SUMMARY OF PRODUCT CHARACHTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

PATENT BLUE V

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

PATENT BLUE V SODIUM ..... 2.50 g

per 100 ml of solution for injection

For a full list of excipients, see Section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

This medicinal product is for diagnostic use only.
Marking lymph vessels and arterial regions.
Marking sentinel nodes before biopsy in patients with operable breast cancer.

4.2. Posology and method of administration

Marking arterial regions: not more than 10 ml intra-arterially
Marking lymph vessels and the sentinel node: 1 to 2 ml subcutaneously around the tumour or areola.

4.3. Contraindications

Hypersensitivity to Patent Blue V, to any of the excipients or to triphenylmethane dyes.

This medicinal product is generally not recommended during pregnancy.

4.4. Special warnings and precautions for use

There is always a risk of hypersensitivity regardless of the route of administration and the dose administered. Patent Blue V can induce minor or major, possibly life-threatening immediate hypersensitivity reactions that can sometimes be fatal (anaphylactic shock). These reactions are often unpredictable, but occur more frequently in patients with a history of hypersensitivity reaction to Patent Blue V or triphenylmethane dyes contained in medicinal products, foods and cosmetics.

Due to the risk of major hypersensitivity reactions, resuscitation equipment must be immediately at hand, especially for patients on beta-blockers, in whom adrenaline and intravascular infusions may be less effective. Consequently, Patent Blue V must be administered only in a setting able to adequately treat these major hypersensitivity reactions.

Before administering Patent Blue V:

- Identify high-risk subjects by means of a detailed clinical interview concerning the patient’s history;
- Insert a venous catheter.

During the examination, ensure:

- Medical surveillance;
- Maintenance of a venous line;
- That resuscitation equipment and medications are immediately at hand.

After administration of Patent Blue V, the patient must be kept under observation for at least 60 minutes.

In the event of an allergic reaction, an investigation must be conducted to determine whether, among all of the medicinal products used during a surgical procedure with general anaesthesia, this reaction can be truly attributed to Patent Blue V. The result of this investigation is important when another surgical procedure is required (e.g. contralateral cancer).

All the team managing the patient must be trained in the sentinel node identification technique.

Data of the literature demonstrate improvement of the sentinel node identification rate by performing double detection with a radiopharmaceutical and a dye.

This medicine contains less than 1 mmol (23 mg) of sodium per 1 mL, meaning that it is essentially "sodium-free."

4.5. Interaction with other medicinal products and other forms of interaction

The partial pressure of oxygen measured by spectrophotometry can be transiently and falsely lowered by about 5 to 10% of baseline values, following an examination with Patent Blue V. When in doubt, arterial blood gases should be checked. Methaemoglobinaemia, measured by the same spectrophotometric method, can be falsely raised.

4.6. Pregnancy and lactation

Pregnancy
No reliable animal teratogenesis data are available.

Currently, there are no, or limited data, to evaluate a possible malformative or foetotoxic effect of Patent Blue V when it is administered during pregnancy.

Consequently, the use of this medicinal product is not recommended during pregnancy.

Breat-feeding
There are no data concerning excretion of Patent Blue V into breast milk.

4.7. Effects on ability to drive and use machines

The potential effects of Patent Blue V on the ability to drive and use machines have not been studied.

4.8. Undesirable effects

Immediate hypersensitivity reactions can occur. These reactions may comprise one or more of the following effects, either concomitantly or successively: skin, respiratory and/or cardiovascular reactions. Each of these effects can be a precursor sign of anaphylactic shock. The most frequently reported effects in a context of hypersensitivity reaction include rash, pruritus, erythema, urticaria, angioedema (such as face oedema or laryngeal oedema), bronchospasm, tachycardia, hypotension, and circulatory collapse.

A bluish discoloration of the integuments is observed after injection, which resolves over the following 24 to 48 hours. The discoloration can persist for longer in the event of lymph stasis or circulatory disorders.

Undesirable effects are given in the table below by System Organ Class and by frequency, using the following classifications: very commom (≥1/10), common (≥1/100 to 1<1/10), uncommon (≥1/1,000 to 1<1/100), rare (≥1/10,000 to <1/1,000), very rare (<1/10,000), unknown (cannot be estimated from available data).

System Organ Class	Frequency: adverse event
Immune system disorders	Unknown frequency: anaphylactic shock, hypersensitivity
Cardiac disorders	Unknown frequency: tachycardia
Vascular disorders	Unknown frequency: circulatory collapse,

	hypotension
Respiratory, thoracic and mediastinal disorders	Unknown frequency: bronchospasm
Skin and subcutaneous tissue disorders	Unkown frequency: angio-oedema, urticaria, rash, pruritus, erythema, blue discolouration of the skin
General disorders and administration site conditions	Unknown frequency: discolouration of the administration site

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.
Any suspected adverse events should be reported to the Ministry of Health according to the National Regulation by using an online form
https://sideeffects.health.gov.il /and emailed to the Registration Holder's Patient Safety Unit at:
drugsafety@neopharmgroup.com

4.9. Overdose

No case of overdose has been reported to date.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Pharmacotherapeutic group: Diagnostic agents, other diagnostic agents, ATC code: V04CX09

5.2. Pharmacokinetic properties

The dye is excreted within 24 to 48 hours, mainly in the urine, which is intensely stained, but also in the bile.

5.3. Preclinical safety data

Preclinical data derived from conventional single-dose and repeated-dose safety pharmacology and toxicology studies have not revealed any particular risk for humans.

A mutagenic effect was observed *in vitro*, at high concentrations, on a bacterial gene mutation test after metabolic activation. This effect was not confirmed on an *in vitro* gene mutation test on mammalian cells (L5178Y murine lymphoma cells), or on a micronucleus test in rats by intravenous injection of doses significantly higher than the maximum dose in humans, and therefore has limited clinical significance.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Sodium chloride, sodium phosphate dibasic, water for injection

6.2. Incompatibilities

Not applicable.

6.3. Shelf life

The expiry date of the product is indicated on the packaging materials.

6.4. Special precautions for storage

Store below 30°C protected from light.

6.5. Nature and contents of container

2 mL type I colorless glass ampoule.

6.6. Special precautions for handling and disposal

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. MANUFACTURER

Guerbet, France
BP 57400
95943 Roissy Charles De Gaulle cedex
France

8. MARKETING AUTHORISATION NUMBER(S)

060-28-27291-05

9. REGISTRATION HOLDER

Promedico Ltd,

P.O.Box 3340, Petach-Tiqva.

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