1 PRODUCT NAME

Scopoderm, 1.5mg transdermal patch.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Active ingredient

Hyoscine 1.5mg (supplied as Hyoscine (scopolamine) hydrobromide trihydrate) per patch.

Dose delivered

Each transdermal therapeutic system (TTS) patch releases approximately 1mg of scopolamine over 72 hours.

Releasing surface

Scopoderm is a flat, round transdermal patch approximately 1.8cm in diameter, with a contact surface area measuring 2.5cm^2

Excipients

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

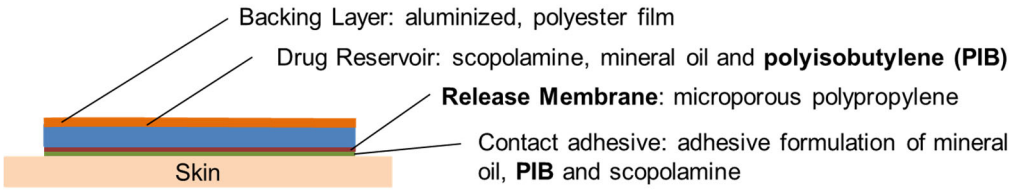
Transdermal patch.

Appearance

One side of the system is tan; the other side is silver and placed on an oversized clear hexagonal film.

Scopoderm is a film 0.2mm thick, with four layers.
Proceeding from the visible layer towards the layer attached to the skin, these are:

1. a backing layer of tan-coloured, aluminized, polyester film;
2. a drug reservoir of scopolamine, light mineral oil, and polyisobutylene;
3. a microporous polypropylene membrane that controls the rate of delivery of
4. scopolamine from the system to the skin surface; and an adhesive formulation of mineral oil, polyisobutylene, and scopolamine. A protective peel strip of siliconized polyester, which covers the adhesive layer, is removed before the system is used.



4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Scopoderm is indicated to prevent symptoms of motion sickness, such as nausea, vomiting, and vertigo.

4.2 Dosage and method of administration

Posology

To obtain an optimum protective effect, a single **Scopoderm** transdermal patch should be applied about 5 - 6 hours before embarking on a journey (or on the evening before the journey) to a clean, dry, hairless area of skin behind the ear (see section 6.6). Application of one **Scopoderm** transdermal patch is sufficient to ensure protection over a period of 72 hours; but, if the patch is only needed for a shorter time, it should be removed at the end of the journey.

Should more prolonged protection be required, the **Scopoderm** transdermal patch must be removed after 72 hours and a fresh patch applied behind the other ear.

If the **Scopoderm** transdermal patch becomes accidentally detached, it should be replaced by a fresh patch if ongoing treatment is needed.

To prevent traces of active substance from entering the eyes the patient should always wash the hands after contact with the patch and wash the site of application after its removal (see section 4.4).

Populations

Elderly

Scopoderm should be used with caution in the elderly (see section 4.4).

Children

Scopoderm can be used in children aged 10 years or above. Safety in children under 10 years has not been established and its use is not recommended.

Hepatic and renal impairment

Scopoderm should be used with caution in patients with impaired hepatic or renal function (see section 4.4).

Route of administration

Transdermal.

For instructions on opening and applying the patches see section 6.6.

4.3 Contraindications

Scopoderm is contraindicated in patients with hypersensitivity to scopolamine, or to any of the excipients (see section 6.1); and in patients with glaucoma.

4.4 Special warnings and precautions for use

General

Scopolamine has anticholinergic effects (see section 5.1). Idiosyncratic reactions may occur with ordinary therapeutic doses.

Side-effects may persist for 24 hours or longer after the patch has been removed (see section 5.2).

Do not apply more than one patch at a time.

Elderly
The elderly may be at increased risk of adverse reactions due to the anticholinerigic effects of scopolamine (see section 4.8). **Scopoderm** should be used with caution in elderly patients.

Hepatic and renal impairment
Scopoderm should be used with caution in patients with metabolic disorders or with impaired hepatic or renal function as its use has not been studied in these populations.

Neuropsychiatric effects
Cases of confusion and/or visual hallucinations have occurred due to the anticholinergic effects of scopolamine. If this occurs, the **Scopoderm** transdermal patch should be removed immediately. If symptoms persist despite removal of the patch appropriate therapeutic measures should be taken. In severe cases, administration of physostigmine should be considered, e.g. 1 - 4mg (in children 0.5mg), by slow intravenous injection to be repeated if necessary.

Gastrointestinal and urinary disorders
Scopolamine can decrease gastrointestinal motility and cause urinary retention due to its anticholinergic effects. **Scopoderm** should be used with caution in patients with pyloric stenosis, intestinal obstruction, or urinary obstruction (e.g. in diseases of the prostate).

Raised intraocular pressure
Scopolamine can increase intra-ocular pressure due to its anticholinergic effects. In patients with suspected raised intra-ocular pressure (e.g. pressure pain, blurred vision, glaucomatous halo), **Scopoderm** should only be used after an ophthalmological examination rules this out (see section 4.3).

Seizures
An increase in seizure frequency in epileptic patients has been reported. **Scopoderm** should be used with caution in patients with a history of seizures.

Blurred vision
After applying, removing, or handling the **Scopoderm** transdermal patch, the hands (and application site if patch is removed) should be thoroughly washed. This is to prevent traces of active substance from entering the eyes, which might lead to temporary blurring of vision and dilatation of the pupils (sometimes in one eye only).

Medical scans
Due the presence of aluminium in one of the layers of the patch, it should be removed before medical scans.

4.5 Interaction with other medicines and other forms of interaction
Scopolamine should be employed with caution in patients taking drugs which act on the central nervous system. This applies particularly to patients under treatment with drugs displaying anticholinergic activity, e.g. belladonna alkaloids, antihistamines, tricyclic antidepressants (such as amitriptyline and imipramine), amantadine, quinidine.

Patients should refrain from consuming alcohol during use of **Scopoderm**.

4.6 Fertility, pregnancy and lactation

Fertility

There are no controlled studies on the potential effects of scopolamine on human fertility. Non-clinical studies in female rats revealed no evidence of impaired fertility (see section 5.3).

Pregnancy

There are no controlled studies on the potential effects of scopolamine in pregnant women. Non-clinical studies in mice and rats have revealed no adverse reproductive or developmental effects at doses comparable to the recommended clinical dose (see section 5.3).

Scopolamine, readily crosses the placenta. Pregnant patients should talk to a healthcare professional before using **Scopoderm**. **Scopoderm** should only be used during pregnancy if the expected benefits to the mother outweigh the potential risks to the foetus.

Breast-feeding

There are no controlled studies on the potential effects of scopolamine in lactating women. Scopolamine is excreted in human milk in trace amounts. Breastfeeding patients should talk to a healthcare professional before using **Scopoderm**.

4.7 Effects on ability to drive and use machines

Scopoderm can causes drowsiness or visual impairment, and in rare cases can also give rise to other side effects (see section 4.8), which may adversely affect the patient's reactions.

Patients should therefore be warned of this possibility and cautioned against engaging in activities that require mental alertness, such as driving a vehicle or operating machinery.

4.8 Undesirable effects

Adverse reactions are listed below by system organ class and frequency. Frequencies are defined as: 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), or not known (cannot to be estimated from available data). Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness.

Table 1 List of Adverse Reactions

MedDRA SOC	Adverse Reaction	Frequency
Psychiatric disorders	Disorientation, confusion and hallucinations	Rare
Nervous system disorders	Somnolence, dizziness	Very common
	Memory impairment, disturbance in attention, restlessness.	Rare
	Agitation	Not known
	Coordination Abnormalities	Not known
	Headache	Not known
Eye disorders	Disturbances of visual accommodation (cycloplegia) including blurred vision, and mydriasis (sometimes unilateral).	Very common
	Angle closure glaucoma	Very rare
Gastrointestinal disorders	Dryness of the mouth	Very common

Skin and subcutaneous tissue disorders	Skin irritation	Common
	Rash generalized	Very rare
	Application site reactions including rash, pruritus, erythema and burning	Not known
Renal and urinary disorders	Urinary retention	Rare

Adverse effects after withdrawal of Scopoderm transdermal patches
After discontinuation of treatment, in rare cases usually after several days of use - symptoms such as dizziness, nausea, vomiting, headache, and disturbances of balance have been reported.

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. Healthcare professionals are asked to report any suspected adverse reactions https://pophealth.my.site.com/carmreportnz/s/

4.9 Overdose

Symptoms and signs
Scopolamine overdose can result in anticholinergic toxicity. Signs and symptoms of overdose can include dry flushed skin, dry mouth, visual disturbance, tachycardia, supraventricular arrhythmias, decreased bowel sounds, urinary retention, hypertension, hyperthermia, lethargy, somnolence, agitation, confusion, and hallucinations. At very high doses seizures, coma, respiratory depression, and circulatory collapse can occur.

Treatment
Remove all patches immediately, as some overdose symptoms may persist for 24 hours or longer even after patch removal.

The most effective antidote is physostigmine, which, depending on the severity of the poisoning, should be injected slowly IV in doses of 1 - 4mg (0.5mg in children). Since physostigmine is rapidly metabolised, symptoms may recur within 1 - 2 hours, and repeated injections may be needed.

Diazepam may be used to manage excitation states and convulsions, but large doses should be avoided in view of the possibility of worsening respiratory depression. In severe cases artificial respiration may be necessary. In the event of hyperthermia, urgent action should be taken to dissipate heat (cold baths). Other appropriate supportive measures should be used as required.

For advice on the management of overdose please contact the National Poisons Centre on 0800 POISON (0800 764766) in New Zealand.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

ATC Code: A04AD01.
Pharmacotherapeutic group: Antiemetics and antinauseants.

Mechanism of action
It has been suggested that the ability of scopolamine to prevent nausea and vomiting due to motion sickness may be related to inhibition of cholinergic impulse conduction from the vestibular nucleus

to the higher centres of the central nervous system, as well as from the reticular formation to the vomiting centre.

Scopolamine is a naturally occurring belladonna alkaloid, the pharmacological properties of which are well known. As a parasympatholytic agent it competitively antagonises acetylcholine (or other direct parasympathomimetics) at the muscarinic receptor. This means that its effect can be abolished by high doses of a parasympathomimetic agent. The effect of scopolamine depends on the sensitivity of the target organs and on the size of the dose employed. In therapeutic doses scopolamine depresses motor function, causes drowsiness, inhibits the secretion of saliva and sweat, and dilates the pupils.

5.2 Pharmacokinetic properties

Absorption

Following application of the **Scopoderm** transdermal patch, equilibrium between the quantity of active substance absorbed and eliminated is reached after about 6 hours. The transdermal therapeutic system produces steady plasma concentrations of scopolamine in the range of 0.17 - 0.33nmol/litre. Provided the system is not removed, the equilibrium is maintained for 72 hours.

Distribution

Little data about the distribution of scopolamine is available; however, the drug distributes well and reaches the central nervous system. Scopolamine seems to be bound to plasma proteins in a reversible manner.

Metabolism

The metabolism of scopolamine has not been fully characterized. The drug appears to be metabolized in the liver (glucoronide or sulfate conjugation).

Elimination

After removal of the **Scopoderm** transdermal patch, the quantity of active substance in the body diminishes slowly within the following 24 hours to approx. one-third, because scopolamine still present in the skin continues to enter the bloodstream.

Excretion

Scopolamine is excreted in urine. The urinary excretion rate of free and total (free plus conjugated) scopolamine was about 0.7 and 3.8 micrograms/hour, respectively after the application of a single transdermal scopolamine patch. Less than 10% of the total dose is excreted in urine as unchanged drug and its metabolites over 108 hours.

Half life

Following a single application of two **Scopoderm** transdermal patches, the average elimination half-life of the drug (free scopolamine) was 9.5 hours.

5.3 Preclinical safety data

NON-CLINICAL INFORMATION

Non-clinical safety data for scopolamine have not revealed findings which are of relevance to the recommended dosage and use of the product.

Fertility

Fertility studies performed in female rats revealed no evidence of impaired fertility following daily subcutaneous administration of scopolamine hydrobromide. Body weights were reduced in females of the highest dose-group. Plasma levels in females of this group were approximately 500-fold greater than the level achieved in humans using scopolamine transdermal patch.

Reproductive and Developmental Toxicity:

A marginal embryotoxic effect was seen in rabbits with scopolamine hydrobromide administered by daily intravenous injection at doses that were approximately 100 times the level achieved with transdermal systems. No adverse effects were recorded in reprotoxicity studies following IV administration in rats.

In a prenatal developmental toxicity study, scopolamine hydrobromide trihydrate was administered to mice on days 6 through 15 of gestation at doses of 0, 10, 100, 450 and 900mg/kg/day (0.8, 8, 36, or 72mg/kg/day human equivalent dose; 77-, 777-, 3495-, or 6990-fold greater than the highest clinical dose). Caesarean sections were performed on gestation day 17. Treatment up to 900mg/kg/day (72mg/kg/day human equivalent dose; 6990-fold greater than the highest clinical dose) had no adverse effect on prenatal viability and produced no evidence of teratogenesis. A marginal reduction in foetal body weight was observed at doses of 450 and 900mg/kg/day (36, or 72mg/kg/day human equivalent dose; 3495-, or 6990-fold greater than the highest clinical dose) which also caused marginal maternal toxicity. Under the conditions of this study, the no observed adverse effect level (NOAEL) was 100mg/kg/day (8mg/kg/day human equivalent dose; 777-fold greater than the highest clinical dose) for both maternal and foetal toxicity.

In another prenatal developmental toxicity study, scopolamine hydrobromide trihydrate was administered to CD rats on days 6 through 15 of gestation at doses of 0, 10, 100, 450 and 900mg/kg/day (1.6, 16, 72, or 144mg/kg/day human equivalent dose; 155-, 1553, 6990-, or 13980-fold greater than the highest clinical dose). A marginal reduction in foetal body weight was noted at doses of 100mg/kg/day (16mg/kg/day human equivalent dose; 1553-fold greater than the highest clinical dose) and greater. There was a significant increase in the incidence of short ribs at doses of 450mg/kg/day (72mg/kg/day human equivalent dose; 6990-fold greater than the highest clinical dose) and greater. These effects were accompanied by a significant dose-related maternal toxicity. Marginal evidence of intrauterine growth retardation and a non-dose-related trend toward an increase in the incidence of malformations was observed only at doses that caused significant maternal toxicity.

Under the conditions of this study, the NOAEL was 10mg/kg/day (1.6mg/kg/day human equivalent dose; 155-fold greater than the highest clinical dose) for both maternal and foetal toxicity.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Light mineral oil
Polyisobutylene.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

48 months from date of manufacture.

6.4 Special precautions for storage

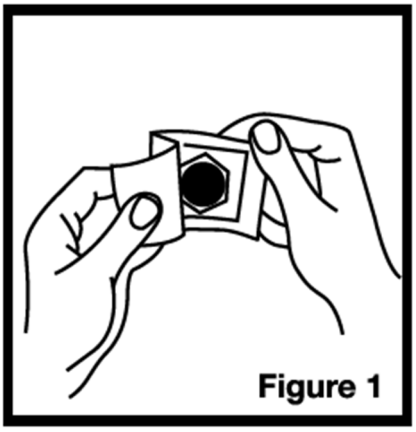
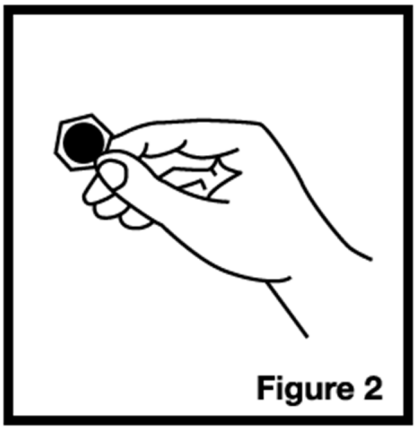
Store at or below 25°C.

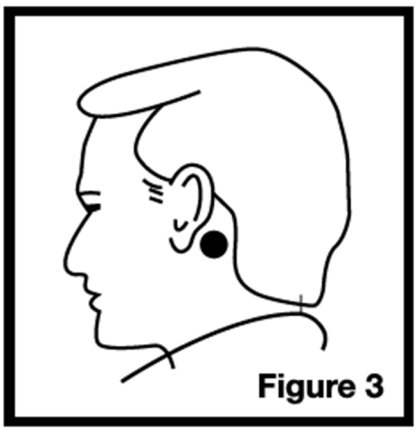
6.5 Nature and contents of container

Scopoderm is available in a pack size of two patches per carton.
Each patch of **Scopoderm** is packaged in a flat, sealed foil lined pouch.

Pouch material is a lamination of paper, low density polyethylene, aluminium foil and Surlyn (heat-seal layer, product contact surface). The secondary packaging consists of a carton and descriptive literature.

6.6 Special precautions for disposal and other handling

Tear open the sachet at the top and take out the flesh-coloured **Scopoderm** transdermal patch complete with its transparent hexagonal protective foil (Fig. 1).	 Figure 1
Holding the system only by its edge - and taking care, if possible not to touch the silvery adhesive side (Fig. 2) - peel off the hexagonal foil.	 Figure 2

Press the system (silvery adhesive side downwards) firmly on to a dry area of skin behind the ear (Fig. 3).	 Figure 3

Once the system has been affixed, it should not be touched again while it is being worn, since pressure exerted on it might possibly cause scopolamine to ooze out at the edge.

After the system has been either applied, hands should be thoroughly washed. Once removed, the site of application and hands should be thoroughly washed.

Do not cut the patch. Dispose of used patches carefully.

7 MEDICINE CLASSIFICATION

Pharmacy Only Medicine.

8 SPONSOR

Scopoderm is distributed in New Zealand by:

Baxter Healthcare Ltd
33 Vestey Drive
Mt Wellington
Auckland 1060.

Baxter Healthcare Ltd
PO Box 14 062
Panmure
Auckland 1741

Phone (09) 574 2400

9 DATE OF FIRST APPROVAL

Date of publication in the New Zealand Gazette of consent to distribute the medicine:
18 November 1982.

10 DATE OF PREPARATION

8 November 2023.

SUMMARY TABLE OF CHANGES

Section changed	Summary of new information
All	Reformatted to Medsafe's data sheet template.
2	Subheadings included as per Data Sheet template.
3	Included pharmaceutical form, appearance, and each layer of the patch.
4.2	Dosage and method of administration updated, specifically, information relating to elderly, children, hepatic and renal impairment populations is included or modified. Route of administration, and instructions for use moved to section 6.6.
4.3	Contraindications updated.
4.4	General safety information updated. Special warnings and precautions updated relating to Elderly, Hepatic and renal impairment, Neuropsychiatric effects, Gastrointestinal and urinary disorders, Seizures, Blurred vision, and Medical scans.
4.6	Section expanded to include warnings regarding fertility, use in pregnancy and breast-feeding.
4.8	Undesirable effects tabulated and updated to MedDRA classification system. Reporting suspected adverse reactions url updated.
4.9	Overdose Symptoms and signs section updated, and Treatment expanded to include advice to remove patches and reference to NPC for advice on overdose management.
5.1 and 5.2	Included ATC and Pharmacotherapeutic group. Mechanism of action updated, subheadings and information under Pharmacokinetic properties updated.
5.3	Included pre-clinical safety data.
6.1, 6.3, 6.4, 6.5	Excipients listed, shelf life and storage information corrected. Nature and contents updated to list marketed pack size.
6.6	Special precautions for disposal and other handling updated. See 4.2
7	Classification corrected.
8	Sponsor details updated.
9	Included date of first approval.

Based on CCDS461 2023April25.

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