PATIENT INFORMATION LEAFLET

SCHEDULING STATUS S3

DIPTATRIS 5 mg/160 mg/ 12,5 mg Film-coated tablets

DIPTATRIS 5 mg/160 mg/ 25 mg Film-coated tablets

DIPTATRIS 10 mg/160 mg/ 12,5 mg Film-coated tablets

DIPTATRIS 10 mg/160 mg/ 25 mg Film-coated tablets

DIPTATRIS 10 mg/320 mg/ 25 mg Film-coated tablets

Amlodipine + Valsartan + Hydrochlorothiazide

Sugar free

Read all of this leaflet carefully before you start taking DIPTATRIS

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

6. Contents of the pack and other information.

1. What DIPTATRIS is and what it is used for

DIPTATRIS tablets contain three substances called amlodipine, valsartan and hydrochlorothiazide.

All of these substances help to control high blood pressure.

- Amlodipine belongs to a group of substances called “calcium channel blockers”. Amlodipine stops calcium from moving into the blood vessel wall, which stops the blood vessels from tightening.
- Valsartan belongs to a group of substances called “angiotensin-II receptor antagonists”.

  Angiotensin II is produced by the body and makes the blood vessels tighten, thus increasing the blood pressure. Valsartan works by blocking the effect of angiotensin II.
- Hydrochlorothiazide belongs to a group of substances called “thiazide diuretics”.

  Hydrochlorothiazide increases urine output, which also lowers blood pressure.

As a result of all three mechanisms, the blood vessels relax and blood pressure is lowered.

DIPTATRIS is used to treat high blood pressure in adult patients whose blood pressure is already controlled while taking amlodipine, valsartan and hydrochlorothiazide separately, and who may benefit from taking one tablet containing all three substances.

2. What you need to know before you take DIPTATRIS

Do not take DIPTATRIS:

- if you are allergic (hypersensitive) to amlodipine, valsartan, hydrochlorothiazide, other sulphonamides or any of the other ingredients of DIPTATRIS (listed in section 6).
- If you are pregnant or breastfeeding– see Pregnancy section.
- If you have previously experienced swelling, especially of the face, hands and feet after taking a medicine like valsartan.
- If you often experience recurrent bouts of swelling with no obvious cause.
- If you have liver disease.
- If you suffer from Addison's disease, where the body does not make enough of certain hormones.
- If you have severe kidney problems.
- If you are unable to produce urine (anuria).
- If you taking any medicines containing lithium.
- If the level of potassium or sodium in your blood is too low.
- If the level of calcium in your blood is too high.
- If you have porphyria, a rare disease of a deficiency of certain enzymes.
- If you have gout (uric acid crystals in the joints).
- If you suffer from a condition called hypertrophic obstructive cardiomyopathy, where the heart muscle becomes abnormally thick.
- If you have narrowing of the valves in the heart.

- If you are taking other medicines or substances, which increase the potassium levels in your blood (such as certain types of diuretics, such as spironolactone, triamterene, amiloride and potassium supplements. These medicines are usually used to treat high blood pressure or swelling.
- If you are treated with a blood pressure lowering medicine containing aliskiren.
- If you have kidney disease and/or you are elderly, do not take DIPTATRIS with antibiotics called fluoroquinolones.
- If you have previously had cancer of the skin or lips.
- If you are under 18 years of age.

Warnings and precautions

Take special care with DIPTATRIS:

− tell your doctor if you experience symptoms such as muscle weakness, muscle spasms, abnormal heart rhythm as this may indicate low levels of potassium or magnesium in your blood.

− tell your doctor if you experience symptoms such as tiredness, confusion, muscle twitching, convulsions) as these may indicate low levels of sodium in your blood.

− tell your doctor if you experience symptoms such as nausea, vomiting, constipation, stomach pain, frequent urination, thirst, muscle weakness and twitching, as these may indicate a high level of calcium in your blood.

− if you have kidney problems, have had a kidney transplant or if you had been told that you have a narrowing of your kidney arteries.

− if you have liver problems.

− if you have or have had heart failure or coronary artery disease, particularly if you are prescribed the maximum dose of DIPTATRIS (10 mg/320 mg/25 mg).

− if you have experienced a heart attack. Follow your doctor's instructions for the starting dose carefully. Your doctor may also check your kidney function.

− if your doctor has told you that you have a narrowing of the valves in your heart (called "aortic or mitral stenosis") or that the thickness of your heart muscle is abnormally increased (called "obstructive hypertrophic cardiomyopathy").

− if you suffer from aldosteronism. This is a disease in which the adrenal glands make too much of the hormone aldosterone If this applies to you, the use of DIPTATRIS is not recommended.

− if you suffer from a disease called systemic lupus erythematosus (also called "lupus" or "SLE"), as DIPTATRIS may make it worse.

− if you have diabetes (high level of sugar in your blood), as DIPTATRIS may alter sugar levels.

if you have high levels of cholesterol or triglycerides in your blood, as DIPTATRIS may alter these levels.

− if you experience skin reactions such as rash after sun exposure.

− if you had an allergic reaction to other high blood pressure medicines or diuretics (a type of medicine also known as "water tablets"), especially if you suffer from asthma and allergies

− if you have been sick (severe vomiting or diarrhoea).

− if you have experienced swelling, particularly of the face and throat, while taking other medicines (including angiotensin converting enzyme inhibitors). If you get these symptoms, stop taking DIPTATRIS and contact your doctor straight away. You should never take DIPTATRIS again.

− if you experience dizziness and/or fainting during treatment with DIPTATRIS, tell your doctor as soon as possible.

− if you experience a decrease in vision or eye pain. These could be symptoms of fluid accumulation in the vascular layer of the eye (choroidal effusion) or an increase of pressure in your eye and can happen within hours to a week of taking DIPTATRIS. This can lead to permanent vision impairment, if not treated.

− if you are taking any of the following medicines used to treat high blood pressure:

- an ACE inhibitor (for example enalapril, lisinopril, ramipril), in particular if you have diabetes-related kidney problems.
- aliskiren.

if you have had skin cancer or if you develop an unexpected skin lesion during the treatment.

Treatment with hydrochlorothiazide, particularly long term use with high doses, may increase the risk of some types of skin and lip cancer (non-melanoma skin cancer). Protect your skin from sun exposure and UV rays while taking DIPTATRIS.

− if you experienced breathing or lung problems (including inflammation or fluid in the lungs) following hydrochlorothiazide intake in the past. If you develop any severe shortness of breath or difficulty breathing after taking DIPTATRIS, seek medical attention immediately.

Your doctor may check your kidney function, blood pressure, and the amount of electrolytes (e.g. potassium) in your blood at regular intervals.

<u>Elderly people (age 65 years and older)</u>

DIPTATRIS can be used by people aged 65 years and over at the same dose as for other adults and in the same way as they have already taken the three substances called amlodipine, valsartan and hydrochlorothiazide. Elderly patients, particularly those taking the maximum dose of DIPTATRIS (10 mg/320 mg/25 mg), should have their blood pressure checked regularly.

Children and adolescents

The use of DIPTATRIS in children and adolescents under 18 years of age is not recommended.

Other medicines and DIPTATRIS

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

Do not take DIPTATRIS with the following medicines:

- lithium (a medicine used to treat some types of depression);
- fluoroquinolones, a type of antibiotic.
- medicines or substances that increase the amount of potassium in your blood. These include potassium supplements or salt substitutes containing potassium, potassium-sparing medicines and heparin;
- ACE inhibitors or aliskiren (see also information under the headings “Do not take DIPTATRIS” and “Warnings and precautions”).

Caution should be used with the following medicines as they may cause a change in the effect of the medicines or cause increased side effects when used with DIPTATRIS:

- alcohol, sleeping pills (barbiturates)
- amantadine (anti-Parkinson therapy, also used to treat or prevent certain illnesses caused by viruses);
- anticholinergic medicines (medicines used to treat a variety of disorders such as gastrointestinal cramps, urinary bladder spasm, asthma, motion sickness, muscular spasms, Parkinson's disease and as an aid to anaesthesia);
- anticonvulsant medicines and mood-stabilising medicines used to treat epilepsy and bipolar disorder (e.g. carbamazepine, phenobarbital, phenytoin, fosphenytoin, primidone);
- cholestyramine, colestipol or other resins (substances used mainly to treat high levels of lipids in the blood);
- simvastatin (a medicine used to control high cholesterol levels);
- ciclosporin (a medicine used in transplantation to prevent organ rejection or for other conditions, e.g: rheumatoid arthritis or atopic dermatitis);
- cytotoxic medicines (used to treat cancer), such as methotrexate or cyclophosphamide;
- digoxin or other digitalis glycosides (medicines used to treat heart problems);
- verapamil, diltiazem (heart medicines);
- iodine contrast media (medicines used for imaging examinations);
- medicines for the treatment of diabetes (oral medicines such as metformin or insulins);
- medicines for the treatment of gout, such as allopurinol;
- medicines that may increase blood sugar levels (beta blockers, diazoxide);
- medicines that may induce “torsades de pointes” (irregular heart beat), such as

antiarrhythmics (medicines used to treat heart problems) and some antipsychotics;

- medicines that may reduce the amount of sodium in your blood, such as antidepressants, antipsychotics, antiepileptics;
- medicines that may reduce the amount of potassium in your blood, such as diuretics (water tablets), corticosteroids, laxatives, amphotericin or penicillin G;
- medicines to increase blood pressure such as adrenaline or noradrenaline;
- medicines used for HIV/AIDS (e.g. ritonavir, indinavir, nelfinavir);
- medicines used to treat fungal infections (e.g. ketoconazole, itraconazole);
- medicines used for oesophageal ulceration and inflammation (carbenoxolone);
- medicines used to relieve pain or inflammation, especially non-steroidal anti-inflammatory agents (NSAIDs), including selective cyclooxygenase-2 inhibitors (Cox-2 inhibitors);
- muscle relaxants (medicines to relax the muscles which are used during operations);
- nitroglycerin and other nitrates, or other substances called “vasodilators”;
- other medicines to treat high blood pressure, including methyldopa;
- rifampicin (used, for example, to treat tuberculosis), erythromycin, clarithromycin (antibiotics);
- St. John’s wort;
- dantrolene (infusion for severe body temperature abnormalities);
- vitamin D and calcium salts.

DIPTATRIS with food, drink and alcohol

Grapefruit and grapefruit juice should not be consumed by people who are prescribed DIPTATRIS. This is because grapefruit and grapefruit juice can lead to an increase in the blood levels of the active substance amlodipine, which can cause an unpredictable increase in the blood pressure lowering effect of DIPTATRIS. Talk to your doctor before drinking alcohol. Alcohol may make your blood pressure fall too much and/or increase the possibility of dizziness or fainting.

Pregnancy, breast-feeding and fertility

If you are pregnant or breastfeeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking DIPTATRIS.

Pregnancy

You must tell your doctor if you think you are (or might become) pregnant. Your doctor will normally advise you to stop taking DIPTATRIS before you become pregnant or as soon as you know you are pregnant and will advise you to take another medicine instead of DIPTATRIS. DIPTATRIS should not be used while pregnant.

Breast-feeding

Do Tell your doctor if you are breast-feeding or about to start breast-feeding. Amlodipine has been shown to pass into breast milk in small amounts. DIPTATRIS should not be used by 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 a newborn, or was born prematurely.

Driving and using machines

It is not always possible to predict to what extent DIPTATRIS may interfere with the daily activities of a patient. Patients should ensure that they do not engage in the above activities until they are aware of the measure to which DIPTATRIS affects them.

DIPTATRIS This medicine may make you feel dizzy, drowsy, nauseous or have a headache. If you experience these symptoms, do not drive or use tools or machines.

3. How to take DIPTATRIS

Do not share medicines prescribed for you with any other person.

Always take DIPTATRIS exactly as your doctor has instructed you. You should check with your doctor or pharmacist if you are unsure.

The usual dose of DIPTATRIS is one tablet per day.

- It is best to take the tablet at the same time each day. Morning is the best time.
- Swallow the tablet whole with a glass of water.
- You can take DIPTATRIS with or without food.

Depending on how you respond to the treatment, your doctor may suggest a higher or lower dose. Do not exceed the prescribed dose.

If you take more DIPTATRIS than you should

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

If you forget to take or give DIPTATRIS

If you forget to take a dose of this medicine, take it as soon as you remember and then take the next dose at its usual time. If it is almost time for your next dose you should simply take the next tablet at the usual time. Do not take a double dose (two tablets at once) to make up for a forgotten tablet.

Effects when treatment with DIPTATRIS is stopped:

Stopping your treatment with DIPTATRIS may cause your disease to get worse. Do not stop taking your medicine unless your doctor tells you to.

4. Possible side effects

DIPTATRIS can have side effects.

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

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

- swelling of the hands, feet, ankles, face, lips and mouth or throat, which may cause difficulty in swallowing or breathing,
- rash or itching.

These are all very serious side effects. If you have them, you may have had a serious reaction to DIPTATRIS. You may need urgent medical attention or hospitalisation.

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

- dizziness,
- low blood pressure (feeling of faintness, light-headedness, sudden loss of consciousness),
- severely decreased urine output (decreased kidney function),
- spontaneous bleeding,
- irregular heart beat,
- liver disorder, the symptoms may include feeling very tired and weak all the time, loss of appetite – which may lead to weight loss, loss of sex drive (libido), yellow skin and whites of the eyes (jaundice), itchy skin, feeling or being sick.
- 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 the mucous membranes (Stevens-Johnson syndrome, toxic epidermal necrolysis) or other allergic reactions,
- heart attack, the symptoms may include chest pain that may feel like pressure, tightness, pain, squeezing or aching; pain or discomfort that spreads to the shoulder, arm, back, neck, jaw, teeth or sometimes the upper belly; cold sweat; fatigue; heartburn or indigestion; light-headedness or sudden dizziness; nausea; shortness of breath,
- inflamed pancreas, which may cause severe abdominal and back pain accompanied with feeling of being very unwell,
- weakness, bruising, fever and frequent infections,

- stiffness.

These are all serious side effects. You may need urgent medical attention.

Tell your doctor if you notice any of the following:

Frequent

- palpitations (awareness of your heart beat), flushing, ankle swelling (oedema),
- abdominal pain, stomach discomfort after meal, reduced appetite, nausea and vomiting,
- sleepiness, tiredness, headache, dizziness, fainting on standing up,
- frequent urination,
- itchy rash and other types of rash,
- inability to achieve or maintain erection.

Less frequent

- fast heartbeat, chest pain,
- low level of blood platelets (sometimes with bleeding or bruising underneath the skin), fever, sore throat or mouth ulcers, more frequent infections (lack or low level of white blood cells), dark-coloured urine (haemolytic anaemia, abnormal breakdown of red blood cells either in the blood vessels or elsewhere in the body), confusion, tiredness, muscle twitching and spasm, rapid breathing (hypochloraemic alkalosis),
- pale skin, tiredness, breathlessness,
- stomach and abdomen discomfort, diarrhoea, disturbed sense of taste/ taste abnormalities, altered bowel habits, indigestion, constipation, abdominal bloating (gastritis), loss of appetite, severe upper stomach ache (inflammation

of the pancreas),

- spinning sensation, inability to either stand or walk in a normal manner, weakness, loss of co-ordination making you unsteady, dizziness on standing up or after exercising,
- neuropathy (weakness, numbness and pain from nerve damage, usually in the hands and feet), sudden temporary loss of consciousness, trembling, mood changes, depression, sleeplessness, fainting, tingling or numbness, confusion,
- kidney disorders with symptoms such as weight loss and poor appetite; swollen ankles, feet or hands – as a result of water retention (oedema); shortness of breath; tiredness; blood in urine; an increased need to urinate, particularly at night; difficulty sleeping; itchy skin,
- vision disorder, visual disturbances, visual impairment,
- breath odour, dry mouth, swelling of the gums,
- weight increase, weight decrease,
- back pain, muscle cramps/weakness/pain, pain in extremity,
- joint swelling,
- cough,
- breathlessness, throat irritation,
- excessive sweating,
- itching/ itchy skin, skin reddening, skin discolouration, purple skin patches, increased sensitivity of skin to sun, yellowing of the skin (jaundice), inflammation of blood vessels often with skin rash,
- swelling, reddening and pain along a vein,
- loss of pain sensation,

- ringing in the ears,
- sneezing/runny nose caused by inflammation of the lining of the nose (rhinitis),
- hair loss,
- disorders in passing of urine, increased need to urinate at night, increased number of times of passing urine discomfort or enlargement of the breasts in men,
- pain, feeling unwell,
- worsening of the diabetic metabolic state, sugar in the urine, high level of sugar in the blood,
- liver disorders which can occur together with yellow skin and eyes, or dark-coloured urine (haemolytic anaemia), inflammation of the liver (hepatitis), liver enzyme increases which may have an effect on some medical tests,
- increased muscle tension,
- sensitivity to light,
- disorders combining rigidity, tremor and/or movement disorders,
- difficulty breathing with fever, coughing, wheezing, breathlessness (respiratory distress, pulmonary oedema, pneumonitis),
- facial rash, joint pain, muscle disorder, fever (lupus erythematosus),
- severe skin disease that causes rash, red skin, blistering of the lips, eyes or mouth, skin peeling, fever (toxic epidermal necrolysis),

Frequency unknown

- weakness, bruising and frequent infections (aplastic anaemia), fever, paleness, dizziness, fatigue – may indicate a condition affecting the blood,

- decrease in vision or pain in your eyes due to high pressure (possible signs of fluid accumulation in the vascular layer of the eye (choroidal effusion) or acute angle-closure glaucoma), breathlessness,
- severely decreased urine output (possible signs of renal disorder or renal failure),
- severe skin disease that causes rash, red skin, blistering of the lips, eyes or mouth, skin peeling, fever (erythema multiforme),
- muscle spasm,
- fever (pyrexia),
- blistering skin (sign of a condition called dermatitis bullous),
- viral infections, upper respiratory tract infection, infection of the sinuses, throat, runny nose,
- any unusual lesions or lumps on the skin that persist or get worse.

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

Reporting of side effects

If you get side effects, talk to your doctor or pharmacist. You can also report side effects to SAHPRA via the "**6.04 Adverse Drug Reactions & Quality Problem Reporting Form**", found online under SAHPRA's publications: https://www.sahpra.org.za/document/adverse-drug-reactions-and-quality-problem-reporting-form/

By reporting side effects, you can help provide more information on the safety of DIPTATRIS.

5. How to store DIPTATRIS

Store all medicines out of reach of children.

- Store at or below 25 °C.
- Do not use after the expiry date stated on the label.

Return all unused medicine to your pharmacist.

Do not dispose of unused medicine in drains or sewerage systems (e.g. toilets).

6. Contents of the pack and other information

What DIPTATRIS contains

The active substances are amlodipine, valsartan and hydrochlorothiazide.

DIPTATRIS 5 mg/160 mg/12,5 mg: Each film-coated tablet contains 6,94 mg amlodipine besylate (equivalent to 5 mg of amlodipine base), 160 mg of valsartan and 12,5 mg hydrochlorothiazide.

DIPTATRIS 5 mg/160 mg/ 25 mg: Each film-coated tablet contains 6,94 mg amlodipine besylate (equivalent to 5 mg of amlodipine base), 160 mg of valsartan and 25 mg hydrochlorothiazide.

DIPTATRIS 10 mg/160 mg/12,5 mg: Each film-coated tablet contains 13,88 mg amlodipine besylate (equivalent to 10 mg of amlodipine base), 160 mg of valsartan and 12,5 mg hydrochlorothiazide.

DIPTATRIS 10 mg/160mg/25 mg: Each film-coated tablet contains 13,88 mg amlodipine besylate (equivalent to 10 mg of amlodipine base), 160 mg of valsartan and 25 mg hydrochlorothiazide.

DIPTATRIS 10 mg/320 mg/25 mg: Each film-coated tablet contains 13,88 mg amlodipine besylate (equivalent to 10 mg of amlodipine base), 320 mg of valsartan and 25 mg hydrochlorothiazide.

Sugar free.

The other ingredients are:

Tablet Core:

Colloidal silicon dioxide, crospovidone, magnesium stearate, microcrystalline cellulose, sodium starch glycolate.

Film Coat:

HPMC 2910/ Hypromellose (E464), iron oxide red (E172), iron oxide yellow (E172), macrogol/ PEG 6000 (E1521), talc (E553b), titanium dioxide (E171).

What DIPTATRIS looks like and contents of the pack

DIPTATRIS 5 mg/160 mg/ 12,5 mg:

A white to off-white, film-coated, oval, biconvex, bevelled edge tablet debossed with "AVH1" on one side of the tablet and "M" on the other side.

DIPTATRIS 5 mg/160 mg/ 25 mg:

A yellow, film-coated, oval, biconvex, bevelled edge tablet debossed with "AVH3" on one side of the tablet and "M" on the other side.

DIPTATRIS 10 mg/160 mg/ 12,5 mg:

An orange, film-coated, oval, biconvex, bevelled edge tablet debossed with "AVH2" on one side of the tablet and "M" on the other side.

DIPTATRIS 10 mg/160 mg/ 25 mg:

Alight brown-yellow, film-coated, oval, biconvex, bevelled edge tablet debossed with AVH4" on one side of the tablet and "M" on the other side.

DIPTATRIS 10 mg/320 mg/ 25 mg:

Alight brown-yellow, film-coated, oval, biconvex, bevelled edge tablet debossed with "AVH5" on one side of the tablet and "M" on the other side.

Contents of the pack:

HDPE bottle pack (marketable pack) comprises of round, blue, opaque, high density polyethylene (HDPE) bottle with blue opaque polypropylene child resistant closure with wad containing aluminium induction sealing liner. The HDPE bottle pack may be placed in an outer cardboard carton along with desiccant based on commercial requirement. Pack size: 30’s.

Holder of Certificate of Registration

VIATRIS HEALTHCARE (PTY) LTD

4 Brewery Street

Isando

Gauteng

Republic of South Africa

This leaflet was last revised in

Registration numbers

Diptatris 5 mg/160 mg/ 12,5 mg: TBA

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Access to the corresponding Professional Information

To be confirmed.