SCHEDULING STATUS

S2

1. NAME OF THE MEDICINE

EFFORTIL® 10 mg/1 ml injection

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 1 ml ampoule contains etilefrine hydrochloride 10 mg.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

A clear colourless solution.

4. CLINICAL PARTICULARS

4.1. Therapeutic Indications

To correct hypotension in:

a) circulatory failure

b) during anaesthesia

c) post-operatively

4.2. Posology and method of administration

Posology

EFFORTIL can be administered as intravenous injection or drip infusion, subcutaneously and intramuscularly.

The recommended doses are as follows:

Children under 1 year - ½ to 1 ampoule (10 mg) daily

4 years - up to 1½ ampoules daily

8 years - 1 to 2 ampoules daily

13 years - 1½ to 3 ampoules daily

Adults - 3 to 6 ampoules daily

For infusion physiological saline solution, lactated Ringer's solution, 5 % glucose solution or 10 % xylitol solution without any further additives should be used.

4.3. Contraindications

- Hypersensitivity to the active substance (etilefrine) or to any of the excipients listed in section 6.1.
- Thyrotoxicosis
- Phaeochromocytoma
- Narrow-angle glaucoma
- Prostatic hypertrophy or prostatic adenoma with urinary retention
- Hypertension
- Coronary heart failure
- Hypertrophic obstructive cardiomyopathy
- Hypotensive dysregulation (produce for a patient a hypertensive reaction upon standing)
- The first trimester of pregnancy (see section 4.6)
- Lactation (see section 4.6)
- Decompensated heart failure
- Stenosis of the heart valves or central arteries

4.4. Special warnings and precautions for use

Stenosis of the heart valves or central arteries must be ruled out as a cause of hypotension before starting treatment with EFFORTIL.

Caution should be exercised in patients with tachycardia, cardiac arrhythmias or severe cardiovascular disorders, diabetes (see section 4.5) or hyperthyroidism.

The product can cause positive results in athlete doping tests.

4.5. Interaction with other medicines and other forms of interaction

- The effects of EFFORTIL may be enhanced by concomitant use of guanethidine, mineralocorticoids, reserpine, thyroid hormones, other sympathomimetics or any substance with sympathomimetic activity such as tricyclic antidepressants, MAO inhibitors, antihistamines.
- Halogenated aliphatic hydrocarbons in inhalational anaesthetics and cardiac glycosides in higher doses may enhance the effects of sympathomimetic agents on the heart and thus lead to the development of cardiac arrhythmias.
- Dihydroergotamine increases the enteral absorption of EFFORTIL and thereby enhances its action.
- Atropine may lead to an enhanced effect of EFFORTIL and to an increased heart rate.
- Adrenergic blocking agents (α-blockers and β-blockers) may partially or completely abolish the effects of etilefrine. Treatment with β-blockers can induce reflex bradycardia.
- The blood sugar lowering effect of antidiabetic medication may be decreased (see section 4.4).

4.6. Fertility, pregnancy and lactation

Pregnancy

EFFORTIL is contraindicated during the first trimester of pregnancy (see section 4.3). Safety of its use during the second and third trimesters has not yet been established.

EFFORTIL may impair uteroplacental perfusion and cause uterine relaxation.

Breastfeeding

Entering of the drug into breast milk cannot be excluded, therefore EFFORTIL should not be administered during lactation (see section 4.3).

Fertility

No studies on the effects on human fertility have been conducted.

4.7. Effects on ability to drive and use machines

No studies on the effects on the ability to drive and use machines have been performed. However, patients should be advised that they may experience undesirable effects such as dizziness during treatment.

Therefore, caution should be recommended when driving or operating machinery. If patients experience the above-mentioned side effects, they should avoid potentially hazardous tasks such as driving or operating machinery.

4.8. Undesirable effects

Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness: Very common (≥ 1/10); common (≥ 1/100 to < 1/10); uncommon (≥ 1/1 000 to < 1/100); rare (≥ 1/10 000 to < 1/1 000); very rare (< 1/10 000); not known (cannot be estimated from the available data).

Immune system disorders

Not known: Hypersensitivity (allergic reaction)

Psychiatric disorders

Uncommon: Anxiety, insomnia

Nervous system disorders

Common: Headache, a sensation of pressure in the head

Uncommon: Restlessness, dizziness, tremor

Cardiac disorders

Uncommon: Tachycardia, palpitations, cardiac arrhythmia

Not known: anginal pain (angina pectoris), unwanted increase in blood pressure

Gastrointestinal disorders

Uncommon: Nausea

General disorders and administration site conditions

Not known: Sweating (hyperhidrosis}

The dose of EFFORTIL should be reduced in patients experiencing these symptoms.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of EFFORTIL is important. It allows continued monitoring of the benefit/risk balance of EFFORTIL. Healthcare 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, or to the Pharmacovigilance Unit at PHARMACO at 011 784 0077 (Tel).

4.9. Overdose

Symptoms

Acute overdosage or excessively rapid intravenous injection intensifies the adverse effects previously described. In addition, agitation and vomiting may occur.

In babies and small children, overdosage may cause central respiratory paralysis and coma.

Treatment

Symptomatic and supportive treatment should be given as appropriate. Intensive care measures should be taken in cases of severe overdosage. Symptoms which are due to β_1-sympathomimetic activity may be treated with β -blockers administered in accordance with the usual therapeutic guidelines for this class of medicines.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Etilefrine hydrochloride belongs to the medicine class A 5.1 Adrenomimetics (sympathomimetics).

Mechanism of action

EFFORTIL in pharmacological terms is regarded as a sympathomimetic. Recent investigations allow for a more precise description as a cardio-selective drug. This term deserves some explanation: EFFORTIL has a mild stimulating effect on peripheral α-adrenoceptors (approximately 1/10 of that of noradrenaline), a mild stimulating effect of β_2-adrenoceptors, and a prominent effect on β_1-adrenoceptors.

The pharmacologically assessed action on adrenoceptors results in a number of typical cardiovascular changes. They are: increase in venous return, increase in stroke volume and cardiac output, unchanged heart rate, slight drop in peripheral arterial resistance, relaxation in precapillary sphincters and increase in transcapillary flow. By the same token, the circulation time is shortened.
The combination of the above cardiovascular actions causes improved tissue perfusion.
Based on the above considerations, EFFORTIL can be used in all conditions where a decreased tissue perfusion is assumed. One of the leading symptoms of reduced tissue perfusion is a drop in blood pressure.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Water for injection.

6.2. Incompatibilities

EFFORTIL should not be mixed with levulose solutions or hydroxyethyl starch (HES/HAES) solution due to incompatibilities.
This medicine must not be mixed with other medicines except those mentioned in section 6.6.

6.3. Shelf life

36 months
From a microbiological point of view, the prepared infusion solution should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user.

6.4. Special precautions for storage

Store at or below 30 °C in a dry place and protect from light.
For storage conditions after dilution, see section 6.3.
Keep out of reach of children.

Do not use this medicine after the expiry date printed on the label.

6.5. Nature and contents of container

Amber glass ampoules containing 1 ml of solution in packs of 5.

6.6. Special precautions for disposal and other handling

For infusion physiological saline solution, lactated Ringer's solution, 5 % glucose solution or 10 % xylitol solution without any further additives should be used.

7. HOLDER OF THE CERTIFICATE OF REGISTRATION

Pharmaco Distribution (Pty) Ltd

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Sandton 2196, Gauteng

South Africa

Ethical assistance Line: +27 (0) 784 00 77

8. REGISTRATION NUMBER(S)

F/5.1/197

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

16 April 1974

10. DATE OF REVISION OF THE TEXT

27 May 2022

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