1. **Trade name of the medicinal product**
   
   Lioton® 1000 gel

2. **Qualitative and quantitative composition**
   
   1 g of gel contains heparin 1,000 I.U.
   
   For excipients, see 6.1

3. **Pharmaceutical form**
   
   Gel

4. **Clinical particulars**

4.1 **Therapeutic indications**

   Treatment of superficial venous diseases such as varicose syndromes and their complications, phlebothrombosis, thrombophlebitis, superficial periphlebitis, varicose ulcers. Postoperative varicophlebitis; sequelae of saphenectomy.
   
   Traumas and contusions; infiltrates and local oedemas; subcutaneous haematoma. Traumas and sprains of the musculotendinous and capsuloligamentous apparatuses.

4.2 **Posology and method of administration**

   One to three applications a day, by gently applying 3 – 10 cm of gel to the affected area.

   Due to the limited experience and to the available data, it should not be used in children.

4.3 **Contraindications**

   Lioton® 1000 gel must not be used in known hypersensitivity to heparin or one of the other ingredients.

4.4 **Special warnings and special precautions for use**

   The use of Lioton® 1000 gel in the presence of haemorrhages should be closely evaluated.

   Lioton® 1000 gel should not be applied in cases of bleeding, open wounds or mucosae, nor on infection sites in case of suppurative processes.
Lioton® 1000 gel contains the excipients methyl and propyl p-hydroxybenzoate and must not be used in patients with paraben allergies.

Keep out of the reach of children!

4.5 Interaction with other medicinal products and other forms of interaction

The use of heparin can further prolong prothrombin time in patients treated with oral anticoagulants.

4.6 Pregnancy and lactation

No specific data exist on the use of the medicinal product during pregnancy and lactation.

4.7 Effects on ability to drive and use machines

Lioton® 1000 gel does not affect alertness and therefore does not exert an effect on the ability to driving vehicles or use machines.

4.8 Undesirable effects

Allergic reactions to heparin on application to the skin are very rare. However, hypersensitivity reactions such as reddening of the skin and itching, which usually disappear rapidly following withdrawal of the preparation, may occur in isolated cases.

4.9 Overdose

No overdose phenomena have been reported to date. In case of overdose, the heparin effect can be neutralised with protamine sulphate.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Antivaricose therapy, Heparins or heparinoids for topical use (ATC index C05B A03)
Experimental pharmacological data demonstrates that Lioton® 1000 gel administered by the percutaneous route exerts a marked antioedemigenic, antigranulomatous, antiexudative, antiinflammatory and anticoagulant activity.

5.2 Pharmacokinetic properties

Pharmacokinetic tests conducted in the rat have shown that heparin concentrations are detectable in the plasma for up to 24 hours after
administration, with peak levels being reached after eight hours. Excretion is predominantly renal. Cutaneous administration of Lioton® 1000 gel did not cause any alterations of coagulation parameters in man.

5.3 Preclinical safety data

Acute toxicology tests conducted in the mouse and the rat have demonstrated that Lioton® 1000 gel has a very low s.c. and i.p. toxicity (LD_{50} 2000 mg/kg). Subchronic and chronic treatment by the cutaneous route has also shown the good local and systemic tolerability of the medicinal product.

6. Pharmaceutical particulars

6.1 List of excipients

Carbomer 940, methyl p-hydroxybenzoate, propyl p-hydroxybenzoate, ethyl alcohol, orange flower oil (neroli oil), lavender oil, triethanolamine, purified water

6.2 Incompatibilities

None known

6.3 Shelf life

Five years

6.4 Special precautions for storage

No special storage conditions.

6.5 Nature and contents of container

Folding box containing 20g, 30 g, 50 or 100 g tube of gel
Not all pack sizes may be marketed.

6.6 Instructions for use and handling

No special instructions
7. **Marketing authorisation holder**

   A. MENARINI
   Industrie Farmaceutiche Riunite s.r.l.
   Via Sette Santi 3
   Florence/Italy

8. **Marketing authorisation number**

9. **Date of first authorisation/renewal of authorisation**

10. **Date of (partial) revision of the text**

   February 2003