

PROFESSIONAL INFORMATION FOR

Oxiprovin®

COMPLEMENTARY MEDICINE

Health Supplement

This unregistered medicine has not been evaluated by the SAHPRA for its quality, safety or intended use.

SCHEDULING STATUS

S0

1 NAME OF THE MEDICINE

OXIPROVIN®, 140 mg capsules

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each capsule contains:

Vitis vinifera (L.) (Grape seed extract) 140 mg
(Source of oligomeric proanthocyanidins)

Sugar free.

For full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Capsules

White and clear, size no. 3 hard gelatine (bovine) capsules, filled with brown powder.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

OXIPROVIN® is a health supplement that contains grape seed extract which is a source of antioxidants (oligomeric proanthocyanidins) for the maintenance and preservation of good health and venous health.

4.2 Posology and method of administration

Posology

Adults over 18 years

For the maintenance of good health:

Take 1 capsule daily.

For times of increased demand or for venous health:

Take 2 – 3 capsules daily.

Special populations

Elderly population:

No dosage adjustment is required for this population.

Paediatric population

This product is not indicated in patients younger than 18 years (see section 4.3).

Method of administration

For oral use only.

Take with water.

4.3 Contraindications

- Hypersensitivity to the active substance, *Vitis vinifera* (L.) (grape and/or grape seed extract), or to any of the excipients listed in section 6.1.
- Anticoagulant or antiplatelet medicine (see section 4.5).
- OXIPROVIN® may be contraindicated if taken prior to surgery, as there may be an increased risk of bleeding (see section 4.4).
- Patients younger than 18 years (see sections 4.2 and 4.4)

4.4 Special warnings and precautions for use

- Patients should be informed to consult their doctor, pharmacist, or health care provider:
 - If they are pregnant or breastfeeding (see section 4.6).
 - In venous conditions, if there is inflammation of the skin, thrombophlebitis or subcutaneous induration, severe pain, ulcers, sudden swelling of one or both legs, cardiac and/or renal insufficiency.
 - For venous health use of OXIPROVIN® beyond 3 months or if symptoms worsen.
- For venous health, use for a minimum of 1 month for beneficial effects.
- Perioperative: Grape seed extracts may increase the risk of excessive bleeding and bruising if used prior to surgery. *In vitro* evidence suggests that grape extracts can decrease platelet aggregation. Discontinue at least 2 weeks prior to elective surgical procedures.

Paediatric population

OXIPROVIN® is not recommended for use in patients younger than 18 years.

4.5 Interaction with other medicines and other forms of interaction

No interaction studies have been performed.

The following interactions with other medicines may be possible:

- Grape extracts may have antiplatelet effects and may increase the risk of bleeding if used with anticoagulant/antiplatelet medicine.
- OXIPROVIN® could influence the levels of the following liver enzymes: Cytochrome P450 2D6 (CYP2D6), Cytochrome P450 2E1 (CYP2E1), Cytochrome P450 3A4 (CYP3A4), and Cytochrome P450 2C9 (CYP2C9). Although no interactions have been reported, the use of OXIPROVIN® together with medicines that are also metabolised with the same pathway should be discussed with and monitored by a doctor or relevant health care provider.
- OXIPROVIN® when used over a long period may decrease the effects of midazolam.

4.6 Fertility, pregnancy and lactation

Pregnancy

The safety of OXIPROVIN® during pregnancy has not been established. Consult a relevant health care provider prior to use if you are pregnant (see section 4.4).

Breastfeeding

The safety of OXIPROVIN® during lactation has not been established. Consult a relevant health care provider prior to use if you are breastfeeding (see section 4.4).

Fertility

Fertility studies have not been performed.

4.7 Effects on ability to drive and use machines

No studies on the effect on the ability to drive and use machines have been performed.

It is not always possible to predict to what extent OXIPROVIN® may affect mental and/or physical ability to perform or execute tasks or activities requiring mental alertness, judgment and/or sound coordination and vision. Patients should ensure that they do not engage in the above activities until they are aware of the measure to which OXIPROVIN® affects them.

4.8 Undesirable effects

a. Summary of safety profile

Orally, grape seed extract is generally well tolerated.

b. Tabulated list of adverse reactions

System Organ Class	Frequency	Adverse reactions
Immune system disorders	Frequency unknown	Hypersensitivity or allergic reactions (e.g., itching, rash, urticaria)
Nervous system disorders	Less frequent	Headache
Respiratory, thoracic and mediastinal disorders	Less frequent	Sore throat, cough, allergic rhinitis, nasopharyngitis
Gastrointestinal disorders	Less frequent	Abdominal pain, nausea, diarrhoea
Musculoskeletal, connective tissue and bone disorders	Less frequent	Joint pain, lumbago

Above reactions have been reported with use of grape seed extract, but these effects occur at rates similar to placebo.

c. Description of selected adverse reactions

Adverse effects are more likely to occur at doses above the tolerable upper intake.

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. Health care providers are asked to report any suspected adverse reactions to SAHPRA via the "6.04 Adverse Drug Reaction Reporting Form", found online under SAHPRA's publications: <https://www.sahpra.org.za/Publications/Index/8>

4.9 Overdose

In overdose, side effects can be precipitated and/or be of increased severity (see section 4.8).

Treatment of overdose should be symptomatic and supportive.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

D34.8 Polyphenols (including Bioflavonoids)

Mechanism of action

Antioxidant effects: Free radical-scavenging activity.
Other mechanisms of action are known.

Pharmacodynamic effects

Grape seed extract contains antioxidants and supports venous health.

5.2 Pharmacokinetic properties

Absorption:

Proanthocyanidins and flavonoids from grape seed extract is absorbed and distributed into serum within two to three hours of ingestion. Oligomeric proanthocyanidins (OPCs) are poorly absorbed in the human small intestine.

Distribution:

Proanthocyanidins and flavonoids from grape seed extract can be detected in serum within two to three hours of ingestion.

Biotransformation and Elimination:

Grape seed extract is probably metabolised to some extent in the liver. *In vitro* data suggests that grape seed extract can inhibit Cytochrome P450 2D6 (CYP2D6), Cytochrome P450 2E1 (CYP2E1), and Cytochrome P450 2C9 (CYP2C9). Evidence from animal studies shows that grape seed extract may induce Cytochrome P450 3A4 (CYP3A4).

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Capsule content

Magnesium stearate (E470b)
Microcrystalline cellulose (E460)

Hard gelatine capsule

Bovine gelatine (E441)
Titanium dioxide (E171)

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

24 months.

6.4 Special precautions for storage

Store at or below 25 °C in a cool, dry place.
Store in the original package.

6.5 Nature and contents of container

White PP securitainer with a white, LDPE plastic closure and a tamper evident seal. Enclosed with a silica gel sachet and foam insert on top of the capsules.
Pack sizes: 40, 60 or 120 capsules.
Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements.

7 HOLDER OF CERTIFICATE OF REGISTRATION

PHARMACORP (PTY) LTD.
29 Victoria Link
Route 21 Corporate Park
Irene, 0178, RSA

8 REGISTRATION NUMBER: Complementary medicine

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

To be allocated.

10 DATE OF REVISION OF TEXT

March 2023