Front Side

470 mm

435 mm

NIOSAR
40/80/160/320 mg
(film-coated tablet)
PM03915101

SCHEDULING STATUS: S3

1 NAME OF THE MEDICINE

NIOSAR 40 mg Film-coated tablets
NIOSAR 80 mg Film-coated tablets
NIOSAR 160 mg Film-coated tablets
NIOSAR 320 mg Film-coated tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each film-coated tablet contains 40 mg, 80 mg, 160 or 320 mg of valsartan.
Sugar free.
For full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Film-coated tablets.
NIOSAR 40 mg: Yellow, oval shaped, biconvex, film coated tablets debossed with "L" and "12" on either side of scoreline on one side and plain on other side.
NIOSAR 80 mg: Pale red, oval shaped, biconvex, film coated tablets debossed with "L13" on one side and plain on other side.
NIOSAR 160 mg: Light Brown, oval shaped, biconvex, film coated tablets debossed with "L14" on one side and plain on other side.
NIOSAR 320 mg: Violet, oval shaped, biconvex, film coated tablets debossed with "L15" on one side and plain on other side.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Hypertension:
Treatment of mild to moderate hypertension.

Post-myocardial infarction:
To improve survival following myocardial infarction in clinically stable patients with signs, symptoms or radiological evidence of left ventricular failure and/or with left ventricular systolic dysfunction.

Heart-Failure:
NIOSAR is indicated for the treatment of heart failure (NYHA class II – IV).

4.2 Posology and method of administration

Posology:
Hypertension:
The recommended dose of **NIOSAR** is 80 mg or 160 mg once daily, irrespective of race, age or gender.
The antihypertensive effect is substantially present within 2 weeks and maximal effects are seen after 4 weeks. In patients whose blood pressure is not adequately controlled, the daily dose may be increased to 320 mg, or a diuretic may be added.
NIOSAR may also be administered with other antihypertensive medicines.

Post-myocardial infarction:
Therapy may be initiated as early as 12 hours after a myocardial infarction. After an initial dose of 20 mg twice daily, **NIOSAR** therapy should be titrated to 40 mg, 80 mg, and 160 mg twice daily over the next few weeks. The starting dose is provided by the 40 mg divisible tablet.
The target dose is 160 mg twice daily. In general, it is recommended that patients achieve a dose level of 80 mg twice daily by two weeks after treatment initiation and that the target maximum dose be achieved by three months, based on the patient's tolerability to valsartan during titration. If symptomatic hypotension or renal dysfunction occurs, consideration should be given to a dosage reduction.
NIOSAR may be used in patients treated with other post-myocardial infarction therapies, e.g. thrombolytics, acetylsalicylic acid, beta blockers, or statins.

Evaluation of post-myocardial infarction patients should always include assessment of renal function.

Heart failure:
The recommended starting dose of **NIOSAR** is 40 mg twice daily. Up-titration to 80 mg and 160 mg twice daily should be done to the highest dose, tolerated by the patient. Consideration should be given to reducing the dose of concomitant diuretics. The maximum daily dose administered in clinical trials is 320 mg in divided doses.
Evaluation of patients with heart failure should always include assessment of renal function.

Special Populations

NOTE for all indications: No dosage adjustment is required for patients with mild renal impairment (where the creatinine clearance is above 70 ml/min) or for patients with hepatic insufficiency of non-biliary origin and without cholestasis.

Use in children and adolescents:
The safety and efficacy of **NIOSAR** have not been established in children and adolescents (below the age of 18 years).

Method of administration
Oral use.
NIOSAR is given orally with or without food.

4.3 Contraindications

- Known hypersensitivity to valsartan or to any of the excipients of **NIOSAR** (see section 6.1).
- A history of angioedema related to previous therapy with angiotensin-converting enzyme (ACE) inhibitors or angiotensin receptor blockers (ARBs): These patients must never again be given these medicines.
- Hereditary or idiopathic angioedema.
- Hypertrophic obstructive cardiomyopathy (HOCM).
- Severe renal function impairment (creatinine clearance less than 30 mL/min).
- Bilateral renal artery stenosis.
- Renal artery stenosis in patients with a single kidney.
- Aortic stenosis.
- Concomitant therapy with potassium sparing diuretics such as spironolectone, triamterene, amiloride (see section 4.4).
- Concomitant use of fluoroquinolones with ACE inhibitors/Angiotensin receptor blockers is contraindicated in patients with moderate to severe renal impairment (Creatinine Clearance ≤ 30mL/min) and in elderly patients
- Porphyria.
- Lithium therapy: Concomitant administration with **NIOSAR** may lead to toxic blood concentrations of lithium (see section 4.5).
- Pregnancy and lactation (see section 4.6).
- The concomitant use of **NIOSAR** with aliskiren-containing medicines is contraindicated (see section 4.4).

4.4 Special warnings and precautions for use

Pregnancy

Should a woman become pregnant while receiving **NIOSAR**, the treatment should be stopped promptly and switched to a different class of antihypertensive medicine (see sections 4.3 and 4.6).

Hyperkalaemia
Concomitant use with potassium supplements, potassium-sparing diuretics, salt substitutes containing potassium, or other medicines that may increase potassium levels (heparin, etc.) is not recommended. Monitoring of potassium should be undertaken as appropriate.

Impaired renal function
There is currently no experience on the safe use in patients with a creatinine clearance <10 mL/min and patients undergoing dialysis, therefore **NIOSAR** should be used with caution in these patients. No dose adjustment is required for adult patients with a creatinine clearance > 70mL/min (see sections 4.2 and 5.2).

The concomitant use of ARBs – including valsartan – or of ACEIs with aliskiren is contraindicated in patients with renal impairment (GFR < 60 mL/min/1,73 m^2) (see sections 4.3 and 4.5).

Hepatic impairment
In patients with mild to moderate hepatic impairment without cholestasis, **NIOSAR** should be used with caution (see sections 4.2 and 5.2).

Sodium- and/or volume-depleted patients
In severely sodium-depleted and/or volume-depleted patients, such as those receiving high doses of diuretics, symptomatic hypotension may occur after initiation of therapy with **NIOSAR**. Sodium and/or volume depletion should be corrected before starting treatment with **NIOSAR**, for example by reducing the diuretic dose.
If hypotension occurs, the patient should be placed in the supine position and, if necessary, given an intravenous infusion of normal saline. Treatment can be continued once blood pressure has stabilised.

Renal artery stenosis
In patients with bilateral renal artery stenosis or stenosis to a solitary kidney, the safe use of **NIOSAR** has not been established.

Short-term administration of valsartan to twelve patients with renovascular hypertension secondary to unilateral renal artery stenosis did not induce any significant changes in renal haemodynamics, serum creatinine, or blood urea nitrogen (BUN). However, other medicines that affect the renin-angiotensin system may increase blood urea and serum creatinine in patients with unilateral renal artery stenosis, therefore monitoring of renal function is recommended when patients are treated with **NIOSAR**.

Kidney transplantation
There is currently no experience on the safe use of **NIOSAR** in patients who have recently undergone kidney transplantation.

Primary hyperaldosteronism
Patients with primary hyperaldosteronism should not be treated with **NIOSAR** as their renin-angiotensin system is not activated.

Aortic and mitral valve stenosis, obstructive hypertrophic cardiomyopathy
NIOSAR is contraindicated in patients suffering from aortic or mitral stenosis, or hypertrophic obstructive cardiomyopathy (HOCM). (see section 4.3)

Recent myocardial infarction (only 40 mg, 80 mg and 160 mg)
The combination of captopril and valsartan has shown no additional clinical benefit, instead the risk for adverse events increased compared to treatment with the respective therapies (see sections 4.2 and 5.1). Therefore, the combination of valsartan as in **NIOSAR** with an ACE inhibitor is not recommended.

Caution should be observed when initiating therapy in post-myocardial infarction patients. Evaluation of post-myocardial infarction patients should always include assessment of renal function (see section 4.2).

Use of **NIOSAR** in post-myocardial infarction patients commonly results in some reduction in blood pressure, but discontinuation of therapy because of continuing symptomatic hypotension is not usually necessary provided dosing instructions are followed (see section 4.2).

Heart Failure (only 40 mg, 80 mg and 160 mg)
The risk of adverse reactions, especially hypotension, hyperkalaemia and decreased renal function (including acute renal failure), may increase when **NIOSAR** is used in combination with an ACE-inhibitor. In patients with heart failure, the triple combination of an ACE inhibitor, a beta-blocker and valsartan has not shown any clinical benefit (see section 5.1). This combination apparently increases the risk for adverse events and is therefore not recommended. Triple combination of an ACE-inhibitor, a mineralocorticoid receptor antagonist and valsartan as in **NIOSAR** are also not recommended. Use of these combinations should be under specialist supervision and subject to frequent close monitoring of renal function, electrolytes and blood pressure.

Caution should be observed when initiating therapy in patients with heart failure. Evaluation of patients with heart failure should always include assessment of renal function (see section 4.2).

Use of **NIOSAR** in patients with heart failure commonly results in some reduction in blood pressure, but discontinuation of therapy because of continuing symptomatic hypotension is not usually necessary provided dosing instructions are followed (see section 4.2).

Other conditions with stimulation of the renin-angiotensin system
In patients whose renal function may depend on the activity of the renin-angiotensin system (e.g. patients with severe congestive heart failure), treatment with angiotensin converting enzyme inhibitors has been associated with oliguria and/or progressive azotaemia and in rare cases with acute renal failure and/or death. As valsartan is an angiotensin II antagonist, it cannot be excluded that the use of **NIOSAR** may be associated with impairment of the renal function.

History of angioedema
Angioedema, including swelling of the larynx and glottis, causing airway obstruction and/or swelling of the face, lips pharynx, and/or tongue has been reported in patients treated with valsartan; some of these patients previously experienced angioedema with other medicines including ACE inhibitors.

NIOSAR should be immediately discontinued in patients who develop angioedema, and valsartan should not be re-administered.

Dual Blockade of the Renin-Angiotensin-Aldosterone System (RAAS)
There is evidence that the concomitant use of ACE-inhibitors, angiotensin II receptor blockers or aliskiren increases the risk of hypotension, hyperkalaemia and decreased renal function (including acute renal failure). Dual blockade of RAAS through the combined use of ACE-inhibitors, angiotensin II receptor blockers or aliskiren is therefore contraindicated (see sections 4.3).

NIOSAR should not be used concomitantly with aliskiran (see section 4.3).

Concomitant use of fluoroquinolones and ACE inhibitors/Angiotensin receptor blockers
Concomitant use of fluoroquinolones and ACE inhibitors/Angiotensin receptor blockers may precipitate acute kidney injury in patients, especially those with moderate to severe renal impairment and elderly patients. (See section 4.3).

Paediatric population
Impaired Renal function
Use in paediatric patients with a creatinine clearance < 30 mL/min and paediatric patients undergoing dialysis has not been studied, therefore valsartan is not recommended in these patients. No dose adjustment is required for paediatric patients with a creatinine clearance > 30 mL/min (see sections 4.2 and 5.2).

Renal function and serum potassium should be closely monitored during treatment with valsartan. This applies particularly when valsartan is given in the presence of other conditions (fever, dehydration) likely to impair renal function.

Impaired Hepatic function
As in adults, **NIOSAR** is contraindicated in paediatric patients with severe hepatic impairment, biliary cirrhosis and in patients with cholestasis (see sections 4.3 and 5.2). There is limited clinical experience with **NIOSAR** in paediatric patients with mild to moderate hepatic impairment.

4.5 Interaction with other medicines and other forms of interaction

Dual blockade of Renin-Angiotensin – System (RAS) with ARBs, AACEIs or aliskiren:
Clinical trial data has shown that dual blockade of the renin-angiotensin-aldosterone-system (RAAS) through the combined use of ACE-inhibitors, angiotensin II receptor blockers or aliskiren is associated with a higher frequency of adverse events such as hypotension, hyperkalaemia and decreased renal function (see sections 4.3, 4.4 and 5.1).

Concomitant use of angiotensin receptor antagonists (ARBs) – including valsartan – or of angiotensin- converting enzyme inhibitors (ACEIs) with aliskiren is contraindicated (see sections 4.3 and 4.4).

Concomitant use of fluoroquinolones and ACE inhibitors/Angiotensin receptor blockers:
Concomitant use of fluoroquinolones and ACE inhibitors/Angiotensin receptor blockers may precipitate acute kidney injury. The mechanism of the possible interaction between the different classes of medicines, over and above different mechanisms of kidney damage, is unknown (see section 4.3).

Concomitant use not recommended
Lithium
Reversible increases in serum lithium concentrations and toxicity have been reported during concurrent use of ACE inhibitors. Due to the lack of experience with concomitant use of valsartan and lithium, this combination is not recommended.

Potassium-sparing diuretics, potassium supplements, salt substitutes containing potassium and other substances that may increase potassium levels
Concomitant therapy with potassium sparing diuretics such as spironolactone, triamterene, amiloride is contraindicated.

Caution required with concomitant use
Non-steroidal anti-inflammatory medicines (NSAIDs), including selective COX-2 inhibitors, acetylsalicylic acid >3 g/day), and non-selective NSAIDs
When angiotensin II antagonists are administered simultaneously with NSAIDs, attenuation of the antihypertensive effect may occur. Furthermore, concomitant use of angiotensin II antagonists and NSAIDs may lead to an increased risk of worsening of renal function and an increase in serum potassium. Therefore, monitoring of renal function at the beginning of the treatment is recommended, as well as adequate hydration of the patient.

Transporters
In vitro data indicates that valsartan is a substrate of the hepatic uptake transporter OATP1B1/OATP1B3 and the hepatic efflux transporter MRP2. The clinical relevance of this finding is unknown. Co-administration of inhibitors of the uptake transporter (e.g. rifampicin, ciclosporin) or efflux transporter (e.g. ritonavir) may increase the systemic exposure to valsartan. Exercise appropriate care when initiating or ending concomitant treatment with such medicines.

Others
In interaction studies with valsartan, no interactions of clinical significance have been found with valsartan or any of the following substances: cimetidine, warfarin, furosemide, digoxin, atenolol, indomethacin, hydrochlorothiazide, amlodipine, glibenclamide.

Paediatric population
In hypertension in children and adolescents, where underlying renal abnormalities are common, caution is recommended with the concomitant use of valsartan and other medicines that inhibit the renin angiotensin aldosterone system which may increase serum potassium. Renal function and serum potassium should be closely monitored.

4.6 Fertility, pregnancy and lactation

Women of childbearing potential
Women of childbearing age should ensure effective contraception.

Pregnancy
Safety in pregnancy has not been established and therefore, **NIOSAR** is contraindicated in pregnancy (see section 4.3). When pregnancy is planned or confirmed **NIOSAR** should be discontinued. Medicines affecting the renin-angiotensin system, such as **NIOSAR**, can cause embryonal toxicity, foetal and neonatal morbidity and mortality when administered to pregnant women.

Breast-feeding
Because no information is available regarding the use of valsartan during breastfeeding, **NIOSAR** is contraindicated during lactation (see section 4.3). Alternative treatments with better established safety profiles during breast-feeding are preferable, especially while nursing a newborn or preterm infant.

Fertility
Valsartan had no adverse effects on the reproductive performance of male or female rats at oral doses up to 200 mg/kg/day. This dose is 6 times the maximum recommended human dose on a mg/m^2 basis (calculations assume an oral dose of 320 mg/day and a 60-kg patient).

4.7 Effects on ability to drive and use machines

No studies on the effects on the ability to drive have been performed. When driving vehicles or operating machines it should be taken into account that occasionally dizziness or weariness may occur when taking **NIOSAR**.

4.8 Undesirable effects

Tabulated summary of adverse reactions

MedDRA system organ class	Frequency	Adverse reactions
Infections and Infestations	Frequent Less frequent	Viral infections Upper respiratory tract infection, pharyngitis, sinusitis, rhinitis
Blood and the lymphatic system disorders	Frequency unknown	Decrease in haemoglobin, decrease in haematocrit, neutropenia, thrombocytopenia
Immune system disorders	Frequency unknown	Hypersensitivity including serum sickness
Metabolism and nutrition disorders	Less frequent Frequency unknown	Hyperkalaemia Increase of serum potassium, hyponatraemia
Psychiatric disorders	Less frequent	Insomnia, decreased libido
Nervous system disorders	Frequent Less frequent Frequency unknown	Postural dizziness Syncope, dizziness Headache
Ear and labyrinth disorders	Less frequent	Vertigo
Cardiac disorders	Less frequent	Cardiac failure
Vascular disorders	Frequent Frequency unknown	Hypotension, orthostatic hypotension Vasculitis
Respiratory, thoracic and mediastinal disorders:	Less frequent	Cough
Gastrointestinal disorders:	Less frequent	Abdominal pain Diarrhoea Nausea
Hepatobiliary disorders	Frequency unknown	Elevation of liver function values including increase of serum bilirubin
Skin and subcutaneous tissue disorders:	Frequency unknown	Angioedema, rash, pruritus
Musculoskeletal and connective tissue disorders:	Less frequent Frequency unknown	Back pain Myalgia Arthralgia
Renal and urinary disorders:	Frequency unknown	Renal failure and impairment, elevation of serum creatinine
General disorders and administration site conditions:	Frequency unknown	Fatigue, asthenia, oedema

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Health care providers are asked to report any suspected adverse reactions to SAHPRA via the "8.04 **Adverse Drug Reactions Reporting Form**", found online under SAHPRA's publications: https://www.sahpra.org.za/

4.9 Overdose

Symptoms
Overdose with **NIOSAR** may result in marked hypotension, which could lead to depressed level of consciousness, circulatory collapse and/or shock.

Treatment
The therapeutic measures depend on the time of ingestion and the type and severity of the symptoms; stabilisation of the circulatory condition is of prime importance.
If hypotension occurs, the patient should be placed in a supine position and blood volume correction should be undertaken. Otherwise, the usual treatment would be intravenous infusion of normal saline.
NIOSAR is unlikely to be removed by haemodialysis.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Angiotensin II Antagonists, plain.
ATC code: C09CA03
Pharmacological classification: A7.1.3 Vascular medicines – other hypotensives
Valsartan is an orally active, specific angiotensin II (Ang II) receptor antagonist. It acts selectively on the angiotensin 1 (AT_1) receptor subtype, which is responsible for the known actions of angiotensin II. The increased plasma levels of Ang II following AT_1 receptor blockade with valsartan may stimulate the unblocked AT_2 receptor, which appears to counterbalance the effect of the AT_1 receptor. Valsartan does not exhibit any partial agonist activity at the AT_1 receptor and has much greater affinity (about 20 000 fold) for the AT_1 receptor than for the AT_2 receptor.
The angiotensin 2 (AT_2) receptor subtype is unrelated to cardiovascular effect.

Abrupt withdrawal of valsartan has not been associated with rebound hypertension or other adverse clinical events.

5.2 Pharmacokinetic properties

Absorption
Valsartan is absorbed after oral administration, although the amount absorbed varies widely. Mean absolute bioavailability for valsartan is 23 %. Valsartan shows multi-exponential decay kinetics ($t½\,\alpha < 1$ h and $t½\,\beta$ about 9 h).
The pharmacokinetics of valsartan is linear in the dose range tested. There is no change in the kinetics of valsartan on repeated administration and little accumulation when dosed once daily. Plasma concentrations are similar in males and females.

Distribution
Valsartan is highly bound to serum protein (94 to 97 %), mainly serum albumin. Steady-state volume of distribution is low (about 17 L). Plasma clearance is relatively slow (about 2 L/h) when compared with hepatic blood flow (about 30 L/h). Of the absorbed dose of valsartan 70 % is excreted in the faeces and after iv administration, 30 % in the urine, mainly as unchanged compound.

Biotransformation
When valsartan is given with food, the area under the plasma concentration curve (AUC) of valsartan is reduced by 48 %, although from about 8 h post dosing plasma valsartan concentrations are similar for the fed and fasted group. This reduction in AUC, however, is not accompanied by a clinically significant reduction in the therapeutic effect, and valsartan can therefore be given either with or without food.

Elimination
The average time to peak concentration and elimination half-life of valsartan in heart failure patients are similar to that observed in healthy volunteers. AUC and C_{max} values of valsartan increase linearly and are almost proportional with increasing dose over the clinical dosing range (40 to 160 mg twice a day). The average accumulation factor is about 1,7. The apparent clearance of valsartan following oral administration approximately 4,5 l/h. Age does not affect the apparent clearance in heart failure patients.

Special Populations:
Elderly:
A significantly higher systemic exposure to valsartan was observed in elderly subjects than in young subjects; however, this has not been shown to have any clinical significance.

Impaired Renal Function:
Renal clearance accounts for only 30 % of total plasma clearance and no correlation is seen between renal function and systemic exposure to valsartan. Dose adjustment is therefore not required in patients with mild renal impairment. No studies have been performed in patients undergoing dialysis. However, valsartan is highly bound to plasma protein and is unlikely to be removed by dialysis.

Hepatic impairment:
About 70 % of the absorbed dose is excreted in the bile mainly as unchanged compound. Valsartan does not undergo extensive biotransformation and systemic exposure to valsartan is not correlated with the degree of liver dysfunction. No dose adjustment for valsartan is therefore necessary in patients with hepatic insufficiency of non-biliary origin and without cholestasis. The AUC with valsartan has been observed to be approximately double in patients with biliary cirrhosis or biliary obstruction (see section 4.4).

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

NIOSAR contains:
microcrystalline cellulose,
crospovidone,
silica colloidal anhydrous,
magnesium stearate
Coating:
hypromellose,
polyethylene glycol 8000,
talc,
titanium dioxide (C.I. no. 77891).
In addition, **NIOSAR 40 mg** contains iron oxide yellow (C.I. no. 77492);
NIOSAR 80 mg contains iron oxide red (C.I. no. 77491) and iron oxide yellow (C.I. no. 77492);
NIOSAR 160 mg contains iron oxide red (C.I. no. 77491), iron oxide yellow (C.I. no. 77492), iron oxide black (C.I. no. 77499); **NIOSAR 320 mg** contains iron oxide red (C.I. no. 77491) and iron oxide black (C.I. no. 77499).

6.2 Incompatibilities

Not applicable

6.3 Shelf life

36 months from the manufacturing date for container pack and blister pack.

6.4 Special precautions for storage

Store at or below 25 °C. No excursions permitted.
Protect from moisture.
Keep the blister in the carton until required for use.
Keep the container closed.
KEEP OUT OF THE REACH OF CHILDREN.

6.5 Nature and contents of container

1) Blister Pack:
Tablets are packed in Clear triplex film PVC/PE/PVDC 250/25/60 with 60 gsm PVDC as the forming material and 25 micron Aluminium foil coated with 6-8 gsm heat seal lacquer as the lidding material, packed in a pre-printed carton.
Pack size include 28's and 30's tablets.

2) HDPE Container Pack:
NIOSAR 40 mg:
Tablets are packed in 40 ml white round HDPE container with 33-400 mm neck finish which are closed with 33 mm child resistant closure with pulp and heat seal liner and packed in outer carton.
NIOSAR 80 mg:
Tablets are packed in 40 ml white round HDPE container with 33-400 mm neck finish which are closed with 33 mm child resistant closure with pulp and heat seal liner and packed in outer carton.
NIOSAR 160 mg:
Tablets are packed in 75 ml white round HDPE container with 38-400 mm neck finish which are closed with 38 mm child resistant closure with pulp and heat seal liner and packed in outer carton.
NIOSAR 320 mg:
Tablets are packed in 150 ml white round HDPE container with 38-400 mm neck finish which are closed with 38 mm child resistant closure with pulp and heat seal liner and packed in outer carton.
Pack size include 30's tablets for 40 mg and 90's tablets for 80 mg, 160 mg and 320 mg.
Not all packs and pack sizes are necessarily marketed.

6.6 Special precautions for disposal and other handling

No special requirements.
Any unused product or waste material should be disposed of in accordance with local requirements.

7 HOLDER OF CERTIFICATE OF REGISTRATION

MACLEODS PHARMACEUTICALS SA (PTY) LTD
Office block 1, Bassonia Estate Office Park (East),
1 Cussonia Drive, Bassonia Rock, Ext. 12, Alberton.

8 REGISTRATION NUMBERS

NIOSAR 40 mg: 47/7.1.3/0683
NIOSAR 80 mg: 47/7.1.3/0684
NIOSAR 160 mg: 47/7.1.3/0685
NIOSAR 320 mg: 47/7.1.3/0686

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

30 NOVEMBER 2021

10 DATE OF REVISION OF THE TEXT

–

PATIENT INFORMATION LEAFLET

SCHEDULING STATUS S3

NIOSAR 40 mg Film-coated tablets
NIOSAR 80 mg Film-coated tablets
NIOSAR 160 mg Film-coated tablets
NIOSAR 320 mg Film-coated tablets
Valsartan
Sugar free

Read all of this leaflet carefully before you start taking NIOSAR
- 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.
- **NIOSAR** 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 **NIOSAR** is and what it is used for
2. What you need to know before you take **NIOSAR**
3. How to take **NIOSAR**
4. Possible side effects
5. How to store **NIOSAR**
6. Contents of the pack and other information

1. What NIOSAR is and what it is used for

Valsartan belongs to a class of medicines known as angiotensin II receptor antagonists, which help to control high blood pressure. Angiotensin II is a substance in the body that causes vessels to tighten, thus causing your blood pressure to increase. Valsartan works by blocking the effect of angiotensin II. As a result, blood vessels relax and blood pressure is lowered.
NIOSAR can be used for three different conditions:
- to treat mild to moderate high blood pressure in adults,
- to treat adult patients after a recent heart attack (myocardial infarction),
- to treat symptomatic heart failure in adult patients.

2. What you need to know before you take NIOSAR

Do not take NIOSAR:
- If you are allergic (hypersensitive) to valsartan or any of the other ingredients of **NIOSAR** (listed in section 6).
- If you have developed swelling of the face, lips, mouth, tongue or throat and giant wheals on your skin when previously taking medicines called angiotensin-converting enzyme (ACE) inhibitors or angiotensin receptor blockers (ARBs) – you should never take these medicines again.
- if you suffer from severe liver disease or biliary obstruction (a problem with the drainage of the bile from the gall bladder).
- if you suffer from obstruction of blood vessels to your heart or kidneys.
- if you suffer from severe kidney function impairment.
- If you suffer from porphyria.
- If you are currently taking lithium.
- If you are currently taking potassium sparing water tablets containing spironolactone, triamterene or amiloride.
- If you are taking fluoroquinolones (antibiotics to treat infections)
- If you are currently taking aliskiren-containing medicines.
- if you are pregnant or breast-feeding.

Warnings and precautions
Take special care with NIOSAR:
- if you have liver disease.
- If you have severe kidney disease or if you are undergoing dialysis.
- If you are suffering from a narrowing of the kidney artery.
- If you have recently undergone kidney transplantation (received a new kidney).
- If you are treated after a heart attack or for heart failure, your doctor may check your kidney function.
- If you have severe heart disease other than heart failure or heart attack.
- if you are taking medicines that increase the amount of potassium in your blood. These include potassium supplements or salt substitutes containing potassium, potassium-sparing medicines and heparin. It may be necessary to check the amount of potassium in your blood at regular intervals.

Back Side

470 mm

- If you suffer from **aldosteronism.** This is a disease in which your adrenal glands make too much of the hormone aldosterone. If this applies to you, the use of **NIOSAR** is not recommended.
- If you have lost a lot of fluid (dehydration) caused by diarrhoea, vomiting, or high doses of water pills (diuretics).
- If you have ever experienced swelling of the tongue and face caused by an allergic reaction called angioedema when taking another medicine (including ACE-inhibitors), tell your doctor. If these symptoms occur when you are taking **NIOSAR**, stop taking **NIOSAR** immediately and never take it again. See section 4 "Possible side effects".
- 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 are being treated with an ACE-inhibitor together with certain other medicines to treat your heart failure, which are known as mineralocorticoid receptor antagonists (MRA) (for example spironolactone, eplerenone) or beta-blockers (for example metoprolol).

Contact your doctor to re-evaluate your treatment. If you are treated with ACE inhibitors/Angiotensin receptor blockers together with a fluoroquinolone antibiotic
Your doctor may check your kidney function, blood pressure, and the amount of electrolytes (e.g. potassium) in your blood at regular intervals.

Other medicines and NIOSAR
Always tell your health care provider if you are taking any other medicine. (This includes **all** complementary or traditional medicines.)
The effect of the treatment can be influenced if **NIOSAR** is taken together with certain other medicines. It may be necessary to change the dose, to take other precautions, or in some cases to stop taking one of the medicines. This applies to both prescription and non-prescription medicines, especially:
- other medicines that lower blood pressure, especially water tablets (diuretics),
- medicines that increase the amount of potassium in your blood. These include potassium supplements or salt substitutes containing potassium, potassium-sparing medicines and heparin,
- certain type of pain killers called non-steroidal anti-inflammatory medicines (NSAIDs),
- lithium, a medicine used to treat some types of psychiatric illness,
- some antibiotics (rifamycin group), a medicine used to protect against transplant rejection (ciclosporin) or an antiretroviral medicine used to treat HIV/AIDS infection (ritonavir). These medicines may increase the effect of **NIOSAR.**

In addition:
- If you are being treated after a heart attack, a combination with ACE inhibitors (a medicine to treat heart attack) is not recommended.
- If you are being treated for heart failure, a triple combination with ACE inhibitors and beta blockers (medicines to treat heart failure) is not recommended.

Your doctor may need to change your dose and/or to take other precautions:
- If you are being treated with an ACE-inhibitor together with certain other medicines to treat your heart failure, which are known as mineralocorticoid receptors antagonists (MRA) (for example spironolactone, eplerenone) or beta-blockers (for example metoprolol).

NIOSAR with food and drink
You can take **NIOSAR** tablets with or without food. Swallow **NIOSAR** tablets with a glass of water.

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 **NIOSAR.**

Do not take **NIOSAR** if you are pregnant, are considering becoming pregnant or are breastfeeding.
If you are a woman of childbearing age, you must use effective contraception.

Driving and using machines
Before you drive a vehicle, use tools or operate machines, or carry out other activities that require concentration, make sure you know how **NIOSAR** affects you. Like many other medicines used to treat high blood pressure, **NIOSAR** may cause dizziness and affect the ability to concentrate.

3. How to take NIOSAR

Do not share medicines prescribed for you with any other person.
Always take **NIOSAR** exactly as your doctor has told you. Check with your doctor if you are not sure.

High blood pressure: The usual starting dose is 80 mg of **NIOSAR** once daily. In some cases your doctor may prescribe higher doses (the dose can be increased to 160 mg and to a maximum of 320 mg). **NIOSAR** may also be administered with other medicines for high blood pressure.

Adult patients after a recent heart attack: After a heart attack the treatment is generally started as early as after 12 hours, usually at a low dose of 20 mg twice daily. You obtain the 20 mg dose by dividing the 40 mg tablet. Your doctor will increase this dose gradually over several weeks to a maximum of 160 mg twice daily. The final dose depends on what you as an individual patient can tolerate.
NIOSAR can be given together with other treatment for heart attack, and your doctor will decide which treatment is suitable for you.

Adult patients with heart failure: Treatment starts generally with 40 mg twice daily. Your doctor will increase the dose gradually over several weeks to a maximum of 160 mg twice daily. The final dose depends on what you as an individual patient can tolerate. **NIOSAR** can be given together with other treatment for heart failure, and your doctor will decide which treatment is suitable for you.
If you have the impression that **NIOSAR** is too strong or too weak, talk to your doctor or pharmacist.

NIOSAR tablets are only for adults and should not be taken by children and adolescents up to 18 years.

If you take more NIOSAR than you should
If you experience severe dizziness and/or fainting, contact your doctor immediately and lie down. 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 NIOSAR
If you forget to take a dose, take it as soon as you remember. However, if it is almost time for your next dose, skip the dose you missed. Do not take a double dose to make up for a forgotten dose.

Effects when treatment with NIOSAR is stopped:
Stopping your treatment with **NIOSAR** may cause your disease to get worse. Do not stop taking your medicine unless your doctor tells you to.

4. Possible side effects

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

If any of the following happens, stop taking **NIOSAR** 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 **NIOSAR.** 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:
- breathlessness, difficulty breathing when lying down, swelling of the feet or legs (signs of cardiac failure),
- severe blistering of the skin (bullous dermatitis),

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

Tell your doctor if you notice any of the following:
Frequent:
- dizziness,
- low blood pressure with or without symptoms such as dizziness and fainting when standing up,
- decreased kidney function (signs of renal impairment).

Less frequent:
- sudden loss of consciousness (syncope),
- dizziness
- spinning sensation (vertigo),
- severely decreased kidney function (signs of acute renal failure),
- heart failure
- muscle spasms, abnormal heart rhythm (signs of hyperkalaemia),
- headache, cough, sore throat, hay fever, inflamed sinuses
- abdominal pain, nausea, diarrhoea
- tiredness, weakness.
- Sleeplessness
- Low sex drive

Unknown frequency:
- allergic reactions with rash, itching and hives; symptoms of fever, swollen joints and joint pain, muscle pain, swollen lymph nodes and/or flu-like symptoms may occur (signs of serum sickness),
- purplish-red spots, fever, itching (signs of inflammation of blood vessels also called vasculitis),
- unusual bleeding or bruising (signs of thrombocytopenia),
- muscle pain (myalgia),
- fever, sore throat or mouth ulcers due to infections (symptoms of low level of white blood cells also called neutropenia),
- decrease of level of haemoglobin and decrease of the percentage of red blood cells in the blood (which can lead to anaemia in severe cases),
- increase of level of potassium in the blood (which can trigger muscle spasms, abnormal heart rhythm in severe cases),
- elevation of liver function values (which can indicate liver damage) including an increase of bilirubin in the blood (which can trigger yellow skin and eyes in severe cases),
- increase of level of blood urea nitrogen and increase of level of serum creatinine (which can indicate abnormal kidney function),
- low level of sodium in the blood (which can trigger tiredness, confusion, muscle twitching and/or convulsions in severe cases).

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

Reporting of side effects
You can also report side effects to SAHPRA via the "8.04 Adverse Drug Reaction Reporting Form", found online under SAHPRA's publications: https://www.sahpra.org.za/
By reporting side effects, you can help provide more information on the safety of **NIOSAR.**

5. How to store NIOSAR

Store **all** medicines out of reach of children.
Store at or below 25 °C. (Room temperature). No excursions permitted.
Keep the blister in the carton until required for use.
Keep the container tightly closed.
Do not store in a bathroom.
Do not use after the expiry date stated on the blister / label / carton / bottle.
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 NIOSAR contains
- The active substance is Valsartan
- The other ingredients are microcrystalline cellulose, crospovidone, Silica colloidal anhydrous, magnesium stearate
- The film coating contains hypromellose, polyethylene glycol 8000, talc, titanium dioxide (C.I. no. 77891), Iron oxide red (C.I. no. 77491), Iron oxide yellow (C.I. no. , 77492), Iron oxide black (C.I. no. 77499)

What NIOSAR looks like and contents of the pack
NIOSAR 40 mg
Yellow, oval shaped, biconvex, film coated tablets debossed with "L" and "12" on either side of scoreline on one side and plain on other side.
NIOSAR 80 mg
Pale red, oval shaped, biconvex, film coated tablets debossed with "L13" on one side and plain on other side.
NIOSAR 160 mg
Light Brown, oval shaped, biconvex, film coated tablets debossed with "L14" on one side and plain on other side.
NIOSAR 320 mg
Violet, oval shaped, biconvex, film coated tablets debossed with "L15" on one side and plain on other side.

Contents of the pack:
1) Blister Pack:
Tablets are packed in a blister pack which has a clear-plastic upper and aluminium foil backing, packed in a pre-printed carton.
Pack size include 28's and 30's tablets.

2) HDPE Container Pack:
NIOSAR 40 mg:
Tablets are packed in 40 ml white round container with child resistant closure and packed in outer carton.
NIOSAR 80 mg:
Tablets are packed in 40 ml white round container with child resistant closure and packed in outer carton.
NIOSAR 160 mg:
Tablets are packed in 75 ml white round container with child resistant closure and packed in outer carton.
NIOSAR 320 mg:
Tablets are packed in 150 ml white round container with child resistant closure and packed in outer carton.
Pack size include 30's tablets for 40 mg and 90's tablets for 80 mg, 160 mg and 320 mg.
Not all packs and pack sizes are necessarily marketed.

MACLEODS PHARMACEUTICALS SA (PTY) LTD
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Registration numbers
NIOSAR 40 mg: 47/7.1.3/0683
NIOSAR 80 mg: 47/7.1.3/0684
NIOSAR 160 mg: 47/7.1.3/0685
NIOSAR 320 mg: 47/7.1.3/0686

PASIËNTINLIGTINGSTUK

SKEDULERINGSTATUS: S3

NIOSAR 40 mg Filmbedekte tablette
NIOSAR 80 mg Filmbedekte tablette
NIOSAR 160 mg Filmbedekte tablette
NIOSAR 320 mg Filmbedekte tablette
Valsartan
Suikervry

Lees hierdie inligtingstuk sorgvuldig voordat jy NIOSAR begin neem
- Hou hierdie inligtingstuk. Dit mag nodig wees dat jy dit weer moet lees.
- Vra asseblief jou dokter, apteker, verpleegkundige of ander gesondheidsorgverskaffer indien jy verdere vrae het
- **NIOSAR** is vir jou persoonlik voorgeskryf, en jy moet nie jou medisyne met ander persone deel nie. Dit mag skadelik vir hulle wees, selfs al is hul simptome dieselfde as joune.

Wat in hierdie inligtingstuk is
1. Wat **NIOSAR** is en waarvoor dit gebruik word
2. Wat jy behoort te weet voordat jy **NIOSAR** neem
3. Hoe om **NIOSAR** te neem
4. Moontlike newe-effekte
5. Hoe om **NIOSAR** te bewaar
6. Inhoud van die pak en ander inligting

1. Wat NIOSAR is en waarvoor dit gebruik word

Valsartan behoort tot 'n groep van medisyne bekend as angiotensien II reseptor antagoniste, wat help om hoë bloeddruk te beheer. Angiotensien II is 'n stof in die liggaam wat veroorsaak dat bloedvate saamtrek en sodoende veroorsaak dat jou bloeddruk verhoog. Valsartan werk deur die effek van angiotensien II te blokkeer. As 'n resultaat, ontspan bloedvate en word bloeddruk verlaag.
NIOSAR kan gebruik word vir die verskillende toestande:
- om ligte tot matige hoë bloeddruk in volwassenes te behandel.
- om volwasse pasiënte ná 'n onlangse hartaanval te behandel (miokardiale infarksie),
- om simptomatiese hartversaking in volwasse pasiënte te behandel.

2. Wat jy behoort te weet voordat jy NIOSAR neem

Moet nie NIOSAR neem:
- Indien jy **allergies** (hipersensitief) vir valsartan of enige van die ander bestanddele van **NIOSAR** is nie (gelys in afdeling 6),
- Indien jy **swelling** van die gesig, lippe, mond, tong of keel, en reusagtige swelsels op jou vel ontwikkel het wanneer jy voorheen medisyne, genaamd angiotensien omskakelings enzism (ACE) inhibeerders of angiotensien reseptor blokkeerders (ARB's) geneem het nie – jy moet nooit weer hierdie medisyne gebruik nie.
- Indien jy ly aan ernstige lewersiekte of bilière obstruksie ('n probleem met die dreinering van die gal vanuit die galblaas).
- Indien jy ly aan obstruksie van bloedvate na jou hart of niere.
- Indien jy ly aan ernstige inkorting van nierfunksie.
- Indien jy ly aan porfirie.
- Indien jy lans litium neem.
- Indien jy lans kaliumbesparende watertablette gebruik wat spironolaktoon, triamtereen of amiloried bevat.
- Indien jy fluorokinolone (antibiotika om infeksies te behandel) gebruik.
- Indien jy lans aliskiren bevattende medisyne neem.
- Indien jy swanger is of borsvoed.

Waarskuwings en voorsorgmaatreëls
Wees veral versigtig met NIOSAR:
- Indien jy 'n lewersiekte het.
- as jy 'n ernstige niersiekte het of indien jy dialise ondergaan.
- indien jy aan 'n vernouing van die nierslagaar ly.
- indien jy onlangs 'n nieroorplanting ondergaan het (jy het 'n nuwe nier ontvang).
- indien jy behandel word na 'n hartaanval, of vir hartversaking, kan jou dokter jou nierfunksie nagaan.
- indien jy ernstige hartsiekte, anders as hartversaking of hartaanval, het.
- as jy medisyne neem wat die hoeveelheid kalium in jou bloed verhoog. Dit sluit kalium-aanvullings of soutvervangers wat kalium bevat, kaliumbesparende medisyne en heparien in. Dit mag nodig wees om die hoeveelheid kalium in jou bloed met gereelde tussenposes na te gaan.
- indien jy aan aldosteronisme ly. Dit is 'n siekte waarin jou byniere te veel van die hormoon aldosteroon maak. Indien dit op jou van toepassing is, word die gebruik van **NIOSAR** nie aanbeveel nie.
- as jy baie vloeistof verloor het (dehidrasie), as gevolg van diarree, braking, of hoë dosisse waterpille (diuretika).
- vertel jou dokter as jy al ooit swelling van die tong en gesig ervaar het wat veroorsaak is deur 'n allergiese reaksie, naamlik angioedeem, wanneer jy 'n ander middel (insluitend ACE-inhibeerders) gebruik. Indien hierdie simptome voorkom wanneer jy **NIOSAR** neem, stop dadelik om **NIOSAR** te gebruik en moet dit nooit weer neem nie. Sien afdeling 4 'Moontlike newe-effekte'.
- indien jy enige van die volgende medisyne neem, wat gebruik word om hoë bloeddruk te behandel:
  - 'n ACE-remmer (byvoorbeeld enalapril, lisinopril, ramipril), veral as jy diabetes verwante nierprobleme het.
  - aliskiren.
- indien jy met 'n ACE-remmer behandel word saam met sekere ander medisyne, om jou hartversaking te behandel, wat bekend staan as mineraalkortikoied reseptor antagoniste (MRA) (byvoorbeeld spironolaktoon, eplerenoon) of betablokkers (byvoorbeeld metoprolol).

Kontak jou dokter om jou behandeling te herevalueer. Indien jy met ACE-/Angiotensien reseptor blokkeerders behandel word, saam met 'n fluorokinolon-antibiotikum.
Jou dokter kan jou nierfunksie, bloeddruk en die hoeveelheid elektroliete (bv. kalium) in jou bloed met gereelde tussenposes nagaan.

Ander medisyne en NIOSAR
Vertel altyd vir jou gesondheidsorgverskaffer indien jy enige ander medisyne neem. (Dit sluit alle komplementêre of tradisionele medisyne in).
Die uitwerking van die behandeling kan beïnvloed word wanneer **NIOSAR** saam met sekere ander medisyne geneem word. Dit mag nodig wees om die dosis te verander, om ander voorsorgmaatreëls te tref, of in sommige gevalle om op te hou om een van die medisyne te neem. Dit geld vir beide voorskrif- en nie-voorskrif medisyne, veral:
- ander medisyne wat bloeddruk verlaag, veral watertablette (diuretika).
- medisyne wat die hoeveelheid kalium in jou bloed verhoog. Dit sluit kaliumaanvullings of soutvervangers wat kalium bevat, kaliumbesparende medisyne en heparien in.
- sekere tipe pynstillers wat nie-steroïdale anti-inflammatoriese medisyne (NSAIM's) genoem word.
- litium, 'n medisyne wat gebruik word om sommige soorte psigiatriese siektes te behandel.
- sommige antibiotika (rifamisien groep), 'n medisyne wat gebruik word om teen verwerping na oorplanting te beskerm (siklosporien) of 'n anti-retrovirale medisyne wat gebruik word om MIV/VIGS infeksie te behandel (ritonavir). Hierdie medisyne kan die uitwerking van **NIOSAR** verhoog.

Daarbenewens:
- as jy na 'n hartaanval behandel word, word 'n kombinasie met ACE-inhibeerders ('n medisyne om 'n hartaanval te behandel) nie aanbeveel nie.
- Indien jy vir hartversaking behandel word, word 'n drievoudige kombinasie met ACE- inhibeerders en betablokkers (medisyne om hartversaking te behandel) nie aanbeveel nie.

Jou dokter sal moontlik jou dosis moet verander en/of ander voorsorgmaatreëls moet tref:
- indien jy behandel word met 'n ACE-inhibeerder saam met sekere ander medisyne om jou hartversaking te behandel, wat bekend staan as mineraalkortikoied reseptor antagoniste (MRA) (byvoorbeeld spironolaktoon, eplerenoon) of betablokkers (byvoorbeeld metoprolol).

NIOSAR met voedsel en drank
Jy kan **NIOSAR** tablette met, of sonder voedsel neem. Sluk **NIOSAR** tablette met 'n glas water.

Swangerskap, borsvoeding en fertiliteit
Indien jy swanger is of borsvoed, dink dat jy moontlik swanger kan wees of beplan om 'n baba te hê, vra jou dokter of apteker vir advies voordat jy **NIOSAR** neem.

Moet nie **NIOSAR** neem **as jy swanger is**, oorweeg om swanger te raak, of borsvoed nie.
Indien jy 'n vrou van kinderbarende ouderdom is, moet jy effektiewe voorbehoeding gebruik.

Bestuur en gebruik van masjinerie
Voordat jy 'n voertuig bestuur, gereedskap gebruik of masjinerie bedryf, of ander aktiwiteite uitvoer wat konsentrasie vereis, maak seker dat jy weet hoe **NIOSAR** jou affekteer. Soos baie ander medisyne wat gebruik word om hoë bloeddruk te behandel, kan **NIOSAR** duiseligheid veroorsaak en die vermoë om te konsentreer, beïnvloed.

3. Hoe om NIOSAR te neem

Moet nie medisyne wat vir jou voorgeskryf is met enige ander persoon deel nie
Neem altyd **NIOSAR** presies soos jou dokter vir jou gesê het. Vra vir jou dokter indien jy onseker is.

Hoë bloeddruk: Die gewone aanvangsdosis is 80 mg van **NIOSAR** een keer per dag. In sommige gevalle kan jou dokter hoër doserings voorskryf (die dosis kan verhoog word tot 160 mg en tot 'n maksimum van 320 mg). **NIOSAR** kan ook saam met ander medisyne vir hoë bloeddruk toegedien word.

Volwasse pasiënte na 'n onlangse hartaanval: Die behandeling word gewoonlik so vroeg as 12 ure na 'n hartaanval begin, gewoonlik teen 'n lae dosis van 20 mg twee keer per dag. Jy verkry die 20 mg dosering deur die 40 mg tablet te deel. Jou dokter sal hierdie dosis geleidelik oor 'n aantal weke verhoog tot 'n maksimum van 160 mg twee keer per dag. Die finale dosis hang af van wat jy as individuele pasiënt kan verdra.
NIOSAR kan saam met ander behandeling vir hartaanval gegee word, en jou dokter sal besluit watter behandeling vir jou geskik is.

Volwasse pasiënte met hartversaking: Behandeling begin gewoonlik met 40 mg twee keer per dag. Jou dokter sal die dosis geleidelik oor 'n aantal weke verhoog tot 'n maksimum van 160 mg twee keer per dag. Die finale dosis hang af van wat jy as individuele pasiënt kan verdra. **NIOSAR** kan saam met ander behandeling vir hartversaking gegee word, en jou dokter sal besluit watter behandeling vir jou geskik is. Indien jy onder die indruk is dat **NIOSAR** te sterk of te swak is, praat met jou dokter of apteker.

NIOSAR tablette is slegs vir volwassenes en moet nie deur kinders en adolessente tot op 18 jaar geneem word nie.

Indien jy meer NIOSAR geneem het as wat jy behoort te neem
Indien jy erge duiseligheid en/of floute ervaar, kontak jou dokter dadelik, en gaan lê. In die geval van oordosering, raadpleeg jou dokter of apteker. Indien nie een beskikbaar is nie, kontak die naaste hospitaal of giftebeheersentrum.

Indien jy vergeet om NIOSAR te neem
Indien jy vergeet om 'n dosis te neem, neem dit sodra jy onthou. Indien dit egter amper tyd is vir jou volgende dosis, slaan die dosering oor wat jy gemis het. Moet nie 'n dubbele dosis neem om vir 'n vergete dosering op te maak nie

Effekte wanneer behandeling met NIOSAR gestaak word:
Indien jy jou behandeling met **NIOSAR** staak, kan jou siekte vererger. Moet nie ophou om jou medisyne te neem nie, tensy jou dokter jou beveel om dit te doen.

4. Moontlike newe-effekte

NIOSAR kan newe-effekte hê.
Nie alle newe-effekte wat vir NIOSAR aangemeld is, is in hierdie inligtingstuk ingesluit nie. Sou jou algemene gesondheid verslag of indien jy enige onaangename gevolge ondervind terwyl jy **NIOSAR** neem, raadpleeg asseblief jou dokter, apteker of ander gesondheidsorgwerker vir advies.

Indien enige van die volgende gebeur, hou op om **NIOSAR** te gebruik en vertel jou dokter onmiddellik of gaan na die ongevalle afdeling van jou naaste hospitaal:
- swelling van die hande, voete, enkels, gesig, lippe en mond of keel, wat dit moeilik kan maak om te sluk of asem te haal.
- uitslag of jeuk

Hierdie is alles baie ernstige newe-effekte. Indien jy dit het, het jy moontlik 'n ernstige reaksie op **NIOSAR** gehad. Jy mag dalk dringende mediese aandag of hospitalisasie benodig.
Vertel vir jou dokter onmiddellik of gaan na die ongevalle afdeling van jou naaste hospitaal indien jy enige van die volgende opmerk:
- kortasem, moeilike asemhaling wanneer jy lê, swelling van die voete of bene (tekens van hartversaking).
- erge blase op die vel (blasige dermatitis).

Hierdie is alles ernstige newe-effekte. Jy mag moontlik dringende mediese aandag benodig.

Vertel vir jou dokter indien jy enige van die volgende waarneem:
Gereeld:
- duiseligheid.
- lae bloeddruk met of sonder simptome soos duiseligheid en floute wanneer jy opstaan.
- verminderde nierfunksie (tekens van renale inkorting).

Minder gereeld:
- skielike verlies van bewussyn (sinkopee),
- duiseligheid
- draai sensasie (vertigo),
- ernstig verminderde nierfunksie (tekens van akute nierversaking),
- hartversaking
- spierspasmas, abnormale hartritme (tekens van hiperkalemie),
- hoofpyn, hoes, seer keel, hooikoors, ontsteekte sinusse
- maagpyn, naarheid, diarree.
- moegheid, swakheid.
- slaaploosheid
- lae seksdrang

Frekwensie onbekend:
- allergiese reaksies met uitslag, jeuk en galbulte; simptome van koors, geswelde gewrigte en gewrigspyn, spierpyn, geswelde limfknope en/of griepagtige simptome kan voorkom (tekens van serumsiekte).
- pers-rooi kolle, koors, jeuk (tekens van inflammasie van bloedvate ook genoem vaskulitis),
- ongewone bloeding of kneusing (tekens van trombositopenie),
- spierpyn (mialgie),
- koors, seer keel of mondsere as gevolg van infeksies (simptome van **lae** vlak van witbloedselle ook genoem neutropenie),
- vermindering in die hemoglobienvlak en vermindering in die persentasie van rooibloedselle in die bloed (wat in ernstige gevalle, tot bloedarmoede kan lei),
- toename in die kaliumvlak in die bloed (wat spierspasmas, abnormale hartritme in ernstige gevalle kan veroorsaak),
- verhoging van lewerfunksiewaardes (wat leverskade kan aandui) insluitend 'n toename van bilirubien in die bloed (wat geel vel en oë in ernstige gevalle kan veroorsaak),
- toename in bloedureumstikstofvlak en toename in serumkreatinienvlak (wat abnormale nierfunksie kan aandui),
- lae natriumvlak in die bloed (wat moegheid, verwarring, spiertrekkings en/of stuiptrekkings in ernstige gevalle kan veroorsaak).

Lig assebliefjou dokter of apteker in indien jy enige newe-effek ervaar wat nie in hierdie inligtingstuk genoem word nie.

Aanmelding van newe-effekte
Indien jy newe-effekte kry, praat met jou dokter, apteker of verpleegkundige.
Jy kan ook newe-effekte aan SAHPRA rapporteer via die "8.04 Adverse Drug Reaction Reporting Form". wat aanlyn gevind kan word onder SAHPRA se publikasies: https://www.sahpra.org.za/.
Deur newe-effekte aan te meld kan jy help om meer inligting beskikbaar te stel aangaande die veiligheid van **NIOSAR.**

5. Hoe om NIOSAR te bewaar

Bewaar alle medisyne buite bereik van kinders.
Bewaar by of bobaie 25°C. (Kamertemperatuur). Geen afwyking word toegelaat nie.
Hou die blister in die buitenste karton totdat dit benodig word vir gebruik.
Hou die houer dig gesluit.
Moet nie in die badkamer bêre nie.
Moet nie na die vervaldatum, wat aangebring is op die blister/etiket/karton/bottel, gebruik nie.
Neem alle ongebruikte medisyne terug na jou apteker.
Moet nie ongebruikte medisyne in afvoerpype of rioolsleisels (bv. toilette) gooi nie.

6. Inhoud van die pak en ander inligting

Wat NIOSAR bevat
- Die aktiewe bestanddeel is Valsartan.
- Die ander bestanddele is mikrokristallyne sellulose, krospovidoon, anhidriese kolloïdale silika, magnesiumstearaat.
- Die filmbedekking bevat hipromellose, poliëtileenglikol 8 000, talk, titaniumdioksied (C.I.nr. 77891) rooi ysteroksied (C.I.nr. 77491), geel ysteroksied (C.I.nr. 77492), swart ysteroksiek (C.I.nr. 77499).

Hoe NIOSAR lyk en inhoud van die pak
NIOSAR 40 mg
Geel, ovaalvormige, bikonvekse, filmbedekte tablette, gedruk met "L" en "12" aan weerskante van die keeplyn aan die een kant, en glad op die ander kant.
NIOSAR 80 mg
Ligrooi, ovaalvormige, bikonvekse, filmbedekte tablette, gedruk met "L13" aan die een kant, en glad op die ander kant.
NIOSAR 160 mg
Ligbruin, ovaalvormige, bikonvekse, filmbedekte tablette, gedruk met "L14" aan die een kant, en glad op die ander kant.
NIOSAR 320 mg
Pers, ovaalvormige, bikonvekse, filmbedekte tablette, gedruk met "L15" aan die die een kant en glad op die ander kant.

Inhoud van die pak:
1) Stulpverpakking:
Tablette word in 'n stulpverpakking verpak, wat 'n deurskynige plastiek boonste en aluminiumfoielle nagkant het, verpak in 'n voorafgedrukte karton.
Verkpakkingsgrootte sluit 28's en 30's tablette in.

2) HDPE houer verpakking:
NIOSAR 40 mg:
Tablette word verpak in 40 ml wit ronde houer met kinderbestande sluiting en verpak in buitenste karton.
NIOSAR 80 mg:
Tablette word verpak in 40 ml wit ronde houer met kinderbestande sluiting en verpak in buitenste karton.
NIOSAR 160 mg:
Tablette word verpak in 75 ml wit ronde houer met kinderbestande sluiting en verpak in buitenste karton.
NIOSAR 320 mg:
Tablette word verpak in 150 ml wit ronde houer met kinderbestande sluiting en verpak in buitenste karton.
Verkpakkingsgrootte sluit in 30's tablette vir 40 mg en 90's tablette vir 80 mg, 160 mg en 320 mg.
Nie alle verpakkings en verpakkingsgroottes word noodwendig bemark nie.

Houer van die Registrasiesertifikaat
MACLEODS PHARMACEUTICALS SA (Edms) Bpk
Kantoorblok 1, Bassonia Estate Kantoorpark (Oos),
Cussonia Weg 1, Bassonia Rock, Uitbr. 12,
Alberton, Suid Afrika

Hierdie inligtingstuk was hersien in
30 NOVEMBER 2021

Registrasienommers
NIOSAR 40 mg: 47/7.1.3/0683
NIOSAR 80 mg: 47/7.1.3/0684
NIOSAR 160 mg: 47/7.1.3/0685
NIOSAR 320 mg: 47/7.1.3/0686

435 mm

PACKAGING RESEARCH & DEVELOPMENT

MACLEODS

Restricted Circulation

(Front Page)

ARTWORK / PRINTPROOF APPROVAL FORM

1. Product: NIOSAR 40/80/160/320 mg (Valsartan Tablets 40/80/160/320 mg)	
2. Country: South Africa (Private Market)	3. Packaging component: Patient Information
4. No. of Colours: 1 Colour	5. Pantone Shade No.: Black
6. Specification: 40 gsm bible paper	
7. Machine Layout No.: NA	8. Dimensions: 470 (L) x 435 (W) mm
9. Design / Style: NA	10. Item code No.: PM03915101
11. Artwork has been made: Actual Size	12. Pharma code No.: 32302 mini (4thicks, 1thin, 1thick, 3thins, 5thicks)
13. Barcode/NDC No: NA	14. Supersedes Item code No: NA
15. Revision No: 00	16. A/W File name:Y:\Valsartan\SA Private Market\01\NIOSAR PI & PIL - PM03915101.cdr
Approved By:	17. Location: Daman

PRD	M.A. HOLDER	RAD	QC	PRODN	QA
07/12/22	Vanita Rajool	07/12/22	08/12/22	08/12/22	09/12/22

Note: 1. To follow overleaf checklist for approval of Artwork / Print proof.

Instructions to Vendor :

1. Before processing, please ensure First pull out / Commercial supply should match with approved Artwork with respect to Design, Size, Fonts & Text.
2. Print proof to represent full printing area with Station Numbers.

FRM/CQA/021/04-01

Reason for revision :	Item code	Artwork Release Date	Artwork Implementation Date
1) New Artwork for South Africa (Private Market)	PM03915101		