

New Zealand Datasheet

1 PRODUCT NAME

FIBROVEIN 3.0%, 1.0%, 0.5% and 0.2% intravenous injection

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Sodium Tetradecyl Sulphate 3.0%, 1.0%, 0.5% and 0.2% intravenous injection

Contains benzyl alcohol 20mg/ml. For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Solution for injection.

Clear, colourless, sterile solution.

pH 7.5 – 7.9.

Osmolarity 247 – 273 mOsm/kg.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Fibrovein 3% and 1%: For the treatment of varicose veins of the leg by injection sclerotherapy.

Fibrovein 0.5%: For the treatment of varicose veins and venous flares of the leg by injection sclerotherapy.

Fibrovein 0.2%: For the treatment of minor venules and spider veins (venous flares) by injection sclerotherapy.

4.2 Dose and method of administration

Route of Administration

For intravenous administration into the lumen of an isolated segment of emptied vein followed by immediate continuous compression.

Recommended doses and dosage schedules:

Adults

Fibrovein 3.0%: 0.5 to 1.0ml of 3.0% Fibrovein injected intravenously at each of 4 sites (maximum 4ml).

Fibrovein 1.0%: 0.25 to 1.0ml of 1.0% Fibrovein injected intravenously into the lumen of an isolated segment of emptied superficial vein, followed by immediate compression. A maximum of 10 sites (10ml total) may be injected during one treatment session.

Fibrovein 0.5%: 0.25 to 1.0ml of 0.5% Fibrovein injected intravenously into the lumen of an isolated segment of emptied superficial vein, followed by immediate compression. A maximum of 10 sites (10ml total) may be injected during one treatment session.

Fibrovein 0.2%: 0.1 to 1.0ml of 0.2% Fibrovein injected intravenously at each of 10 sites (maximum 10ml).

The smallest of needles (30 gauge) should be used to perform the injection, which should be made slowly so that the blood content of these veins is expelled. In the treatment of spider veins an air block technique may be used.

Children

All strengths: not recommended in children

The Elderly

As for adults.

4.3 Contraindications

- Hypersensitivity to sodium tetradecyl sulphate or to any component of the preparation and allergic conditions.
- Patients unable to walk due to any cause, bedridden patients.
- Patients with a high risk of thrombosis e.g. patients with a congenital predisposition to blood clots or with multiple risk factors such as hormonal contraceptives or hormone replacement therapy, significant obesity, smoking or extended periods of immobility
- Recent acute superficial thrombophlebitis, deep vein thrombosis or pulmonary embolism
- Recent surgery
- Local or systemic infection.
- Varicosities caused by pelvic or abdominal tumours unless the tumour has been removed
- Uncontrolled systemic disease such as diabetes mellitus, toxic hyperthyroidism, tuberculosis, asthma, neoplasm, sepsis, blood dyscrasias and acute respiratory or skin diseases
- Evolutive cancer
- Significant valvular incompetence of the deep veins
- Occlusive arterial disease
- Huge superficial veins with wide open communications to deeper veins
- Phlebitis migrans
- Acute cellulitis
- Acute infections

4.4 Special warnings and precautions for use

Fibrovein should only be administered by practitioners experienced in venous anatomy and the diagnosis and treatment of conditions affecting the venous system and familiar with proper injection technique. Thorough pre-injection assessment for valvular competence and deep vein patency must be carried out. Extreme care in needle placement and slow injection of the minimal effective volume at each injection site are essential for safe and efficient use.

Before treatment, the healthcare professional should investigate patient's risk factors and inform them about the risks of the technique. As a reminder, sclerotherapy is contraindicated in patients with high risk of thromboembolic events but should also be avoided in most situations at lower risk. Sclerotherapy is notably not recommended in patients with a history of thromboembolic events. Nevertheless, if sclerotherapy is judged necessary, preventive anticoagulation can be initiated.

Due to the risk of circulation of product, bubbles or particulates in the right heart, the presence of a PFO may enhance the occurrence of serious arterial adverse events. In patients with history of migraine with aura, serious cerebrovascular events or pulmonary hypertension, it is recommended to search for PFO before sclerotherapy. In patients with

asymptomatic but known PFO, it is recommended to use smaller volumes and avoid Valsalva manoeuvre in the minutes after injection. Use smaller volumes in patients with history of migraine.

Severe adverse local effects, including tissue necrosis, may occur following extravasation; therefore, extreme care in intravenous needle placement and using the minimal effective volume at each injection site are important.

Sclerosants must never be injected into an artery as this can cause extended tissue necrosis and may result in loss of the extremity. Injection under duplex ultrasound is recommended in order to avoid extravasations and arterial injection.

Healthcare professional should monitor the patient during and after the administration of Fibrovein. Symptoms of hypersensitivity (redness, pruritis, cough) or neurological symptoms (scotoma, amaurosis, migraine with aura, paraesthesia, focal deficit) may happen

Special care should be taken in patients with laboured breathing (bronchial asthma) or a strong predisposition to allergies (see Dosage and Administration). Emergency resuscitation equipment should be immediately available. Allergic reactions, including anaphylaxis have been reported. The possibility of an anaphylactic reaction should be kept in mind, and the physician should be prepared to treat it appropriately.

Because of the danger of thrombosis extension into the deep venous system, thorough pre-injection evaluation for valvular competency should be carried out and slow injections with a small amount (not over 2 ml) of the preparation should be injected into the varicosity. Deep venous patency must be determined by non-invasive testing such as duplex ultrasound. Venous sclerotherapy should not be undertaken if tests such as Trendelenberg and Perthes, and angiography show significant valvular or deep venous incompetence.

Healthcare professionals should see the patient again after 1 month for a control of treatment efficacy and safety, by clinical and ultrasound evaluation.

The development of deep vein thrombosis and pulmonary embolism have been reported following sclerotherapy treatment of superficial varicosities. Patients should have post-treatment follow-up of sufficient duration to assess for the development of deep vein thrombosis. Embolism may occur as long as four weeks after injection of sodium tetradecyl sulphate. Adequate post-treatment compression may decrease the incidence of deep vein thrombosis.

Extreme caution in use is required in patients with arterial disease such as severe peripheral atherosclerosis or thromboangitis obliterans (Buerger's Disease).

Special care is required when injecting above and posterior to the medial malleolus where the posterior tibial artery may be at risk.

Pigmentation may be more likely to result if blood is extravasated at the injection site (particularly when treating smaller surface veins) and compression is not used.

4.5 Interaction with other medicines and other forms of interaction

No interaction studies have been performed.

4.6 Fertility, pregnancy and lactation

Fertility

It is not known whether sodium tetradecyl sulfate affects fertility.

Use in Pregnancy

Safety for use in pregnancy has not been established. There are no or limited amount of data from the use of sodium tetradecyl sulphate in pregnant women. Animal studies are insufficient with respect to reproductive toxicity. Treatment should be postponed until after childbirth. Fibrovein should be used only when clearly needed for symptomatic relief and when the potential benefits outweigh the potential hazards to the foetus.

Use in Lactation

It is not known whether sodium tetradecyl sulphate is excreted in human milk. Caution should be exercised when used in nursing mothers.

4.7 Effects on ability to drive and use machines

A bandage and/or compression stockings may be added after treatment. This could affect the ability to drive.

4.8 Undesirable effects

The most commonly reported side effects are pain on injection urticaria, superficial thrombophlebitis and temporary skin pigmentation after treatment. Very rarely a permanent discoloration may remain along the path of the sclerosed vein segment. Ulceration may occur following extravasation of the drug. It is important to use the lowest strength that will sclerose the vein as many of the common side effects are caused by using a concentration that is too high.

Intra-arterial injection although very rare has been reported resulting in significant tissue necrosis including loss of the extremity.

The most serious side effects are anaphylactic shock and pulmonary embolism and deaths have been reported in patients receiving sodium tetradecyl sulphate.

Adverse events are listed below by system organ class and estimated frequency from published clinical data. Frequencies are defined using the following convention:

Very common $\geq 1/10$

Common $\geq 1/100$ to $< 1/10$

Uncommon $\geq 1/1000$ to $< 1/100$

Rare $\geq 1/10,000$ to $< 1/1000$

Very rare (includes isolated reports) $\leq 1/10,000$

Immune disorders	
Systemic allergic reactions e.g. anaphylactic shock, asthma, generalised hives.	Very Rare
Nervous system disorders	
Headache, migraine, local sensitivity disturbances (paraesthesias). Vaso-vagal reactions e.g. fainting, confusion, dizziness, loss of consciousness.	Very Rare
Nerve damage after extravasation of the drug	Very Rare
Weakness (hemiparesis, hemiplegia), transient ischaemic attack (TIA), palpitations.	Very Rare
Stroke	Very rare
Eye disorders	
Scotoma, scintillating scotoma.	Very rare
Vascular disorders	
Superficial thrombophlebitis, phlebitis.	Common
Matting (growth of very fine spider veins in treated area).	Uncommon
Deep vein thrombosis (mostly muscular and distal).	Very rare
Pulmonary embolism, vasculitis, circulatory collapse.	Very Rare
Distal tissue necrosis following intra-arterial injection, may lead to gangrene. Most cases have involved the posterior tibial artery above the medial malleolus. Arterial spasm can occur despite intravenous injection.	Very Rare
Respiratory disorders	
Coughing, shortness of breath, sensation of pressure/tightness in the chest.	Very rare
Gastro-intestinal disorders	
Nausea, vomiting, diarrhoea, feeling of swollen/thick tongue, dry mouth.	Very rare
Skin and subcutaneous tissue disorders	
Skin discolouration (hyperpigmentation, more rarely - haematoma & ecchymosis).	Uncommon
Local allergic and non-allergic skin reactions e.g. erythema, urticaria, dermatitis, swelling/induration.	Uncommon
Local sloughing and necrosis of skin & tissues.	Rare
General disorders	
Pain or burning (short term at the injection site).	Common
Fever, hot flushes.	Very Rare

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. Healthcare professionals are asked to report any suspected adverse reactions <https://nzphvc.otago.ac.nz/reporting/>.

4.9 Overdose

No case of systemic overdose has been reported. Using a higher concentration than recommended in small veins may lead to pigmentation and/or local tissue necrosis.

For advice on the management of overdose please contact the National Poisons Centre on 0800 POISON (0800 764766).

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Sclerosing agents for local injections, ATC code: C05BB04

Sodium tetradecyl sulphate is a sclerosing agent. Intravenous injection causes intima inflammation and thrombus formation. This usually occludes the injected vein. Subsequent formation of fibrous tissue results in partial or complete vein obliteration that may or may not be permanent.

5.2 Pharmacokinetic properties

Absorption

Fibrovein containing sodium tetradecyl sulphate is administered directly into the lumen of the isolated segment of vein/venule.

Distribution

In humans, the majority (75%) of an injected dose of radiolabelled 3% sodium tetradecyl sulphate rapidly disappeared from the empty varicose vein injection site into communicating blood vessels with rapid passage into the deep calf veins.

In rats, at 72 hours after intravenous dosing of radiolabelled sodium tetradecyl sulphate, tissue levels of radiolabel found in the sampled tissues (liver, kidney, lipid and skeletal muscle) were extremely low. Although there was some evidence of radiolabel associated with the injection site, the levels were very low.

Biotransformation

The metabolism of sodium tetradecyl sulphate has not been confirmed.

Elimination

Of an intravenously administered radiolabelled dose, 70% was recovered in the urine of rats within the first 24 hours post-dosing. At the end of the 72 hour post-dose period, 73.5% of the radiolabel had been recovered from the urine and 18.2% recovered from the faeces.

Hepatic/Renal Impairment

No pharmacokinetics studies have been performed in patients with hepatic or renal impairment.

5.3 Preclinical safety data

There are no additional data of relevance to the prescriber other than those already mentioned in other sections of the datasheet.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Benzyl Alcohol BP, Disodium Hydrogen Phosphate BP, Potassium dihydrogen phosphate, Water for injections BP.

6.2 Incompatibilities

This product is not compatible with heparin.

In the absence of compatibility studies, this medicinal product should not be mixed with other medicinal products.

6.3 Shelf life

Shelf life is 36 months (3 years) from manufacture.

Each 2ml glass ampoule is for single use only. The in-use period of each 5ml multi-dose vial is a single session of therapy and for use in the treatment of a single patient. Unused vial contents should be discarded immediately afterwards.

6.4 Special precautions for storage

Store below 25°C. Do not freeze. Keep the vial/ampoule in the outer carton in order to protect from light.

6.5 Nature and contents of container

Fibrovein 3.0%: 2ml ampoules and 5ml vials

Fibrovein 1.0%: 2ml ampoules

Fibrovein 0.5%: 2ml ampoules

Fibrovein 0.2%: 5ml vials.

2ml ampoule (Type 1 glass). Pack size 5 ampoules.

5ml vial (Type 1 glass) with a stopper (chlorobutyl) and aluminium seal with flip-off cap (polypropylene). Pack size of 5 vials.

6.6 Special precautions for disposal

The foam must be prepared just before use and administered by a physician appropriately trained in the correct generation and administration of foam.

Strict aseptic technique must be maintained while manufacturing the foam.

Manufacture of foam using the Tessari technique

To create the foam 1ml of liquid sclerosant is drawn into a sterile syringe and 3ml or 4ml of sterile air is drawn into another sterile syringe. The air is drawn through a 0.2 µm filter to ensure it is sterile. The syringes are then connected using a sterile three way tap/valve (Fig. 1).

The sclerosant/air mixture is then forced back and forth from one syringe to the other through the 3-way valve approximately 20 times to produce a smooth, consistent foam (Fig. 2&3).

The syringe containing the foam, is then removed and the vein is injected immediately (Fig. 4).

The sclerosant foam must be used within sixty seconds of production. After sixty seconds any remaining foam should be discarded. More foam should be prepared if required.

The quality of the foam should be checked before administration. It should appear homogeneous with no large bubbles visible to the naked eye.



Figure 1



Figure 2



Figure 3



Figure 4

The quality of foam depends on specific criteria:

1. The product concentration: Foam can only be prepared with concentrations of 1 to 3% sodium tetradecyl sulfate.
2. The proportion of liquid to air: Usually, this proportion is 1 volume of liquid for 3 volumes of air.
3. Number of backwards and forwards passes: The physician should follow precisely the number of movements defined for each technique.
4. Macroscopic consistency of the foam: The quality of the foam should be checked outside of the syringe before administration. The foam should be homogenous, soft and cohesive with no visible large bubbles. If large bubbles are visible, the foam should be thrown away and a new foam prepared.
5. The total time of preparation of the foam: The preparation should take around 10 seconds from the first to the last backwards and forwards movement.
6. The maximum time between preparation and injection: The sclerosant foam must be used within sixty seconds of production. After sixty seconds, any remaining foam should be discarded. More foam should be prepared if required.

Disposal

There are no special requirements for disposal.

7 MEDICINE SCHEDULE

Prescription medicine

8 SPONSOR

New Zealand Medical and Scientific Ltd
PO Box 24-138
Royal Oak
AUCKLAND
Ph: 09 259 4062
Fax: 09 259 4067

9 DATE OF FIRST APPROVAL

31 December 1969

10 DATE OF REVISION OF THE TEXT

6 April 2018

SUMMARY TABLE OF CHANGES

Section changed	Summary of new information
3.0	Inclusion of physiochemical data
4.6	Inclusion of fertility statement
4.8	Addition of reporting of adverse events
4.9	Addition of Poison Centre information
5.1	Addition of Pharmacotherapeutic group and ATC code
5.3	Addition of pre-clinical safety data
6.6	Addition of instructions for use and disposal information