

Package leaflet: Information for the patient

Arplexam 2.5mg/0.625mg/5mg film-coated tablets

Arplexam 5mg/1.25mg/5mg film-coated tablets

Arplexam 5mg/1.25mg/10mg film-coated tablets

Arplexam 10mg/2.5mg/5mg film-coated tablets

Arplexam 10mg/2.5mg/10mg film-coated tablets

perindopril arginine/indapamide/amlodipine

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, or pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet:

1. What Arplexam is and what it is used for
2. What you need to know before you take Arplexam
3. How to take Arplexam
4. Possible side effects
5. How to store Arplexam
6. Content of the pack and other information

1. What Arplexam is and what it is used for

Arplexam is a combination of three active ingredients: perindopril, indapamide and amlodipine. It is an anti-hypertensive medicine used in the treatment of high blood pressure (hypertension).

Patients already taking perindopril/indapamide as fixed dose combination and amlodipine from separate tablets may instead receive one tablet of Arplexam which contains the three active ingredients in the same strength.

Each of the active ingredients reduces blood pressure and they work together to control your blood pressure:

- Perindopril belongs to a class of medicines called Angiotensin Converting Enzyme (ACE) inhibitors. It works by widening the blood vessels, which makes it easier for your heart to pump blood through them.
- Indapamide is a diuretic (which belongs to a class of medicines called sulphonamide derivatives with an indole ring). Diuretics increase the amount of urine produced by the kidneys. However, indapamide is different from other diuretics, as it only causes a slight increase in the amount of urine produced.
- Amlodipine is a calcium channel blockers (which belongs to a class of medicines called dihydropyridines). It works by relaxing blood vessels, so blood passes through easily.

2. What you need to know before you take Arplexam

Do not take Arplexam

- if you are allergic to perindopril or other ACE-inhibitors, indapamide or other sulphonamides, amlodipine or other dihydropyridines, or any of the other ingredients of this medicine (listed in Section 6),
- if you have experienced symptoms such as wheezing, swelling of the face or tongue, intense itching or severe skin rashes with previous ACE inhibitor treatment or if you or a member of your family have had these symptoms in any other circumstances (a condition called angioedema),
- if you have severe liver disease or suffer from a condition called hepatic encephalopathy (disease of the brain caused by liver illness),

- if you are suspected of having untreated decompensated heart failure (severe water retention, difficulty in breathing),
- if you take non antiarrhythmic medicines causing life-threatening irregular beat (torsades de pointes)
- if you have narrowing of the aortic heart valve (aortic stenosis) or cardiogenic shock (a condition where your heart is unable to supply enough blood to the body),
- if you suffer from heart failure after a heart attack.
- if you have severe low blood pressure (hypotension),
- if you have low blood potassium,
- if you have severe kidney problems
- if you are receiving dialysis
- if you have moderate kidney problems (for Arplexam doses containing 10mg/2.5mg/5mg and 10mg/2.5mg/10mg).
- if you are more than 3 months pregnant (it is also better to avoid Arplexam in early pregnancy – see pregnancy section.),
- if you are breastfeeding.
- if you have diabetes mellitus or kidney problems and you are treated with aliskiren.

Warning and precaution

Talk to your doctor or pharmacist or nurse before taking Arplexam:

- if you have hypertrophic cardiomyopathy (heart muscle disease) or renal artery stenosis (narrowing of the artery supplying the kidney with blood),
- if you have heart failure or any other heart problems,
- if you have severe increase in blood pressure (hypertensive crisis),
- if you have liver problems,
- if you suffer from a collagen disease (skin disease) such as systemic lupus erythematosus or scleroderma,
- if you have atherosclerosis (hardening of the arteries),
- if you need to have a test to check how well your parathyroid gland is working,
- if you suffer from gout,
- if you have diabetes,
- if you are on a salt restricted diet or use salt substitutes which contain potassium (a well-balanced potassium blood level is essential),
- if you take lithium or potassium-sparing diuretics (spironolactone, triamterene) as their use with Arplexam should be avoided (see “Taking other medicines”),
- if you take aliskiren (medicines used to treat hypertension)
- if you are elderly and your dose needs to be increased,
- if you had photosensitivity reactions,
- if you are black people you may have higher incidence of angioedema (swelling of the face, lips, mouth , tongue or throat which may cause difficulty in swallowing or breathing) and less effective in lowering blood pressure,
- if you are Haemodialysis patients dialysed with high-flux membranes,
- if you have kidney problems,
- if you have too much acid in blood, which may cause an increased rate of breathing,
- if you have cerebral circulatory insufficiency (low blood pressure in the brain),
- if you have swelling of the face, lips, mouth , tongue or throat which may cause difficulty in swallowing or breathing (angioedema), which can occur at any time during treatment, stop your treatment immediately and directly contact your doctor.

Your doctor may prescribe you blood tests to check for low sodium or potassium levels or high calcium levels.

You must tell your doctor if you think that you are (or might become) pregnant. Arplexam is not recommended in early pregnancy, and must not be taken if you are more than 3 months pregnant, as it may cause serious harm to your baby if used at that stage (see “Pregnancy and breastfeeding”).

When you are taking Arplexam, you should also inform your doctor or the medical staff:

- if you are to undergo anaesthesia and/or surgery,

- if you have recently suffered from diarrhoea or vomiting, or are dehydrated,
- if you are to undergo dialysis or LDL apheresis (which is removal of cholesterol from your blood by a machine),
- if you are going to have desensitisation treatment to reduce the effects of an allergy to bee or wasp stings,
- if you are to undergo a medical test that requires injection of an iodinated contrast agent (a substance that makes organs like kidney or stomach visible on an X-ray).

Children and adolescents

Arplexam should not be given to children and adolescents.

Other medicines and Arplexam

Please tell your doctor or pharmacist if you are taking or have recently taken or might take any other medicines.

Do not take aliskiren (used to treat high blood pressure) if you have diabetes or kidney problems.

You should avoid Arplexam with:

- ✓ lithium (used to treat some mental health disorders such as mania, manic depressive illness and recurrent depression),
- ✓ potassium-sparing drugs (e.g. triamterene, amiloride), potassium supplements or potassium-containing salt substitutes,
- ✓ dantrolene (infusion) is also used to treat malignant hyperthermia during anaesthesia (symptoms including very high fever and muscle stiffness),
- ✓ estramustine (used in cancer therapy),
- ✓ other medicines used to treat high blood pressure: angiotensin-converting-enzyme inhibitor and angiotensin receptor blockers.

Treatment with Arplexam can be affected by other medicines. Make sure to tell your doctor if you are taking any of the following medicines as special care may be required:

- ✓ other medicines for treating high blood pressure, including diuretics (medicines which increase the amount of urine produced by the kidneys),
- ✓ potassium-sparing drugs used in the treatment of heart failure : eplerenone and spironolactone at doses between 12.5mg to 50mg per day,
- ✓ anaesthetic medicines
- ✓ iodinated contrast agent
- ✓ bepridil (used to treat angina pectoris),
- ✓ moxifloxacin, sparfloxacin (antibiotic: medicine used to treat infection),
- ✓ methadone (used to treat addiction)
- ✓ dofetilide, ibutilide, bretylium, cisapride, diphemamil, procainamide, quinidine, hydroquinidine, disopyramide, amiodarone, sotalol (for the treatment of an irregular heart beat),
- ✓ verapamil, diltiazem (heart medicines)
- ✓ digoxin or other cardiac glycosides (for the treatment of heart problems),
- ✓ some antibiotics used to treat infections, such as rifampicin, erythromycin, clarithromycin,
- ✓ itraconazole, ketoconazole, amphotericin B by injection (to treat fungal disease),
- ✓ allopurinol (for the treatment of gout),
- ✓ mizolastine, terfenadine or astemizole (antihistamines for hay fever or allergies),
- ✓ corticosteroids used to treat various conditions including severe asthma and rheumatoid arthritis, and non-steroidal anti-inflammatory drugs (e.g. ibuprofen) or high dose salicylates (e.g. acetylsalicylic acid),
- ✓ immunosuppressants used for the treatment of auto-immune disorders or following transplant surgery to prevent rejection (e.g. ciclosporin, tacrolimus),
- ✓ tetracosactide (to treat Crohn's disease)
- ✓ gold salts, especially with intravenous administration (used to treat symptoms of rheumatoid arthritis),
- ✓ halofantrine (used to treat certain types of malaria),
- ✓ baclofen used to treat muscle stiffness in diseases such as multiple sclerosis,
- ✓ medicines to treat diabetes such as insulin or metformin,

- ✓ calcium including calcium supplements,
- ✓ stimulant laxatives (e.g. senna),
- ✓ medicines for the treatment of cancer,
- ✓ vincamine (used to treat symptomatic cognitive disorders in elderly including memory loss),
- ✓ medicines to treat mental health disorders such as depression, anxiety, schizophrenia... (e.g. tricyclic antidepressants, antipsychotics, imipramine-like antidepressants, neuroleptics),
- ✓ pentamidine (used to treat pneumonia),
- ✓ ritonavir, indinavir, nelfinavir (so called protease inhibitors used to treat HIV).
- ✓ hypericum perforatum (St. John's Wort),
- ✓ trimethoprim (for the treatment of infections),
- ✓ heparin (medicines used to thin blood),
- ✓ medicines used for the treatment of low blood pressure, shock or asthma (e.g. ephedrine, noradrenaline or adrenaline),
- ✓ nitroglycerin and other nitrates, or other vasodilators that may further reduce blood pressure.

Arplexam with food and drink

Grapefruit juice and grapefruit should not be consumed by people who are taking Arplexam. This is because grapefruit and grapefruit juice can lead to an increase in the blood levels of the active ingredient amlodipine, which can cause an unpredictable increase in the blood pressure lowering effect of Arplexam.

Pregnancy and breast-feeding

If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine

Pregnancy

You must tell your doctor if you think that you are (or might become) pregnant.

Your doctor will normally advise you to stop taking Arplexam before you become pregnant or as soon as you know you are pregnant and will advise you to take another medicine instead of Arplexam. Arplexam is not recommended in early pregnancy, and must not be taken when more than 3 months pregnant, as it may cause serious harm to your baby if used after the third month of pregnancy.

Breast-feeding

Tell your doctor if you are breast-feeding or about to start breast-feeding. Arplexam is not recommended for mothers who are breast-feeding, and your doctor may choose another treatment for you if you wish to breast-feed, especially if your baby is new-born, or was born prematurely.

Driving and using machines

Arplexam may affect your ability to drive or use machines. If the tablets make you feel sick, dizzy, tired, or give you a headache, do not drive or use machines and contact your doctor immediately.

3. How to take Arplexam

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

Swallow the tablet with a glass of water preferably in the morning and before a meal. Your doctor will decide on the correct dose for you. This will normally be one tablet once a day.

If you take more Arplexam than you should

Taking too many tablets may cause your blood pressure to become low or even dangerously low sometimes associated with nausea, vomiting, cramps, dizziness, sleepiness, mental confusion, oliguria (passing less urine than is normal), anuria (no production or passing of urine). You may feel lightheaded, faint, or weak. If blood pressure drop is severe enough shock can occur. Your skin could feel cool and clammy and you could lose consciousness. Seek immediate medical attention if you take too many Arplexam tablets.

If you forget to take Arplexam

It is important to take your medicine every day as regular treatment is more effective. However, If you forget to take a dose of Arplexam, take the next dose at the usual time. Do not take a double dose to make up for a forgotten dose.

If you stop taking Arplexam

As the treatment for high blood pressure is usually life-long, you should discuss with your doctor before stopping this medicinal product.

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.

Stop taking the medicinal product and see a doctor immediately, if you experience any of the following side effects:

- sudden wheeziness, chest pain, shortness of breath, or difficulty in breathing, (Uncommon) (may affect up to 1 in 100 people)
- swelling of eyelids, face or lips, (Uncommon) (may affect up to 1 in 100 people)
- swelling of the mouth, tongue and throat, which causes great difficulty breathing, (Uncommon) (may affect up to 1 in 100 people)
- severe skin reactions including intense skin rash, hives, reddening of the skin over your whole body, severe itching, blistering, peeling and swelling of the skin, inflammation of mucous membranes (Stevens Johnson Syndrome) or other allergic reactions, (Very rare) (may affect up to 1 in 10,000 people)
- severe dizziness or fainting, (Common) (may affect up to 1 in 10 people)
- heart attack, (Very rare) (may affect up to 1 in 10,000 people life-threatening irregular beat.(Not known)
- inflamed pancreas which may cause severe abdominal and back pain accompanied with feeling very unwell (Very rare) (may affect up to 1 in 10,000 people)

In decreasing order of frequency, side effects can include:

- Common (may affect up to 1 in 10 people):
Headache, dizziness, palpitations (awareness of your heartbeat), flushing, vertigo, pins and needles, visual impairment, tinnitus (sensation of noises in the ears), light-headedness due to low blood pressure, cough, shortness of breath, gastro-intestinal disorders (nausea, vomiting, abdominal pain, taste disturbances, , dyspepsia or difficulty of digestion, diarrhoea, constipation), allergic reactions (such as skin rashes, itching), cramps, feeling of tiredness, somnolence, ankle swelling (oedema)
- Uncommon (may affect up to 1 in 100 people):
Mood swings, anxiety, depression, sleep disturbances, trembling, hives, fainting, loss of pain sensation, rhinitis (blocked up or runny nose), , change of bowel habits, hair loss, purpura (red pinpoint spots on skin), skin discoloration, itchy skin, sweating, chest pain, joint or muscle pain, back pain, pain, feeling unwell (malaise), kidney problems, disorder in passing urine, increased need to urinate at night, increased number of times of passing urine, inability to obtain an erection, fever or high temperature, discomfort or enlargement of the breasts in men, weight increase or decrease, increase in some white blood cells, high potassium levels in the blood, hypoglycaemia (very low blood sugar level), low sodium levels in the blood, double vision, rapid heartbeat, vasculitis (inflammation of blood vessels), photosensitivity reactions (change in skin appearance) after exposure to the sun or artificial UVA, blister clusters over the skin, swelling of hands, ankles or feet, blood creatinine increased and blood urea increase, fall, dry mouth.
- Rare (may affect up to 1 in 1000 people):
Confusion, changes in laboratory parameters: Increased level of liver enzymes, high level of serum bilirubin.
- Very rare (may affect up to 1 in 10,000 people):

Decreased numbers of white blood cells, decrease in the number of platelets (which causes easy bruising and nasal bleeding), anaemia (decrease in red blood cells), cardiovascular disorders (irregular heartbeat, angina pectoris (pains to the chest, jaw and back, brought on by physical effort, and due to problems with the blood flow to the heart)), eosinophilic pneumonia (a rare type of pneumonia), swelling of the gums, severe skin reactions including intense skin rash, reddening of the skin over your whole body, severe itching, blistering, peeling and swelling of the skin, erythema multiforme (a skin rash which often starts with red itchy patches on your face, arms or legs), bleeding, tender or enlarged gums, abnormal liver function, inflammation of the liver (hepatitis), severe kidney problems, yellowing of the skin (jaundice), abdominal bloating (gastritis), disorder of the nerves which can cause weakness, tingling or numbness, increased muscle tension, hyperglycaemia (very high blood sugar level), high level of calcium in the blood, stroke possibly secondary to excessive low blood pressure.

- Not known (frequency cannot be estimated from the available data):
Hepatic encephalopathy (disease of the brain caused by liver illness), abnormal ECG heart tracing, low potassium levels in the blood, if you suffer from systemic lupus erythematosus (a type of collagen disease), this might get worse.
Short sightedness (myopia), blurred vision.

Changes in laboratory parameters (blood tests) can occur. Your doctor may need to give you blood tests to monitor your condition.

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 HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: www.hpra.ie; E-mail: medsafety@hpra.ie. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Arplexam

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 and tablet container. The expiry date refers to the last day of that month.

This medicinal product does not require any special storage conditions.

For the container of 30 film-coated tablet, the in-use stability after first opening is 30 days.
For the container of 100 film-coated tablet, the in-use stability after first opening is 100 days.

Do not throw away any medicine via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer used. These measures will help to protect the environment.

6. Content of the pack and other information

What Arplexam contains

- The active substances are perindopril arginine, indapamide and amlodipine
One film-coated tablet of Arplexam 2.5/0.625/5 mg contains 1.6975 mg perindopril equivalent to 2.5 mg perindopril arginine, 0.625 mg indapamide and 6.935mg amlodipine besilate equivalent to 5mg of amlodipine.
One film-coated tablet of Arplexam 5/1.25/5 mg contains 3.395 mg perindopril equivalent to 5mg perindopril arginine, 1.25 mg indapamide and 6.935mg amlodipine besilate equivalent to 5 mg of amlodipine. One film-coated tablet of Arplexam 5/1.25/10 mg contains 3.395 mg perindopril equivalent to 5mg perindopril arginine, 1.25 mg indapamide and 13.870mg amlodipine besilate equivalent to 10

mg of amlodipine. One film-coated tablet of Arplexam 10 /2.5/5 mg contains 6.790 mg perindopril equivalent to 10 mg perindopril arginine, 2.5 mg indapamide and 6.935mg amlodipine besilate equivalent to 5 mg of amlodipine.

One film-coated tablet of Arplexam 10 /2.5/10 mg contains 6.790 mg perindopril equivalent to 10 mg perindopril arginine, 2.5 mg indapamide and 13.870 mg amlodipine besilate equivalent to 10 mg of amlodipine.

- The other ingredients are:
 - Tablet core: Calcium carbonate starch compound: Calcium carbonate 90 %, Pregelatinised maize starch 10%, cellulose microcrystalline (E460), croscarmellose sodium (E468), magnesium stearate (E572), colloidal anhydrous silica, pregelatinised starch.
 - Tablet film-coating: Glycerol(E422), hypromellose 6mPa.s(E464), macrogol 6000, magnesium stearate(E572), titanium dioxide (E171).

What Arplexam looks like and contents of the pack

Arplexam 2.5/0.625/5 mg tablets are white, oblong, film-coated tablet, 8.5 mm long and 4.5 mm wide, engraved with  on one face and  on the other face.

Arplexam 5/1.25/5 mg are white, oblong, film-coated tablet, 9.75 mm long and 5.16 mm wide, engraved with  on one face and  on the other face.

Arplexam 5/1.25/10 mg are white, oblong, film-coated tablet, 10.7 mm long and 5.66 mm wide, engraved with  on one face and  on the other face.

Arplexam 10/2.5/5 mg are white, oblong, film-coated tablet, 11.5 mm long and 6.09 mm wide, engraved with  on one face and  on the other face.

Arplexam 10/2.5/10 mg are white, oblong, film-coated tablet, 12.2 mm long and 6.46 mm, engraved with  on one face and  on the other face.

The tablets are available in box of 10, 30, 60 (2 tablet containers of 30), 90 (3 tablet containers of 30), 100 and 500 tablets (5 tablet containers of 100).

The desiccant is present in the stopper of the tablet containers.
Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer

Marketing Authorisation Holder :

Les Laboratoires Servier
50, rue Carnot
92284 Suresnes cedex – France

Manufacturers:

Servier (Ireland) Industries Ltd
Gorey Road
Arklow - Co. Wicklow – Ireland

and

Les Laboratoires Servier Industrie
905 route de Saran
45520 Gidy – France

and

Anpharm Przedsiębiorstwo Farmaceutyczne S.A.

03-236 Warszawa
ul. Annopol 6b – Poland

and

EGIS Pharmaceuticals PLC
H-9900 Körmend, Mátyás király u.65
Hungary

This medicinal product is authorised in the Member States of the EEA under the following names:

| | |
|----------------|---|
| Austria | ARPLEXAM, Filmtabletten |
| Belgium | ARPLEXAM, comprimé pelliculé |
| Bulgaria | ARPLEXAM, филмирани таблетки |
| Cyprus | ARPLEXAM, επικαλυμμένα με λεπτό υμένιο δισκία |
| Czech Republic | ARPLEXAM, potahované tablety |
| Estonia | ARPLEXAM |
| Finland | ARPLEXAM, kalvopäällysteinen tabletti |
| France | ARPLEXAM, comprimé pelliculé |
| Greece | ARPLEXAM, επικαλυμμένα με λεπτό υμένιο δισκία |
| Hungary | ARPLEXAM filmtabletták |
| Ireland | ARPLEXAM film-coated tablets |
| Italy | TRIPLIAM, compresse rivestite con film |
| Latvia | ARPLEXAM, apvalkotās tabletes |
| Lithuania | ARPLEXAM, plėvele dengtos tabletės |
| Luxembourg | ARPLEXAM, comprimé pelliculé |
| Malta | ARPLEXAM film-coated tablets |
| Netherlands | ARPLEXAM, filmomhulde tabletten |
| Poland | ARPLEXAM |
| Portugal | ARPLEXAM |
| Romania | ARPLEXAM comprimate filmate |
| Slovakia | ARPLEXAM, filmom obalené tablety |
| Slovenia | ARPLEXAM filmsko obložene tablete |
| Spain | ARPLEXAM comprimidos recubiertos con película |

This leaflet was last revised in September 2015

Other sources of information

Detailed information on this medicine is available on the Medicines Authority web site:
www.medicinesauthority.gov.mt