PROFESSIONAL INFORMATION FOR TRINRALIN 10, 25, 50 & 100

SCHEDULING STATUS

S3

1 NAME OF THE MEDICINE

TRINRALIN 10 (Tablets)

TRINRALIN 25 (Tablets)

TRINRALIN 50 (Tablets)

TRINRALIN 100 (Tablets)

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

TRINRALIN 10: Each tablet contains hydralazine hydrochloride 10 mg

TRINRALIN 25: Each tablet contains hydralazine hydrochloride 25 mg

TRINRALIN 50: Each tablet contains hydralazine hydrochloride 50 mg

TRINRALIN 100: Each tablet contains hydralazine hydrochloride 100 mg

Contains sugar: Lactose anhydrous, mannitol

TRINRALIN 10: Contains 82,62 mg mannitol.

TRINRALIN 25: Contains 140,07 mg lactose anhydrous.

TRINRALIN 50: Contains 280,14 mg lactose anhydrous.

TRINRALIN 100: Contains 314,30 mg lactose anhydrous.

For full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Tablets.

TRINRALIN 10: Orange coloured, circular, biconvex tablets, debossed "10" on one side and plain on other side.

TRINRALIN 25: Orange coloured, circular, flat bevel edged tablets, debossed ‘25’ on one side and plain on other side.

TRINRALIN 50: Orange coloured, circular, flat bevel edged tablets, debossed ‘50’ on one side and plain on other side.

TRINRALIN 100: Orange coloured, circular, flat bevel edged tablets, debossed ‘100’ on one side and plain on other side.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

TRINRALIN is indicated for the treatment of hypertension.

4.2 Posology and method of administration

Posology

The usual oral dose is 100 mg to 200 mg per day, starting with 10 mg or 20 mg two to four times daily. This is increased gradually until the desired effect is obtained or unacceptable side effects develop. The dose should not exceed 300 mg per day.

Special populations

Reduced doses of hydralazine should be given to patients who are slow acetylators.

Hypotension may occur during anaesthesia in patients being treated with hydralazine.

Paediatric population

No data are available.

Method of administration

TRINRALIN is for oral use.

4.3 Contraindications

TRINRALIN is contraindicated in:

- Hypersensitivity to hydralazine or to any of the excipients of TRINRALIN (see section 6.1).

- Patients with tachycardia.
- Used with caution in patients with a history of coronary disease.

4.4 Special warnings and precautions for use

Chronic administration of hydralazine, particularly in doses of 400 mg or more per day, can produce an acute rheumatoid state. A syndrome indistinguishable from disseminated lupus erythematosus, including glomerulonephritis, may develop. The symptoms regress after hydralazine is discontinued but relatively long-term treatment with adrenocorticosteroids (steroids) may be required.

Reduced doses of hydralazine should be given to patients who are slow acetylators and women.

Myocardial stimulation produced by hydralazine can cause anginal attacks and ECG changes of myocardial ischemia. Hydralazine must be used with caution in patients with suspected coronary artery disease.

The “hyperdynamic” circulation caused by hydralazine may accentuate specific cardiovascular inadequacies. For example, hydralazine may increase pulmonary artery pressure in patients with mitral valvular disease.

Postural hypotension may result from hydralazine but is less common than with ganglionic blocking medicines. It should be used with caution in patients with cerebral vascular accidents.

In hypertensive patients with normal kidneys who are treated with hydralazine, there is evidence of increased renal blood flow and a maintenance of glomerular filtration rate. Hydralazine should be used with caution in patients with advanced renal damage.

Hypotension may occur during anaesthesia in patients being treated with hydralazine.

Adrenaline should not be given to antagonise the hypotensive effects of hydralazine since it enhances the cardiac-accelerating effects.

Caution should be observed if hydralazine is administered concurrently with monoamine oxidase inhibitors or tricyclic antidepressants (see section 4.5).

The hypotensive effects of hydralazine may be enhanced by thiazide diuretics and by β-adrenergic blocking medicines which may also diminish the cardiac-accelerating effects.

Peripheral neuritis, evidenced by paraesthesia, numbness, and tingling, has been observed.

Laboratory Tests

Complete blood counts and antinuclear antibody titer determinations are indicated before and periodically during prolonged therapy with hydralazine even though the patient is asymptomatic. These studies are also indicated if the patient develops arthralgia, fever, chest pain, continued malaise, or other unexplained signs or symptoms.

A positive antinuclear antibody titer requires that the medical practitioner carefully weigh the implications of the test results against the benefits to be derived from antihypertensive therapy with hydralazine.

Blood dyscrasias, consisting of reduction in haemoglobin and red cell count, leukopenia, agranulocytosis, and purpura, have been reported. If such abnormalities develop, therapy should be discontinued.

Excipients with known effect

TRINRALIN contains lactose. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine

Paediatric population

The safety of TRINRALIN for use in children has not been established.

4.5 Interaction with other medicines and other forms of interaction

The following medicine enhance the hypotensive effects of hydralazine:

- Other antihypertensives (diuretics, ACE inhibitors, calcium channel blockers, vasodilators)
- Anaesthetics
- Tricyclic antidepressants

- Major tranquillisers
- Nitrates or drugs exerting central depressant actions (including alcohol)

MAO inhibitors and tricyclic antidepressants should be used with caution in patients receiving hydralazine.

When other potent parenteral antihypertensive medicines, such as diazoxide, are used in combination with hydralazine, patients should be continuously observed for several hours for any excessive fall in blood pressure. Profound hypotensive episodes may occur when diazoxide injection and hydralazine are used concomitantly.

4.6 Fertility, pregnancy and lactation

The safety of hydralazine for use during pregnancy and lactation have not been established.

4.7 Effects on ability to drive and use machines

TRINRALIN has no or negligible influence on the ability to drive and use machines. However, undesirable effects may occur (e.g. allergic reaction, dizziness, convulsions), which may influence the ability to drive and use machines (see section 4.8).

4.8 Undesirable effects

a. Summary of the safety profile

Adverse reactions with hydralazine are usually reversible when dosage is reduced. However, in some cases it may be necessary to discontinue use. Common side effects are headache, anorexia, nausea, vomiting, diarrhoea, palpitations, tachycardia, angina pectoris.

b. Tabulated summary of adverse reactions

System Organ Class	Frequency	Undesirable effect
Blood and the lymphatic system disorders	Less frequent	Blood dyscrasias, consisting of reduction in haemoglobin and red cell count, leukopenia, agranulocytosis, purpura, lymphadenopathy; splenomegaly, eosinophilia
Metabolism and nutrition disorders	*Frequent*	Anorexia
Nervous system disorders	*Frequent*	Sweating, severe headache
	Less frequent	Peripheral neuritis, evidenced by paraesthesia, numbness, and tingling, tremors; muscle cramps; chills, fever, flushing, psychotic reactions characterized by depression, disorientation, or anxiety
Eye disorders	*Less frequent*	Conjunctivitis, lacrimation
Ear and labyrinth disorders	*Less frequent*	Vertigo, dizziness
Cardiac disorders	*Frequent*	Tachycardia, palpitations, angina
	Less frequent	Hypotension, paradoxical pressor response, oedema
Respiratory, thoracic and mediastinal disorders	*Frequent*	Nasal congestion
	Less frequent	Dyspnoea and pleural pain

System Organ Class	Frequency	Undesirable effect
Gastrointestinal disorders	*Frequent*	Nausea, vomiting, diarrhoea
	Less frequent	Constipation, paralytic ileus
Hepato-biliary disorders	*Frequency unknown*	Hepatitis
Skin and subcutaneous tissue disorders	*Less frequent*	Rash, urticaria, pruritus
Renal and urinary disorders	*Less frequent*	Proteinuria, haematuria sometimes associated with glomerulonephritis
	Frequency unknown	Acute renal failure, urinary retention

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 "**6.04 Adverse Drug Reactions Reporting Form**", found online under SAHPRA's publications:

https://www.sahpra.org.za/Publications/Index/8

4.9 Overdose

Symptoms: Tachycardia, palpitations, severe headache. anorexia, nausea, vomiting, postural hypotension, lacrimation. nasal congestion and peripheral neuritis.

Treatment for tachycardia and relative hypovolaemia may be indicated.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

A 7.1.3 Other hypotensives

The major action of hydralazine is direct relaxation of vascular smooth muscle with a greater

effect on arterioles than on veins. Therefore, in adequate doses it decreases arterial blood pressure, diastolic often more than systolic, and peripheral vascular resistance, and increases heart rate, stroke volume, and cardiac output. The preferential dilatation of arterioles as compared to veins, minimises postural hypotension and promotes the increase in cardiac output. The latter may limit the reduction in mean blood pressure produced by the drug. The peripheral vasodilatation is widespread but not uniform. Glomerular filtration, renal tubular function, and urine volume are not consistently affected; however, in common with many other hypertensive medicines, hydralazine can produce sodium retention and decreased urine volume. Hydralazine usually increases plasma renin activity. Vascular resistance in the cutaneous and muscle beds may decrease, but this is usually in parallel with the fall in blood pressure and blood flow does not increase.

Effects of hydralazine on organs other than those of the cardiovascular system are minor and variable.

5.2 Pharmacokinetic properties

Hydralazine is rapidly absorbed after oral administration, and peak plasma levels are reached at 1 to 2 hours. Plasma levels of apparent hydralazine decline with a half-life of 3 to 7 hours. Binding to human plasma protein is 87%. Plasma levels of hydralazine vary widely among individuals. Hydralazine is subject to polymorphic acetylation; slow acetylators generally have higher plasma levels of hydralazine and require lower doses to maintain control of blood pressure. Hydralazine undergoes extensive hepatic metabolism; it is excreted mainly in the form of metabolites in the urine.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Lactose anhydrous

Microcrystalline cellulose

Mannitol (TRINRALIN 10)

Magnesium stearate (TRINRALIN 10)

Sodium starch glycolate

Sunset yellow Lake

Stearic acid

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

2 years.

6.4 Special precautions for storage

Store at or below 25 °C. Protect product from moisture and light.

KEEP OUT OF REACH OF CHILDREN

6.5 Nature and contents of container

100, 500 or 1000 tablets packed in white, opaque HDPE container with a white, opaque polypropylene closure and a cotton coil filler.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal of a used medicine or waste materials derived from such medicine and other handling of the product

No special requirements.

7 HOLDER OF CERTIFICATE OF REGISTRATION

Strides Pharma SA (Pty) Ltd

106 16th Road

Midrand,

1686

8 REGISTRATION NUMBER(S)

TRINLANIN 10: 55/7.1.3/0890.889

TRINLANIN 25: 54/7.1.3/0820.817

TRINLANIN 50: 54/7.1.3/0821.818

TRINLANIN 100: 54/7.1.3/0822.819

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 06 June 2022

10 DATE OF REVISION OF THE TEXT