1. DENOMINATION OF THE MEDICINE
Trombovar® 1 POUR CENT (20 mg/2 mL), solution for injection (IV) in ampoule
Trombovar® 3 POUR CENT (60 mg/2 mL), solution for injection (IV) in ampoule

2. QUALITATIVE AND QUANTITATIVE COMPOSITION
For one ampoule:
1% dosage: Sodium Tetradecyl Sulfate: 20 mg – 3% dosage: Sodium Tetradecyl Sulfate: 60 mg
Excipients: benzylic alcohol, dodeca-hydrated sodium hydrogen phosphate, concentrated phosphoric acid, water for injectable preparation.
Excipient with manifest effect: benzylic alcohol.

3. PHARMACEUTICAL FORM: Solution for injection (I.V.)

4. CLINICAL DATA
4.1. Therapeutic indications:
Sclerosis of varicose veins, œsophageal varices, sebaceous cysts, lipomas and mucoid cysts.

4.2. Method and route of administration
Intravenous route only.
It is recommended to start each session by administration a minimum test dose
1% solution is more frequently used that 3% solution.
The use of TROMBOVAR 3% must be restricted to sclerosis of large varicose veins and varicose veins resistant to treatment with TROMBOVAR 1%.
The usual dosage is 0.5 to 2 ml of injectable solution per session, at points separated by 6 to 12 cm, without exceeding the total dosage of 10 ml per session.
Injections must be repeated every week or two-weeks, while multiplying the injections points and increasing progressively the total dosage per session.

4.3. Contra-indications
- Known allergy to the sodium tetradecyl sulfate or one of the components
- Prolonged immobility
- Recent thrombosis (clot that blocks a bold vessel)
- Progressive cancer
- Known symptomatic cardiac anomaly (Patent foramen ovale)
- Cutaneous lesions (Erysipelas) or inflammation of lymphatic vessels (lymphangitis) in the area to be treated
- Children less than 3 years old, because of benzylic alcohol.

4.4. Special warnings and precautions for use
Special warnings
Any injection outside a vein may occasion severe necrosis
An intra-arterial injection is particularly serious and may result in the need for amputation.
A passage of the product or cellular debris through the right-heart being possible, a POF may facilitate arterial events. It is then recommended to search for POF, before sclerotherapy, for patients with history of cerebrovascular events, HABP or migraine with aura.
The injections must only be realised by an experienced practitioner. Ultrasound guidance is recommended.
Sclerotherapy is not recommended to the following patients with:
- history of thromboembolic events;
- high risk of thromboembolic events;
- known familial or congenital thromboembolic illness.
If sclerotherapy is deemed necessary, preventive anticoagulation treatment may be initiated.

Precautions for use
For patients with known POF but asymptomatic, it is recommended to inject smaller volumes and avoid any effort with closed glottis (Valsalva manoeuvre) during the minutes following the injection.
For migrainous patient, it is recommended to use smaller volumes.
Association with beta-blockers runs the risk to reduce compensation cardiovascular reactions in case of an anaphylactic shock.
During the minutes following the injection, watch manifestations evoking hypersensitivity (cutaneous and conjunctival red patches, itching, cough…) and neurological events (scotoma, transitory vision loss, migraine with aura, paraesthesia and focused deficit).

4.5. Interactions with other drugs and other kind of interactions: NA

4.6. Pregnancy – breast feeding:
If indication requires the treatment with Trombovar 1 or 3 POUR CENT, solution for injection, it will only be initiated after the pregnancy.

4.7. Effects on aptitude to drive vehicles and use machines: NA

4.8. Adverse events
Following adverse-events have been observed with different frequencies.

<table>
<thead>
<tr>
<th>System, organ</th>
<th>Adverse events</th>
</tr>
</thead>
<tbody>
<tr>
<td>Immune-system disorders</td>
<td>Anaphylactic shock, angio-oedema skin rash, asthma.</td>
</tr>
<tr>
<td>Nervous system disorders</td>
<td>Headaches, migraine, paraesthesia, loss of consciousness, confusional state, vertigo.</td>
</tr>
<tr>
<td>Eye disorders</td>
<td>Phosphenes, scotoma, transitory vision loss</td>
</tr>
<tr>
<td>Heart disorders</td>
<td>Palpitations</td>
</tr>
<tr>
<td>Vascular disorders</td>
<td>Neovascularisation, bruise</td>
</tr>
<tr>
<td></td>
<td>Superficial thrombophlebitis, phlebitis</td>
</tr>
<tr>
<td></td>
<td>Deep venous thrombosis</td>
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<tr>
<td></td>
<td>Lung embolism, faintness, vasovagal faint.</td>
</tr>
<tr>
<td></td>
<td>Vasculitis, leukocytoclastic vasculitis</td>
</tr>
<tr>
<td>Respiratory, thoracic and mediastinal disorders</td>
<td>Dyspnoea, tightness of the chest.</td>
</tr>
<tr>
<td>Gastrointestinal disorders</td>
<td>Dysgueusia, nausea.</td>
</tr>
<tr>
<td>Skin and subcutaneous tissue disorders</td>
<td>Cutaneous hyperpigmentation, bruise.</td>
</tr>
<tr>
<td></td>
<td>Allergic dermatitis contact urticaria, erythema.</td>
</tr>
<tr>
<td></td>
<td>Hypertrichosis (in the treated area).</td>
</tr>
<tr>
<td>General disorders and administration site conditions</td>
<td>Pain (short term) at the injection site; thrombosis at the injection site (local intra-varicose clots).</td>
</tr>
<tr>
<td></td>
<td>Induration, œdème.</td>
</tr>
<tr>
<td></td>
<td>Local reactions necrosis type at skin level and underlying tissues in particular (in few rare cases at nerve level) have been observed in the treatment of legs varices after inadvertently injection in the surrounding tissues (perivenous injection). Risk is increased with injection of higher concentrations and volumes.</td>
</tr>
<tr>
<td></td>
<td>Fever, hot flushes.</td>
</tr>
<tr>
<td>Investigations</td>
<td>Abnormal blood pressure.</td>
</tr>
<tr>
<td>Injury and poisoning</td>
<td>Nerve injury.</td>
</tr>
</tbody>
</table>

Declaration of suspected adverse events:
Declaration of suspected adverse events after the authorization of the drug is important. It allows the continuous checking of the benefits/risks ratio of the drug. Health care professionals declare all suspected adverse event through the national system of declaration: in France National Agency for Safety of drugs and health care products (ANSM) and network of Regional Centres of Pharmacovigilance - Site internet: www.ansm.sante.fr

4.9. Overdose: NA

5. PHARMACOLOGICAL PROPERTIES

5.1 pharmacodynamical properties
Pharmacological-therapeutic class:
ANTI VARICOSE VEINS THERAPEUTIC / SCLEROSING AGENT FOR LOCAL INJECTION. Code ATC: C05BB04.
Injection provokes a local destruction of endothelium, generally coming with a vasospasm, followed by a thrombus.

5.2. Pharmacokinetics Properties: NA

5.3. Preclinical safety data: NA

6. PHARMACEUTICAL DATA
6.1. **List of excipients**: see composition in point 2

6.2. **Incompatibilities**: Avoid any association in the injection.

6.3. **Shelf life**: 30 months. After opening and reconstitution: product must be immediately used.

6.4. **Particular precautions for preserving**: no particular precautions for preserving.

6.5. **Nature and content of the external packaging**: 2 ml in bottle ampoule (type I glass). Box of 5.

6.6. **Particular precautions for elimination and manipulation**: no particular must.

7. **MARKETING AUTHORISATION HOLDER**
   Laboratoire KREUSSLER Pharma - 18, Avenue Parmentier - 75011 PARIS

8. **NUMBER OF MARKETING AUTHORISATION**
   AMM 34009 491 198 0 6 (5 amp. of 2mL at 1%); AMM 34009 491 199 7 4 : (5 amp. of 2mL at 3%)

9. **DATE FOR FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION**: June 1987 / Last renewal June 2012

10. **UPDATE OF THE TEXT ON**: 21st March 2016

11. **DOSIMETRY**: NA.

12. **INSTRUCTIONS FOR RADIOPHARMACEUTICAL PREPARATION**: NA.

**CONDITIONS FOR PRESCRIPTION AND DELIVERY**: List II, Non Reimb. Soc. Sec. – Collect.

**OPERATOR**: Laboratoire Kreussler Pharma – 18, avenue Parmentier – 75011 Paris – France - Tel.: 01 58 39 35 80 – Fax: 01 43 70 21 06 – Web: www.kreussler.fr