and carbamazepine, medicines to treat some forms of epilepsy.
- corticosteroids, medicines to treat some inflammatory diseases.
- metamizole, a medicine to treat pain, muscle spasms and fever.
- acetazolamide, a medicine to treat glaucoma.
- nicorandil, a medicine to treat cardiac chest pain.
- the varicella vaccine, a medicine to prevent chickenpox or shingles, within 6 weeks of taking CLOPIWIN PLUS, or if you have an active chickenpox or shingles infection.
- levothyroxine, a medicine to treat low thyroid activity.
- tenofovir, an antiretroviral medicine used in the treatment of HIV.
- repaglinide, a medicine to treat diabetes.
- paclitaxel, a medicine to treat cancer.
- rosuvastatin (used to lower your cholesterol level)
- opioids: while you are treated with clopidogrel, you should inform your doctor before being prescribed any opioids (used to treat severe pain, e.g. morphine).

Alcohol: The consumption of alcohol may affect how well CLOPIWIN PLUS works; it may increase blood loss and stomach irritation. Please ask your doctor for more information.

Alcohol should be used with caution if you are taking CLOPIWIN PLUS.

You should stop other clopidogrel treatments while you are taking CLOPIWIN PLUS.

Contact your doctor before using other aspirin containing medicines concomitantly with CLOPIWIN PLUS.

CLOPIWIN PLUS with food, drink and alcohol

CLOPIWIN PLUS may be taken with or without food.

Alcohol should be used with caution if you are taking CLOPIWIN PLUS (see Other medicine with CLOPIWIN PLUS).

Pregnancy and breastfeeding

If you are pregnant or breast feeding your baby, think you may be pregnant or are planning to have a baby, please consult your doctor, pharmacist or health care provider for advice.

You should not take CLOPIWIN PLUS if you are pregnant (see section 2).

If you become pregnant while taking CLOPIWIN PLUS, consult your doctor immediately.

You should not take CLOPIWIN PLUS if you are breastfeeding.

If you are breastfeeding or planning to breastfeed, talk to your doctor before taking CLOPIWIN PLUS.

Driving and using machines

CLOPIWIN PLUS should not affect your ability to drive or to use machines.

CLOPIWIN PLUS contains lactose and castor oil

CLOPIWIN PLUS contains lactose. If you have been told by your doctor that you have intolerance to some sugars (e.g., lactose), contact your doctor before taking CLOPIWIN PLUS.

CLOPIWIN PLUS also contains hydrogenated castor oil which may cause stomach upset and diarrhoea.

3. How to take CLOPIWIN PLUS

Do not share CLOPIWIN PLUS prescribed for you with any other person.

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

The usual dose is one tablet of CLOPIWIN PLUS per day to be taken orally with a glass of water, with or without food.

You should take your medicines at the same time each day.

You should take CLOPIWIN PLUS for as long as your doctor continues to prescribe it.

If you take more CLOPIWIN PLUS than you should

In the event of overdosage, consult your doctor or pharmacist. If neither is available, contact the nearest hospital or poison control centre.

If you forget to take CLOPIWIN PLUS

If you forget to take a dose of CLOPIWIN PLUS, but remember within 12 hours of your usual time, take your tablet straightaway and then take your next tablet at the usual time.

If you forget for more than 12 hours, simply take the next single dose at the usual time. Do not take a double dose to make up for the forgotten individual doses.

If you stop taking CLOPIWIN PLUS

Do not stop the treatment unless your doctor tells you so. Contact your doctor or pharmacist before stopping.

If you have been told by your doctor to stop treatment temporarily, ask your doctor when to re-start the treatment.

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

4. Possible side effects

Not all side effects reported for CLOPIWIN PLUS are included in this leaflet. Should your general health worsen or if you experience any untoward effects while taking CLOPIWIN PLUS, please consult your health care provider for advice.

CLOPIWIN PLUS can have side effects.

The most frequent side effect which has been seen with CLOPIWIN PLUS is bleeding.

Bleeding may occur as bleeding in the stomach or bowels, bruising, haematoma (unusual bleeding or bruising under the skin), nosebleed, blood in the urine. In a small number of cases, bleeding in the eye, inside the head, the lung or the joints has also been reported.

If you experience prolonged bleeding when taking CLOPIWIN PLUS:

If you cut or injure yourself, it may take slightly longer than usual for bleeding to stop. This is linked to the way CLOPIWIN PLUS works as it prevents the ability of blood clots to form. For minor cuts and injuries e.g., cutting yourself or shaving, this is usually of no concern. However, if you are concerned by your bleeding, you should contact your doctor straight away (see section 2).

If any of the following happens, stop taking CLOPIWIN PLUS and tell your doctor immediately or go to the casualty department at your nearest hospital:

Frequency unknown:

- swelling of the face, lips, mouth, tongue or throat which may cause difficulty in swallowing or breathing
- skin disorders such as rashes and itching, blisters of the skin
- if you develop a medical condition known as Thrombotic Thrombocytopenic Purpura (also known as TTP) – the symptoms may include fever, bruising under the skin that may appear as red pinpoint dots, with or without unexplained extreme tiredness, confusion, yellowing of the skin or eyes (jaundice) - see section 2

- tightness of chest, wheezing, coughing or difficulty breathing
- chest pain that may radiate to the neck or left arm, pallor, sweatiness, nausea, breathlessness, low blood pressure. These symptoms may be signs of heart problems due to an allergy to clopidogrel or aspirin (Kounis syndrome)
- sudden severe headache, seizures with no previous history of seizures, weakness in your arm or leg, nausea or vomiting (severe and continuing), sudden tiredness, difficulty speaking or understanding speech, loss of balance, hand tremors or loss of consciousness. These symptoms may be signs of life-threatening bleeding within your skull
- blistering, peeling or bleeding on any part of your skin (including your lips, eyes, mouth, nose, genitals, hands or feet) with or without a rash. You may also have flu-like symptoms at the same time, such as fever, chills or aching muscles. These may be signs of serious skin disorders such as Stevens-Johnson syndrome and toxic epidermal necrolysis (TEN)

These are very serious side effects. If you have them you may have a serious allergic reaction or other serious reaction to CLOPIWIN PLUS.

Tell your doctor immediately or go to the casualty department at your nearest hospital if you notice any of the following:

Frequent:

- bleeding (including nose bleeds) or bruising more easily than normal. Signs of bleeding may include unusually heavy bleeding from cuts and wounds, coughing up blood, blood in the urine, vomiting of blood or vomit that looks like coffee grounds, bloody or black bowel motions, unusually heavy or unexpected menstrual bleeding, bleeding in the eyes

Less frequent:

- stomach or duodenal ulcer
- fever, signs of infection or extreme tiredness. These may be due to a decrease in the

number of your white blood cells

- headache, dizziness, light-headedness or feeling faint

Frequency unknown:

- a serious skin reaction called acute generalized exanthematous pustulosis (AGEP) - symptoms may include a red, scaly widespread rash with bumps under the skin (including your skin folds, trunk, and upper extremities) and blisters filled with white/yellow fluid accompanied by fever
- a serious skin reaction called drug rash with eosinophilia and systemic symptoms (DRESS) or drug-induced hypersensitivity syndrome (DiHS) - symptoms may include rash, often itchy, fever, inflammation of internal organs, most commonly the liver
- inflammation of the pancreas with symptoms such as severe upper abdominal pain, the abdominal pain may radiate to your back, nausea, vomiting, diarrhoea, tenderness when touching your abdomen, fever
- lung problems called non-cardiogenic pulmonary oedema causing a fluid build-up in the lung - symptoms may include dry cough, fever, difficulty breathing when lying down, chest pain, shortness of breath
- breathing difficulties, sometimes associated with coughing
- a condition where a certain type of white blood cell called eosinophils accumulates in your lungs (eosinophilic pneumonia) - symptoms may include fever, chest pain worsened by deep breathing, shortness of breath, cough and generally feeling unwell
- numbness or problems with co-ordination
- low blood sugar - symptoms may include feeling shaky, anxious or nervous, light-headed, dizzy, chills, sweating or clammy skin, fast heartbeat
- insulin autoimmune syndrome a condition which can cause persistent low blood sugar levels
- increase in blood pressure
- decrease in blood pressure
- severe abdominal pain with or without back pain

- worsening of inflammation of the colon (colitis) which causes abdominal pain and diarrhoea
- kidney failure or inflammation of the kidneys – symptoms may include swelling of legs, ankles, feet or face due to fluid retention, reduction in your urine output, shortness of breath, fatigue, confusion
- liver problems such as liver injury or inflammation of the liver (hepatitis)
- headache (severe or continuing)
- ulcer perforation (where an ulcer burns through the stomach or duodenal wall, causing severe, sharp abdominal pain)
- inflammation of your blood vessels with symptoms such as fever, headache, tiredness, weight loss, general aches and pains, night sweats, rash or nerve problems such as numbness or weakness
- confusion; hallucinations
- reduction in your red and white blood cells and blood platelets (aplastic anaemia) – symptoms may include that you feel weak and tired, and that you are more susceptible to infections and uncontrolled bleeding
- reduction in the number of your red blood cells (anaemia) – symptoms may include that you feel weak and tired, and looking pale
- fever, signs of infection (such as sore throat) or extreme tiredness

These are serious side effects. If you have them, you may need urgent medical attention.

Tell your doctor if you notice any of the following:

Frequent:

- diarrhoea
- abdominal discomfort, indigestion or heartburn

Less frequent:

- vomiting, nausea, constipation, excessive gas in stomach or intestines
- changes in the way things taste

- sensation of tingling and numbness

Unknown frequency:

- ringing in the ears, hearing loss
- breast enlargement in men
- arthritis - pain or stiffness in the joints, joint pain and muscle pain
- gout
- stomatitis - sores and inflammation of the mouth
- fluid retention (oedema) – symptoms may include swelling of the feet, ankles, legs and/or hands.

Your doctor may identify changes in your blood or urine tests.

If you notice any side effects not mentioned in this leaflet, please tell your doctor or pharmacist.

Reporting of side effects

If you get any side effects, talk to your doctor, pharmacist or health care provider. This includes any possible side effects not listed in this leaflet.

You can report any side effects directly to Sanofi's Pharmacovigilance Unit at za.drugsafety@sanofi.com (email) or 011 256 3700 (tel).

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 CLOPIWIN PLUS.

5. How to store CLOPIWIN PLUS

Store all medicines out of reach of children.

Do not use after the expiry date which is stated on the carton or blister.

Store at or below 25 °C.

Do not remove blisters from the carton until required.

Do not use CLOPIWIN PLUS if you notice any visible sign of deterioration.

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. Contents of the pack and other information

What CLOPIWIN PLUS 75/75 contains

The active substances are clopidogrel and acetylsalicylic acid (aspirin).

Each film-coated tablet contains clopidogrel hydrogen sulphate (form II) equivalent of 75 mg clopidogrel base, and 75 mg acetylsalicylic acid (aspirin).

The other ingredients are mannitol, macrogol, microcrystalline cellulose, low-substituted hydroxypropylcellulose, maize starch, hydrogenated castor oil, stearic acid, anhydrous silica, lactose, hypromellose, triacetin, yellow iron oxide, titanium dioxide and carnauba wax.

Contains sugar: lactose and mannitol: Each tablet contains 7,0 mg lactose and 68,925 mg mannitol.

What CLOPIWIN PLUS 75/75 looks like and contents of the pack

CLOPIWIN PLUS 75/75 film-coated tablets are oval, slightly biconvex, yellow, engraved on one side with "C75" and "A75" on the other side.

CLOPIWIN PLUS 75/75 film-coated tablets are packed into aluminium blister strips and placed in cardboard cartons. Each strip contains either 7 or 10 tablets.

Pack sizes: 14 (2 strips of 7), 28 (4 strips of 7), or 84 (12 strips of 7) or 30 (3 strips of 10), 50 (5 strips of 10), 90 (9 strips of 10) or 100 (10 strips of 10).

Holder of Certificate of Registration

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