Aethoxysklerol

Lauromacrogol 400 (Polidocanol)

Summary of Product Characteristics

1. Name of the medicinal product

Aethoxysklerol 2.5 mg/ml solution for injection
Aethoxysklerol 5 mg/ml solution for injection
Aethoxysklerol 10 mg/ml solution for injection
Aethoxysklerol 20 mg/ml solution for injection
Aethoxysklerol 30 mg/ml solution for injection

2. Qualitative and quantitative composition

The active substance in Aethoxysklerol is lauromacrogol 400 also known as polidocanol.

	Each ml solution for injection contains:	Each 2ml ampoule of solution contains:
Aethoxysklerol 2.5 mg/ml	2.5 mg lauromacrogol 400	5 mg lauromacrogol 400
Aethoxysklerol 5 mg/ml	5 mg lauromacrogol 400	10 mg lauromacrogol 400
Aethoxysklerol 10 mg/ml	10 mg lauromacrogol 400	20 mg lauromacrogol 400
Aethoxysklerol 20 mg/ml	20 mg lauromacrogol 400	40 mg lauromacrogol 400
Aethoxysklerol 30 mg/ml	30 mg lauromacrogol 400	60 mg lauromacrogol 400

Excipients with known effect:

All strengths contain 42 mg ethanol per ml.
All strengths contain 0.310 mg sodium per ml.
All strengths contain 0.124 mg potassium per ml.
For the full list of excipients, see section 6.1.

3. Pharmaceutical form

Solution for injection
Clear, colourless to very faintly greenish yellow sterile solution.
pH 7.0 – 8.0
Osmolality 920 – 975 mOsmol/kg

4. Clinical particulars

4.1 Therapeutic indications

Aethoxysklerol is indicated for sclerotherapy of varicose veins of the lower extremities.

4.2 Posology and method of administration

Different concentrations of Aethoxysklerol are required, depending on the type and size of the varicose veins to be treated.

If several concentrations are stated for a certain type of vein (see table below), the diameter of the vein and the patient's individual situation should be considered. In case of doubt the lower concentration should be chosen.

Depending on the degree and extent of the varicose veins, several treatments may be required.

	Aethoxysklerol Concentration					
Sclerotherapy of	2.5 mg/ml	5 mg/ml	10 mg/ml	20 mg/ml	30 mg/ml	
Telangiectasias (spider veins)	●	●				Liquid
						Microfoam
Central veins of telangiectasias	●	●	●			Liquid
						Microfoam
Reticular veins			●			Liquid
						Microfoam
Small varicose veins			●			Liquid
			●			Microfoam
Medium-sized varicose veins				●	●	Liquid
				●	●	Microfoam
Large varicose veins					●	Liquid
					●	Microfoam

Posology

Sclerotherapy of varicose veins

Generally, the dose of 2 mg lauromacrogol 400 per kg body weight per day should not be exceeded.
For a patient weighing 70 kg, a total of up to 140 mg lauromacrogol 400 can be injected. 140 mg lauromacrogol 400 are contained in:

Aethoxysklerol	2.5 mg/ml	5 mg/ml	10 mg/ml	20 mg/ml	30 mg/ml
140 mg lauromacrogol 400	56 ml	28 ml	14 ml	7 ml	4.6 ml

When applying as a sclerosing microfoam, it is recommended not to exceed the total dose of 10 ml microfoam (the sum of the liquid and air components) per session and day – irrespective of the patient's body weight and concentration of lauromacrogol 400.

Sclerotherapy of telangiectasias

Depending on the size of the area to be treated, per puncture 0.1-0.2 ml Aethoxysklerol 2.5 mg/ml or 5 mg/ml are injected intravenously.

Sclerotherapy of central veins of telangiectasias

Depending on the size of the area to be treated, per puncture 0.1-0.2 ml Aethoxysklerol 2.5 mg/ml, 5 mg/ml or 10 mg/ml are injected intravenously.

Sclerotherapy of reticular veins

Depending on the size of the varicose vein to be treated, per puncture 0.1-0.3 ml Aethoxysklerol 10 mg/ml are injected intravenously.

Sclerotherapy of small varicose veins

Depending on the size of the varicose vein to be treated, per puncture 0.1-0.3 ml liquid Aethoxysklerol 10 mg/ml are injected intravenously.
When using Aethoxysklerol 10 mg/ml microfoam, e.g. for the treatment of tributary varicose veins (collateral varices), up to 4-6 ml are injected per puncture. When treating perforating veins with microfoam up to 2-4 ml are injected per puncture.

Sclerotherapy of medium-sized varicose veins

Depending on the diameter of the varicose veins to be treated, Aethoxysklerol 20 mg/ml or 30 mg/ml is used.

Depending on the length of the segment to be treated, several injections with up to 2 ml of liquid Aethoxysklerol 20 mg/ml or 30 mg/ml per injection may be administered, without exceeding the maximum daily dose.

When using Aethoxysklerol 20 mg/ml microfoam, e.g. for the treatment of perforating or tributary varicose veins, up to 2 ml microfoam are injected per puncture. When using Aethoxysklerol 20 mg/ml or 30 mg/ml microfoam, e.g. for the treatment of the saphenous veins, up to 4 ml are injected per puncture for the small saphenous veins and up to 6 ml for the great saphenous veins.

Sclerotherapy of large varicose veins

Depending on the length of the segment to be treated, several injections with up to 2 ml of liquid Aethoxysklerol 30 mg/ml per injection may be administered, without exceeding the maximum daily dose.

When using Aethoxysklerol 30 mg/ml microfoam, e.g. for the treatment of the saphenous veins, up to 4 ml are injected per puncture for the small saphenous veins and up to 6 ml for the great saphenous veins.

Elderly population

No specific dose recommendations apply.

Paediatric population

There is no relevant use of Aethoxysklerol in the paediatric population in children or adolescents for the indication of sclerotherapy of varicose veins of the lower extremities.

Hepatic impairment/Renal impairment

No pharmacokinetic studies have been performed in patients with hepatic or renal impairment. The use of sclerotherapy should be cautious and assessed in patients with moderate hepatic or renal impairment, in whom the treatment benefit clearly outweighs the risk. Aethoxysklerol is not recommended for use in patients with severe hepatic or renal impairment.

Method of administration

Sclerotherapy of varicose veins

All injections must be given intravenously; the position of the needle should be checked (e.g. by aspiration of blood).

Strict aseptic technique must be maintained while handling Aethoxysklerol.

Aethoxysklerol is a single-use parenteral product. Once the container is opened, use immediately and discard any unused portion.

Visually inspect for particulate matter before use. Solutions that contain particulate matter should not be used.

Additionally for microfoam administration refer to the detailed instructions in section 6.6.

- *Sclerotherapy of telangiectasias*
- *Sclerotherapy of central veins of telangiectasias*
- *Sclerotherapy of reticular veins*

Injections are usually carried out in a leg placed horizontally. Smooth-moving disposable syringes are used.

For telangiectasias very fine needles (e.g. insulin needles) are used. The puncture is carried out tangentially and the injection given slowly.

Sclerotherapy of small, medium-sized and large varicose veins

Irrespective of the mode of venepuncture (in a standing patient with the cannula only or in a sitting patient with a syringe ready for injection), injections are usually carried out in a leg placed horizontally.

Smooth-moving disposable syringes are recommended for sclerotherapy as well as needles with different diameters, depending on the indication.

When using microfoam, the leg can be placed horizontally or elevated approx. 30 – 45° above the horizontal for injection. Direct puncture and injection into non-visible veins should be guided by duplex ultrasound. The needle should not be smaller than 25G.

Note:

Thrombi, which occasionally develop, are removed by stab incision and thrombus expression.

Compression treatment after injection of Aethoxysklerol

Once the injection site has been covered, a tight compression bandage or elastic stocking should be applied. After that, the patient should walk for 30 minutes, preferably within reach of the practice.

After sclerotherapy with liquid Aethoxysklerol, compression is applied immediately.

After sclerotherapy with microfoam the patient's leg is initially immobilised for 2-5 minutes. Valsalva's manoeuvre and muscle activation should be avoided during this time. Compression should not be applied immediately but 5 to 10 minutes after injection.

Compression should be applied for a few days up to several weeks, depending on the extent and severity of the varicose veins.

To make sure the bandage does not slip, especially on the thigh and conical limbs, a foam bandage support under the actual compression bandage is recommended.

4.3 Contraindications

- Known hypersensitivity to lauromacrogol 400 or any of the excipients listed in section 6.1
- Uncontrolled systemic diseases (such as diabetes melitus, toxic hyperthyroidism, tuberculosis, asthma, neoplasm, systemic infections, blood dyscrasias, acute respiratory or skin diseases)
- Immobility – inability to walk due to any cause, i.e. the patient is immobile
- Severe arterial occlusive disease (Fontaine stages III and IV)
- Thromboembolic diseases
- High risk of thrombosis (e.g. known hereditary thrombophilia or patients with multiple risk factors such as use of hormonal contraceptives or hormone replacement therapy, obesity, smoking, and extended periods of immobility)

In addition, the following contraindication applies to microfoam sclerotherapy: Known symptomatic right-to-left shunt (e.g. symptomatic patent foramen ovale (PFO)).

4.4 Special warnings and precautions for use

Aethoxysklerol should only be administered by healthcare professionals experienced in sclerotherapy and the required preparation techniques.

Sclerotherapy of varicose veins should be used with caution in the following situations:

- In patients with asymptomatic but known patent foramen ovale (PFO), it is recommended to use smaller volumes and avoid Valsalva manoeuvre in the minutes after injection
- In patients that suffered from visual or neurological symptoms (e.g. migraine) after previous microfoam sclerotherapy, it is recommended that the patients should lie down for a longer time and avoid Vaslava manoeuvre in the minutes after injection. Use smaller volumes in these patients
- Patients showing the symptoms of a fever (febrile state)
- Patients with bronchial asthma or a known strong predisposition to allergies
- When treating telangiectasias in patients with arterial occlusive disease (Fontaine stage II)

- The presence of leg oedema if it cannot be influenced by compression
- Inflammatory skin disease in the area of treatment
- Patients showing symptoms of microangiopathy or neuropathy
- Patients with reduced mobility
- Anticoagulation is not a contraindication to sclerotherapy. In general, special care should be taken in patients using anticoagulation medication

Pre-procedure evaluation

Before treatment, the healthcare professional should investigate patient's risk factors and inform them about the risks of the technique.

A thorough pre-procedure evaluation for valvular competency should be carried out as appropriate.

Sclerotherapy should not be undertaken if significant valvular incompetence is suspected following the evaluation.

Follow-up

The healthcare professional should see the patient again in the weeks after treatment to perform a clinical efficacy and safety evaluation. Patients should have post-treatment follow-up of sufficient duration to assess for the development of deep vein thrombosis. Adequate post-treatment compression may decrease the incidence of deep vein thrombosis.

Improper administration when treating varicose veins

Sclerosants must never be injected intra-arterially because this can cause severe necrosis which may necessitate amputation. A vascular surgeon must be called in immediately if any such incident occurs.

In certain body regions such as in the foot or malleolar region, the risk of inadvertent intra-arterial injection may be increased. Therefore, in these regions only small amounts should be used in low concentrations with particular care.

Adverse effects, including tissue necrosis, may occur following extravasation, therefore it is important to exercise extreme care in intravenous needle placement and use the minimal effective volume at each injection site.

Management of local toxicity after improper administration when treating varicose veins

a) Intra-arterial injection

1. Leave cannula in place; if already removed, relocate the puncture site and aspirate blood and the remaining sclerosing solution back into the syringe
2. Inject 5-10 ml of a local anaesthetic, without the addition of adrenaline
3. Start with anticoagulation e.g. by injection of 5,000 IU heparin or equivalents (if possible, into the affected artery; otherwise i.v.)
4. Pack the ischaemic leg in wadding and lower
5. Hospitalise the patient as a precaution (vascular surgery)

b) Extravenous injection

Depending on the quantity and concentration of Aethoxysklerol injected extravenously, inject 5 to 10 ml of physiological saline, if possible combined with hyaluronidase, at the application site. If the patient is in severe pain, a local anaesthetic (without adrenaline) may be injected.

Emergency measures and antidotes

Anaphylactic reactions

Anaphylactic reactions are very rare, but potentially life-threatening situations. The attending doctor should be prepared for emergency measures and have a suitable emergency kit available. Therapy with beta blockers or ACE (angiotensin converting enzyme) inhibitors may influence emergency procedures for anaphylactic shock because of their cardiovascular effects.

Stress cardiomyopathy and cardiac arrest

Stress cardiomyopathy (Tako Tsubo) and cardiac arrest have been very rarely reported following Aethoxysklerol sclerotherapy. Patients complaining of chest pain or discomfort during or after the procedure should be promptly investigated and monitored. All patients should also be made aware of this possible adverse event and advised to immediately seek medical advice in case of any symptoms.

Excipients with known effect

All Aethoxysklerol products contain:

- 5% (v/v) ethanol which may be harmful for those sufferng from alcoholism or undergoing treatment of alcoholism with Disulfiram. To be taken into account in pregnant or breast-feeding women, children and high risk groups such as patients with liver disease or epilepsy
- Potassium, but less than 1 mmol (39 mg) potassium per ampoule, i.e. essentially 'potassium-free'
- Sodium, but less than 1 mmol (23 mg) sodium per ampoule, i.e. essentially 'sodium-free'

4.5 Interaction with other medicinal products and other forms of interaction

Lauromacrogol 400 is a local anaesthetic. When combined with other anaesthetics, there is a risk of an additive effect of these anaesthetics on the cardiovascular system.

4.6 Fertility, pregnancy and lactation

Pregnancy

Safety for use in pregnancy has not been established. Studies in animals showed reproductive toxicity, but no teratogenic potential (see section 5.3).

Treatment should be postponed until after childbirth.

Aethoxysklerol should be used only when clearly needed for symptomatic relief and when the potential benefits outweigh the potential hazards to the fetus.

Breast-feeding

It is not known whether lauromacrogol 400 is excreted in human milk. Caution should be exercised when used in nursing mothers. If sclerotherapy is necessary during breast-feeding, it is advisable to suspend breast-feeding for 2-3 days.

Fertility

It is not known whether lauromacrogol 400 affects fertility.

4.7 Effects on ability to drive and use machines

No negative effects on the ability to drive and use machines are known for Aethoxysklerol.

4.8 Undesirable effects

The most commonly reported side effects are temporary in most cases and include short-term injection site pain, injection site intravaricose blood clots and temporary skin discolouration after treatment.

Local adverse reactions (e.g. necrosis), especially of the skin and of the underlying tissue (and, in rare cases, of the nerves), were observed when treating varicose veins in the leg after inadvertent injection into the surrounding tissue (paravenous injection). The risk increases with increasing Aethoxysklerol concentrations and volumes.

The most serious side effects reported in patients receiving lauromacrogol 400 are anaphylactic shock, pulmonary embolism, cerebrovascular accident, stress cardiomyopathy (Tako Tsubo) and cardiac arrest.

The adverse events are categorised according to MedDRA (Medical Dictionary for Regulatory Activities) and listed by system organ class. The frequencies seen below estimated from published data and spontaneous reports and are defined using the following convention:

- 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

Very rare: anaphylactic shock, angioedema, urticaria (generalised), asthma (asthmatic attack)

Nervous system disorders

Very rare: cerebrovascular accident (stroke, transient ischaemic attack (TIA)), hemiparesis, headache, migraine, paraesthesia (local), hypoaesthesia oral, loss of consciousness, confusional state, aphasia, ataxia, dizziness

Rare: migraine (when using sclerosing microfoam)

Eye disorders

Very rare ('rare' when using sclerosing microfoam): visual impairment (visual disturbance)

Cardiac disorders

Very rare: cardiac arrest, palpitations, stress cardiomyopathy (Tako Tsubo)

Vascular disorders

Common: neovascularisation, haematoma

Uncommon: thrombophlebitis superficial, phlebitis

Rare: deep vein thrombosis

Very rare: pulmonary embolism, syncope vasovagal, circulatory collapse, vasculitis

Respiratory, thoracic and mediastinal disorders

Very rare: dyspnoea, chest discomfort, cough

Gastrointestinal disorders

Very rare: dysgeusia, nausea, vomiting

Skin and subcutaneous tissue disorders

Common: skin hyperpigmentation, ecchymosis

Uncommon: dermatitis allergic, urticaria contact, skin reaction, erythema

Very rare: hypertrichosis (in the area of sclerotherapy)

Musculoskeletal and connective tissue disorders

Rare: pain in extremity

General disorders and administration site conditions

Common: injection site pain (short-term), injection site thrombosis (local intravaricose blood clots)

Uncommon: necrosis of skin and tissues, induration, swelling

Very rare: pyrexia, hot flush, asthenia, malaise

Investigations

Very rare: blood pressure abnormal, heart rate abnormal (tachycardia, bradycardia)

Injury, poisoning and procedural complications

Uncommon: nerve injury

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via Yellow Card Scheme. Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

4.9 Overdose

Local overdose (caused by the injected volume or concentration being too high) may cause local necrosis, especially after extravenous injection.

For management of local toxicity after improper administration when treating varicose veins refer to section 4.4 above.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: sclerosing agents for local injection, ATC code: C05BB02

Lauromacrogol 400 (also known as polidocanol) is the active ingredient of Aethoxysklerol, has world-wide well-established use for sclerotherapy treatment of varicose veins.

Both primary and secondary nonclinical pharmacodynamic studies show that the pharmacological profile of lauromacrogol 400 is characterized by its local effects on cell membranes and the associated, locally confined, damage to tissue. This pharmacodynamic activity results in the desired sclerosing effect of blood vessels if lauromacrogol 400 is administered correctly, but may cause unintended tissue damage and subsequent adverse reactions if the recommended application procedure is not followed.

Lauromacrogol 400 has a concentration and volume dependent effect on the endothelium of blood vessels and possibly additional layers of the vein wall. In the long term, the affected veins are transformed into a fibrous cord. The result of sclerotherapy is equivalent to the surgical removal of a varicose vein.

Application of compression following sclerotherapy of varicose veins compresses the damaged vein walls so that excessive thrombus formation and recanalisation of the initially formed parietal thrombus is prevented. This gives rise to the desired transformation into fibrous tissue and hence sclerosis.

The main pharmacodynamic effect of lauromacrogol 400 - the induction of tissue damage by interacting with the lipid double layer of cells - diminishes with increasing distance from the site of injection. The pharmacological action of lauromacrogol 400 is therefore considered to be locally restricted.

When converted to a microfoam, lauromacrogol 400 is very effective at treating small, medium and large varicose veins. The microfoam has more time to act compared to the liquid form, using a smaller quantity. However, additional precautions and contraindications are applicable and some adverse events are more frequent following microfoam sclerotherapy compared to liquid sclerotherapy.

5.2 Pharmacokinetic properties

Six healthy subjects received an injection of 37 mg 14C-lauromacrogol 400 as a strongly diluted solution into the great saphenous vein. The concentration-time course of lauromacrogol 400 in plasma was biphasic with a terminal elimination half-life of lauromacrogol 400 and its labelled metabolites of 4.09 h. The AUC_{∞} was 3.16 µg x h/ml and the total clearance 11.68 l/h. 89% of the administered dose was eliminated from the blood within the first 12 hours.

In another study, the plasma concentrations of parent lauromacrogol 400 molecules were determined in 6 patients with varicose veins (diameter > 3 mm) after treatment with Aethoxysklerol 30 mg/ml. The plasma half-life was 0.94-1.27 h and the AUC_{∞} 6.19-10.90 µg x h/ml. The mean total clearance was 12.41 l/h and the distribution volume 17.9 l.

5.3 Preclinical safety data

In animal experiments, Aethoxysklerol has a relatively low acute toxicity. Safety pharmacology studies showed negative chronotropic, inotropic and dromotropic effects, with a blood pressure drop. Additional proarrhythmic effects were seen when other local anaesthetics were given concomitantly. After repeated administration of Aethoxysklerol, some animals of all species investigated showed histological alterations in the intestine, adrenal glands and liver, and rabbits additionally in the kidney.

Lauromacrogol 400 caused haematuria in all species investigated. At doses of 4 mg/kg body weight/day and higher, male rats showed an increase in liver weight after daily administration on 7 consecutive days, and an increase in ALAT/GPT and ASAT/GOT activity at doses of 14 mg/kg/day and higher.

Mutagenicity

Lauromacrogol 400 was tested extensively in vitro and in vivo. All tests were negative, except one in vitro test in which lauromacrogol 400 induced polyploids in mammalian cells. However, if the medicinal product is used according to the instructions, no relevant clinical genotoxic potential is expected.

Reproduction toxicity

The daily intravenous administration of lauromacrogol 400 over several weeks or during organogenesis had no influence on male or female fertility or early embryo development in rats, and did not induce teratogenic effects in rats or rabbits; however, embryotoxic and fetotoxic effects (increased embryo/fetal mortality, reduced fetal weights) were seen in the maternal toxic dose range. When administration was restricted to intervals of 4 consecutive days during organogenesis, neither maternal toxic nor embryotoxic/fetotoxic effects occurred (rabbits). Peri- and postnatal development, behaviour and reproduction were not impaired in rats whose mothers received intravenous lauromacrogol 400 every other day during late gestation and in the lactation period. Lauromacrogol 400 crosses the placental barrier in rats.

6. Pharmaceutical particulars

6.1 List of excipients

Ethanol 96%

Potassium dihydrogen phosphate

Disodium phosphate dihydrate

Water for injections

6.2 Incompatibilities

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

6.3 Shelf life

3 years

The ampoule is intended for single use. After first opening, the medicinal product should be used immediately. Any residual amount must be discarded.

6.4 Special precautions for storage

This medicinal product does not require any special storage conditions.

6.5 Nature and contents of container

2ml ampoule (Type I glass)

	Ampoule identification Stripe colours & format
Aethoxysklerol 2.5 mg/ml	Two red
Aethoxysklerol 5 mg/ml	Two white and one red
Aethoxysklerol 10 mg/ml	One yellow and one red
Aethoxysklerol 20 mg/ml	One green and one red
Aethoxysklerol 30 mg/ml	One blue and one red and one white

6.6 Special precautions for disposal and other handling

No special requirements for disposal.

Preparation of the Microfoam

Preparation of the microfoam using the Tessari and Dual Syringe System (DSS) techniques, respectively, is described below. Other suitable techniques may also be used.

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.

The quality of microfoam depends on specific criteria:

a) **Concentration of lauromacrogol 400:** In order to obtain a very fine-bubbled and stable microfoam, a concentration of 10-30 mg/ml must be used.

b) **Proportion of liquid to gas:** In general, this proportion is 1 volume of liquid for 4 volumes of gas.

c) **Macroscopic appearance:** Observe the macroscopic appearance of the microfoam in the syringe: It must be homogenous and fine-bubbled. No unmixed liquid or gas should be visible.

d) **Maximum time between preparation and injection:** Inject the microfoam soon after preparation (within 60 seconds).

Filling of the syringes for both foam preparation methods

Note: Syringes containing siliconized components produce a less stable foam and their use should be minimised. As two sterile syringes are needed to create the foam, only the second syringe should have a rubber plunger as this will aid a smooth injection.

To create the foam 2 ml of liquid sclerosant is drawn into the first syringe (without a rubber plunger). The second syringe (with a rubber plunger) is fixed to a 0.2 µm sterile filter and 8 ml of sterile air is drawn up.

Preparation of sclerosing microfoam with Tessari technique:

The syringes are firmly connected to a sterile three-way tap/valve (Fig. 1). Foam generation is performed by mixing sclerosant and the air by moving the plungers of both syringes completely forward and backward approximately 20 times under high pressure on both syringes (Fig. 2 and 3). A smooth, consistent foam is obtained. The syringe with the rubber plunger is filled with foam and is then removed from the three-way valve. The vein is injected immediately (Fig. 4).

Preparation of sclerosing microfoam with DSS (Double Syringe System):

The syringes are firmly connected to a sterile Luer Lock female-female adapter (Fig. 5). Foam generation is performed by mixing sclerosant and the air by moving the plungers of both syringes completely forward and backward 5 times with a short, firm thumb pressure of both hands, so that the pumping must be done against a resistance (Fig. 6 and 7). This is followed by 7 quick forward and backward movements without additional pressure to get a homogenous foam. The syringe with the rubber plunger is filled with foam and is then removed from the adapter. The vein is injected immediately (Fig. 8).

7. Marketing authorisation holder

Ferndale Pharmaceuticals Ltd
Unit 740,
Thorp Arch Estate,
Wetherby,
West Yorkshire,
LS23 7FX

8. United Kingdom marketing authorisation number(s)

Aethoxysklerol	2.5 mg/ml	5 mg/ml	10 mg/ml	20 mg/ml	30 mg/ml
Authorisation number	PL20685/ 0042	PL20685/ 0039	PL20685/ 0040	PL20685/ 0043	PL20685/ 0041

9. Date of first authorisation/renewal of the authorisation

24/12/2018

10. Date of revision of the text

24/12/2018

FERNDALE
PHARMACEUTICALS

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Adverse events should be reported.
Reporting forms and information can be found at: https://yellowcard.mhra.gov.uk,
or search for MHRA Yellow Card in the Google Play or Apple App Store.
Adverse events should also be reported to Ferndale Pharmaceuticals Ltd on 01937 541122