HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use TRANSDERM SCŌP safely and effectively. See full prescribing information for TRANSDERM SCŌP.

TRANSDERM SCŌP (scopolamine transdermal system)
Initial U.S. Approval: 1979

---------- -- RECENT MAJOR CHANGES ----------

Dosage and Administration (2.1)	09/2023
Warnings and Precautions (5)	09/2023

---------- INDICATIONS AND USAGE ----------

TRANSDERM SCŌP is an anticholinergic indicated in adults for the prevention of:

- nausea and vomiting associated with motion sickness. (1)
- post-operative nausea and vomiting (PONV) associated with recovery from anesthesia and/or opiate analgesia and surgery. (1)

---------- DOSAGE AND ADMINISTRATION ----------

Application and Removal (2.1):

- Each TRANSDERM SCŌP transdermal system delivers 1 mg of scopolamine over 3 days.
- Only wear one transdermal system at a time.
- Do not cut the transdermal system.
- Wash hands thoroughly after application and do not touch the system again.
- Upon removal, fold used transdermal system in half with sticky side together, discard to prevent accidental contact or ingestion, and wash the hands and application site.

Recommended Dosage:

- *Motion Sickness*: Apply one transdermal system to the hairless area behind one ear at least 4 hours before antiemetic effect is required for use up to 3 days. If therapy for more than 3 days is required, remove the first transdermal system and apply a new transdermal system behind the other ear. (2.2)
- *PONV*: For surgeries other than cesarean section, apply one transdermal system behind the ear the evening before surgery and remove 24 hours following surgery. (2.2)

---------- DOSAGE FORMS AND STRENGTHS ----------

Transdermal system: 1 mg/3 days (3)

---------- CONTRAINDICATIONS ----------

- Angle closure glaucoma. (4, 6.2)
- Hypersensitivity to scopolamine or other belladonna alkaloids or to any ingredient or component of the formulation or delivery system. (4, 7)

---------- WARNINGS AND PRECAUTIONS ----------

- Acute Angle Closure Glaucoma: In patient with symptom of raised intraocular pressure perform the ophthalmological examination. Monitor for increased intraocular pressure in patients with open-angle glaucoma and adjust glaucoma therapy as needed. Discontinue if signs or symptoms of acute angle closure glaucoma develop. (5.1)
- Neuropsychiatric Adverse Reactions: May cause psychiatric and cognitive effects, seizures and impair mental and/or physical abilities. Monitor patients for new or worsening psychiatric symptoms during treatment and during concomitant treatment with other drugs that are associated with similar psychiatric effects. (5.2, 7.1)
- Idiosyncratic Reactions: May occur with ordinary therapeutic doses. (5.3)
- Eclamptic Seizures in Pregnant Women: Avoid use in patients with severe preeclampsia. (5.4)
- Gastrointestinal and Urinary Disorders: Consider more frequent monitoring during treatment in patients suspected of having intestinal obstruction; patients with pyloric obstruction, patients with impeded urine flow or receiving other anticholinergic drugs. Discontinue if patient develops difficulty in urination. (5.5, 7.2)
- Drug Withdrawal/Post-Removal Symptoms: Anticholinergic symptoms may occur 24 hours or more after removal of the transdermal system. (5.6)
- Blurred Vision: Avoid contact with the eyes. (2.1, 5.7)
- Magnetic Resonance Imaging (MRI) Skin Burns: Remove TRANSDERM SCŌP prior to MRI scan. (5.8)

---------- ADVERSE REACTIONS ----------

Most common adverse reactions are:

- Motion Sickness (>15%): dry mouth, drowsiness, blurred vision and dilation of the pupils. (6.1)
- PONV (≥ 3%): dry mouth, dizziness, somnolence, agitation, visual impairment, confusion, mydriasis and pharyngitis. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Baxter Healthcare Corporation at 1-866-888-2472 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

---------- DRUG INTERACTIONS ----------

- Drugs Causing Central Nervous System (CNS) Adverse Reactions: Monitor patients for CNS adverse reactions (drowsiness, dizziness or disorientations). (7.1)
- Anticholinergic Drugs: Consider more frequent monitoring during treatment in patients receiving other anticholinergic drugs. (7.2)
- Oral Drugs Absorbed in the Stomach: Monitor for increased or decreased therapeutic effect of the oral drug. (7.3)
- Interaction with Gastric Secretion Test: Discontinue use of TRANSDERM SCŌP 10 days prior to testing. (7.4)

---------- USE IN SPECIFIC POPULATIONS ----------

- Geriatric Patients: Consider more frequent monitoring during treatment due to increased risk of CNS adverse reactions. (5.2, 8.5)
- Renal or Hepatic Impairment: Consider more frequent monitoring during treatment due to increased risk of CNS adverse reactions. (5.2, 8.6)

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling.

Revised: 09/2023

FULL PRESCRIBING INFORMATION: CONTENTS*

*SECTIONS OR SUBSECTIONS OMITTED FROM THE FULL PRESCRIBING INFORMATION ARE NOT LISTED.

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

TRANSDERM SCŌP is indicated in adults for the prevention of:

- nausea and vomiting associated with motion sickness.
- post-operative nausea and vomiting (PONV) associated with recovery from anesthesia and/or opiate analgesia and surgery.

2 DOSAGE AND ADMINISTRATION

2.1 Important Application and Removal Instructions

- Each TRANSDERM SCŌP transdermal system is formulated to deliver *in vivo* approximately 1 mg of scopolamine over 3 days.
- Only wear one transdermal system at any time.
- **Do not cut the transdermal system.**
- Apply the transdermal system to the skin in the postauricular area (hairless area behind one ear).
- After the transdermal system is applied on the dry skin behind the ear, wash hands thoroughly with soap and water and dry hands *[see Warnings and Precautions (5.7)]*.
- If the transdermal system becomes displaced, discard the transdermal system, and apply a new transdermal system on the hairless area behind the other ear.
- Once the transdermal system has been affixed, it should not be touched again while it is being worn, since pressure exerted on it may cause scopolamine to ooze out at the edge.
- Upon removal, fold the used transdermal system in half with the sticky side together, and discard in household trash in a manner that prevents accidental contact or ingestion by children, pets or others.
- Wash the hands and application site after transdermal system removal *[see Warnings and Precautions (5.7)]*.

2.2 Recommended Adult Dosage

Motion Sickness

Apply one TRANSDERM SCŌP transdermal system to the hairless area behind one ear at least 4 hours before the antiemetic effect is required – for use up to 3 days. If therapy is required for longer than 3 days, remove the first transdermal system and apply a new TRANSDERM SCŌP transdermal system behind the other ear.

PONV

For surgeries other than cesarean section: Apply one TRANSDERM SCŌP transdermal system the evening before scheduled surgery. Remove the transdermal system 24 hours following surgery.

3 DOSAGE FORMS AND STRENGTHS

Transdermal system: a circular, flat, tan-colored transdermal system imprinted with “Scopolamine 1 mg/3 days”

4 CONTRAINDICATIONS

TRANSDERM SCŌP is contraindicated in patients with:

- angle closure glaucoma *[see Warnings and Precautions (5.1)]*.
- hypersensitivity to scopolamine or other belladonna alkaloids or to any ingredient or component in the formulation or delivery system. Reactions have included rash generalized and erythema *[see Adverse Reactions (6.2), Description (11)]*.

5 WARNINGS AND PRECAUTIONS

5.1 Acute Angle Closure Glaucoma

The mydriatic effect of scopolamine may cause an increase in intraocular pressure resulting in acute angle closure glaucoma. In patients whose case history indicates that there might be raised intra-ocular pressure (pressure pain, blurred vision, glaucomatous halo) TRANSDERM SCŌP should only be employed after an ophthalmological examination. Monitor intraocular pressure in patients with open angle glaucoma and adjust glaucoma therapy during TRANSDERM SCŌP use, as needed. Advise patients to immediately remove the transdermal system and contact their healthcare provider if they experience symptoms of acute angle closure glaucoma (e.g., eye pain or discomfort, blurred vision, visual halos or colored images in association with red eyes from conjunctival congestion and corneal edema).

5.2 Neuropsychiatric Adverse Reactions

Psychiatric Adverse Reactions

Scopolamine has been reported to exacerbate psychosis. Other psychiatric reactions have also been reported, including acute toxic psychosis, agitation, speech disorder, hallucinations, paranoia, and delusions *[see Adverse Reactions (6.2)]*. Monitor patients for new or worsening psychiatric symptoms during treatment with TRANSDERM SCŌP. Also, monitor patients for new or worsening psychiatric symptoms during concomitant treatment with other drugs that are associated with similar psychiatric effects *[see Drug Interactions (7.1)]*. In cases of psychiatric reactions occurring TRANSDERM SCŌP should be removed at once. If, despite this, the symptoms persist in a severe form, appropriate therapeutic measures should be taken.

Seizures

Seizures and seizure-like activity have been reported in patients receiving scopolamine. Weigh this potential risk against the benefits before prescribing TRANSDERM SCŌP to patients with a history of seizures, including those receiving anti-epileptic medication or who have risk factors that can lower the seizure threshold.

Cognitive Adverse Reactions

Scopolamine can cause drowsiness, disorientation, and confusion. Discontinue TRANSDERM SCŌP if signs or symptoms of cognitive impairment develop. If, despite this, the symptoms persist in a severe form, appropriate therapeutic measures should be taken. Elderly and pediatric patients may be more sensitive to the neurological and psychiatric effects of TRANSDERM SCŌP. Consider more frequent monitoring during treatment with TRANSDERM SCŌP in elderly patients *[see Use in Specific Populations (8.5)]*. TRANSDERM SCŌP is not approved for use in pediatric patients *[see Use in Specific Populations (8.4)]*.

Hazardous Activities

TRANSDERM SCŌP may impair the mental and/or physical abilities required for the performance of hazardous tasks such as driving a motor vehicle, operating machinery or participating in underwater sports. Concomitant use of other drugs that cause central nervous system (CNS) adverse reactions (e.g., alcohol, sedatives, hypnotics, opiates, and anxiolytics) or have anticholinergic properties (e.g., other belladonna alkaloids, sedating antihistamines, meclizine, tricyclic antidepressants, and muscle relaxants) may increase this effect *[see Drug Interactions (7.1)]*. Inform patients not to operate motor vehicles or other dangerous machinery or participate in underwater sports until they are reasonably certain that TRANSDERM SCŌP does not affect them adversely.

5.3 Idiosyncratic Reactions

Idiosyncratic reactions may occur with ordinary therapeutic doses of scopolamine.

5.4 Eclamptic Seizures in Pregnant Women

Eclamptic seizures have been reported in pregnant women with severe preeclampsia soon after injection of intravenous and intramuscular scopolamine *[see Use in Specific Populations (8.1)]*. Avoid use of TRANSDERM SCŌP in patients with severe preeclampsia.

5.5 Gastrointestinal and Urinary Disorders

Scopolamine, due to its anticholinergic properties, can decrease gastrointestinal motility and cause urinary retention. Consider more frequent monitoring during treatment with TRANSDERM SCŌP in patients suspected of having intestinal obstruction, patients with pyloric obstruction or patients suffering from difficulty in passing water owning to an impeded flow of urine (e.g., in diseases of the prostate or urinary bladder neck obstruction) and patients receiving other anticholinergic drugs *[see Drug Interactions (7.2)]*. Discontinue TRANSDERM SCŌP in patients who develop difficulty in urination.

5.6 Drug Withdrawal/Post-Removal Symptoms

Discontinuation of TRANSDERM SCŌP, usually after several days of use, may result in withdrawal symptoms, such as disturbances of equilibrium, dizziness, nausea, vomiting, abdominal cramps, sweating, headache, mental confusion, muscle weakness, bradycardia and hypotension. The onset of these symptoms is generally 24 hours or more after the transdermal system has been removed. Instruct patients to seek medical attention if they experience severe symptoms.

5.7 Blurred Vision

Scopolamine can cause temporary dilation of the pupils resulting in blurred vision if it comes in contact with the eyes.

Advise patients to wash their hands thoroughly with soap and water and dry their hands immediately after handling the transdermal system, do not touch the system while wearing it, and wash the application site after transdermal system removal *[see Dosage and Administration (2.1)]*.

5.8 Magnetic Resonance Imaging (MRI) Skin Burns

TRANSDERM SCŌP contains an aluminized membrane. Skin burns have been reported at the application site in patients wearing an aluminized transdermal system during an MRI scan. Remove TRANSDERM SCŌP before undergoing an MRI.

6 ADVERSE REACTIONS

The following serious adverse reactions are described elsewhere in labeling:

- Acute Angle Closure Glaucoma *[see Warnings and Precautions (5.1)]*
- Neuropsychiatric Adverse Reactions *[see Warnings and Precautions (5.2)]*
- Idiosyncratic Reactions *[see Warnings and Precautions (5.3)]*
- Eclamptic Seizures in Pregnant Women *[see Warnings and Precautions (5.4)]*
- Gastrointestinal and Urinary Disorders *[see Warnings and Precautions (5.5)]*
- Drug Withdrawal/Post-Removal Symptoms *[see Warnings and Precautions (5.6)]*
- Blurred Vision *[see Warnings and Precautions (5.7)]*
- MRI Skin Burns *[see Warnings and Precautions (5.8)]*

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

Motion Sickness

The most common adverse reaction (approximately two thirds) was dry mouth. Less common adverse reactions, included drowsiness (less than one sixth), blurred vision and dilation of the pupils.

PONV

Common adverse reactions, occurring in at least 3% of patients in PONV clinical trials are shown in Table 1.

Table 1 Common Adverse Reactions* in Surgical Patients for the Prevention of PONV

	TRANSDERM SCŌP % (N = 461)	Placebo % (N = 457)
Dry mouth	29	16
Dizziness	12	7
Somnolence	8	4
Agitation	6	4
Visual Impairment	5	3
Confusion	4	3
Mydriasis	4	0
Pharyngitis	3	2

*occurring in at least 3% of patients and at a rate higher than placebo

6.2 Postmarketing Experience

The following adverse reactions have been identified during post-approval use of scopolamine transdermal system. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Psychiatric disorders: acute psychosis including: hallucinations, disorientation, and paranoia

Nervous system disorders: headache, amnesia, coordination abnormalities, speech disorder, disturbance in attention, restlessness

General disorders and administration site conditions: application site reactions including burning, rash, pruritus

Eye disorders: dry eyes, eye pruritus, angle closure glaucoma, amblyopia, eyelid irritation

Skin and subcutaneous tissue disorders: rash generalized, skin irritation, erythema

Renal and urinary disorders: dysuria

Ear and labyrinth disorders: vertigo

7 DRUG INTERACTIONS

7.1 Drugs Causing Central Nervous System (CNS) Adverse Reactions

The concurrent use of TRANSDERM SCŌP with other drugs that cause CNS adverse reactions of drowsiness, dizziness or disorientation (e.g., sedatives, hypnotics, opiates, anxiolytics and alcohol) or have anticholinergic properties (e.g., other belladonna alkaloids, sedating antihistamines, meclizine, tricyclic antidepressants, and muscle relaxants) may potentiate the effects of TRANSDERM SCŌP *[see Warnings and Precautions (5.2)]*. Either TRANSDERM SCŌP or the interacting drug should be chosen, depending on the importance of the drug to the patient. If the interacting drug cannot be avoided, monitor patients for CNS adverse reactions.

7.2 Anticholinergic Drugs

Concomitant use of scopolamine with other drugs having anticholinergic properties may increase the risk of CNS adverse reactions *[see Drug Interactions (7.1)]*, intestinal obstruction and/or urinary retention. Consider more frequent monitoring during treatment with TRANSDERM SCŌP in patients receiving anticholinergic drugs *[see Warnings and Precautions (5.2, 5.5)]*.

7.3 Oral Drugs Absorbed in the Stomach

TRANSDERM SCŌP, as an anticholinergic, may delay gastric and upper gastrointestinal motility and, therefore, the rate of absorption of other orally administered drugs. Monitor patients for modified therapeutic effect of concomitant orally administered drugs with a narrow therapeutic index.

7.4 Interaction with Gastric Secretion Test

Scopolamine will interfere with the gastric secretion test. Discontinue TRANSDERM SCŌP 10 days prior to testing.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

Available data from observational studies and postmarketing reports with scopolamine use in pregnant women have not identified a drug associated risk of major birth defects, miscarriage, or adverse fetal outcomes. Avoid use of TRANSDERM SCŌP in pregnant women with severe preeclampsia because eclamptic seizures have been reported after exposure to scopolamine *(see Data).*

In animal studies, there was no evidence of adverse developmental effects with intravenous administration of scopolamine hydrobromide revealed in rats. Embryotoxicity was observed in rabbits at intravenous doses producing plasma levels approximately 100 times the levels achieved in humans using a transdermal system.

The estimated background risk of major birth defects and miscarriage for the indicated population is unknown. All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. In the U.S. general population, the background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively.

Data

Human Data

Eclamptic Seizures
In published case reports, two pregnant patients with severe preeclampsia were administered intravenous and intramuscular scopolamine, respectively, and developed eclamptic seizures soon after scopolamine administration *[see Warnings and Precautions (5.4)]*.

Animal Data

In animal reproduction studies, when pregnant rats and rabbits received scopolamine hydrobromide by daily intravenous injection, no adverse effects were observed in rats. An embryotoxic effect was observed in rabbits at doses producing plasma levels approximately 100 times the levels achieved in humans using a transdermal system. Scopolamine administered parenterally to rats and rabbits at doses higher than the dose delivered by TRANSDERM SCŌP did not affect uterine contractions or increase the duration of labor.

8.2 Lactation

Risk Summary

Scopolamine is present in human milk. There are no available data on the effects of scopolamine on the breastfed infant or the effects on milk production. Because there have been no consistent reports of adverse events in breastfed infants over decades of use, the developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for TRANSDERM SCŌP and any potential adverse effects on the breastfed child from TRANSDERM SCŌP or from the underlying maternal condition.

8.4 Pediatric Use

Safety and effectiveness in pediatric patients have not been established. Pediatric patients are particularly susceptible to the adverse reactions of scopolamine; including mydriasis, hallucinations, amblyopia and drug withdrawal syndrome. Neurologic and psychiatric adverse reactions, such as hallucinations, amblyopia and mydriasis have also been reported.

8.5 Geriatric Use

Clinical trials of TRANSDERM SCŌP did not include sufficient number of subjects aged 65 years and older to determine if they respond differently from younger subjects. In other clinical experience, elderly patients had an increased risk of neurologic and psychiatric adverse reactions, such as hallucinations, confusion, dizziness and drug withdrawal syndrome *[*see Warnings and Precautions (*5.2*, *5.6*)*]*. Consider more frequent monitoring for CNS adverse reactions during treatment with TRANSDERM SCŌP in elderly patients *[see Warnings and Precautions (5.2)]*.

8.6 Renal or Hepatic Impairment

TRANSDERM SCŌP has not been studied in patients with renal or hepatic impairment. Consider more frequent monitoring during treatment with TRANSDERM SCŌP in patients with renal or hepatic impairment because of the increased risk of CNS adverse reactions *[see Warnings and Precautions (5.2)]*.

9 DRUG ABUSE AND DEPENDENCE

9.1 Controlled Substance

TRANSDERM SCŌP contains scopolamine, which is not a controlled substance.

9.3 Dependence

Termination of TRANSDERM SCŌP, usually after several days of use, may result in withdrawal symptoms such as disturbances of equilibrium, dizziness, nausea, vomiting, abdominal cramps, sweating, headache, mental confusion, muscle weakness, bradycardia and hypotension. These withdrawal symptoms indicate that scopolamine, like other anticholinergic drugs, may produce physical dependence. The onset of these symptoms, generally 24 hours or more after the transdermal system has been removed, can be severe and may require medical intervention *[see Warnings and Precautions (5.6)]*.

10 OVERDOSAGE

The signs and symptoms of anticholinergic toxicity include: lethargy, somnolence, coma, confusion, agitation, hallucinations, convulsion, visual disturbance, dry flushed skin, dry mouth, decreased bowel sounds, urinary retention, tachycardia, hypertension, and supraventricular arrhythmias. These symptoms can be severe and may require medical intervention.

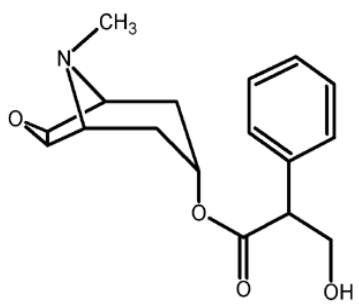
In cases of toxicity remove the TRANSDERM SCŌP transdermal system. Serious symptomatic cases of overdosage involving multiple transdermal system applications and/or ingestion may be managed by initially ensuring the patient has an adequate airway and supporting respiration and circulation. This should be rapidly followed by removal of all transdermal systems from the skin and the mouth. If there is evidence of transdermal system ingestion, endoscopic removal of swallowed transdermal systems, or administration of activated charcoal should be considered, as indicated by the clinical situation. In any case where there is serious overdosage or signs of evolving acute toxicity, continuous monitoring of vital signs and ECG, establishment of intravenous access, and administration of oxygen are all recommended.

The signs and symptoms of overdose/toxicity due to scopolamine should be carefully distinguished from the occasionally observed syndrome of withdrawal *[see Warnings and Precautions (5.6)]*. Although mental confusion and dizziness may be observed with both acute toxicity and withdrawal, other characteristic findings differ: tachyarrhythmias, dry skin, and decreased bowel sounds suggest anticholinergic toxicity, while bradycardia, headache, nausea and abdominal cramps, and sweating suggest post-removal withdrawal.

If over-exposure occurs, call your Poison Control Center at 1-800-222-1222 for current information on the management of poisoning or overdosage.

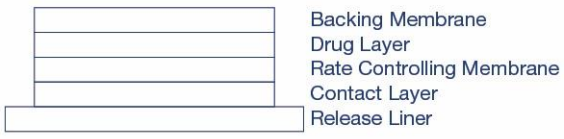
11 DESCRIPTION

TRANSDERM SCŌP (scopolamine transdermal system) is designed for continuous release of scopolamine following application to an area of intact skin on the head, behind the ear. Each system contains 1.5 mg of scopolamine base. Scopolamine is (9-methyl-3-oxa-9-azatricyclo[3.3.1.$0^{2,4}$]nonan-7-yl) 3-hydroxy-2-phenylpropanoate. The empirical formula is $C_{17}H_{21}NO_4$ and its structural formula is:



Scopolamine has a molecular weight of 303.35 and a pKa of 7.55-7.81. The TRANSDERM SCŌP transdermal system is a circular, 0.2 mm thick, 2.5 cm^2 film with four layers. Proceeding from the visible surface towards the surface attached to the skin, these layers are: (1) a backing membrane of tan-colored, aluminized, polyester film; (2) a drug layer of scopolamine, light mineral oil, and polyisobutylene; (3) a microporous polypropylene membrane that controls the rate of delivery of scopolamine from the system to the skin surface; and (4) a contact layer formulation of mineral oil, polyisobutylene, and scopolamine. A release liner of siliconized polyester, which covers the adhesive layer, is removed before the system is used.

Cross section of the system:



12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Scopolamine, a belladonna alkaloid, is an anticholinergic. Scopolamine acts: i) as a competitive inhibitor at postganglionic muscarinic receptor sites of the parasympathetic nervous system, and ii) on smooth muscles that respond to acetylcholine but lack cholinergic innervation. It has been suggested that scopolamine acts in the central nervous system (CNS) by blocking cholinergic transmission from the vestibular nuclei to higher centers in the CNS and from the reticular formation to the vomiting center. Scopolamine can inhibit the secretion of saliva and sweat, decrease gastrointestinal secretions and motility, cause drowsiness, dilate the pupils, increase heart rate, and depress motor function.

12.3 Pharmacokinetics

The system is formulated to deliver approximately 1 mg of scopolamine to the systemic circulation over 3 days.

Absorption

Following application to the skin behind the ear, circulating plasma concentrations are detected within 4 hours with peak concentrations being obtained, on average, within 24 hours. The average plasma concentration produced is 87 pg/mL (0.28 nM) for free scopolamine and 354 pg/mL for total scopolamine (free + conjugates). Following removal of the used transdermal system, there is some degree of continued systemic absorption of scopolamine bound in the skin layers.

Distribution
The distribution of scopolamine is not well characterized. It crosses the placenta and the blood brain barrier and may be reversibly bound to plasma proteins.

Elimination

Metabolism and Excretion
Scopolamine is metabolized and conjugated with less than 5% of the total dose appearing unchanged in the urine. The enzymes responsible for metabolizing scopolamine are unknown. The exact elimination pattern of scopolamine has not been determined. Following transdermal system removal, plasma concentrations of scopolamine decline in a log linear fashion with an observed half-life of 9.5 hours. Less than 10% of the total dose is excreted in the urine as the parent drug and metabolites over 108 hours.

Drug Interaction Studies

An *in vitro* study using human hepatocytes examined the induction of CYP1A2 and CYP3A4 by scopolamine. Scopolamine did not induce CYP1A2 and CYP3A4 isoenzymes at the concentrations up to 10 nM. In an *in vitro* study using human liver microsomes which evaluated the inhibition of CYP1A2, 2C8, 2C9, 2C19, 2D6 and 3A4, scopolamine did not inhibit these cytochrome P450 isoenzymes at the concentrations up to 1 micromolar. No *in vivo* drug-drug interaction studies have been conducted.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

No long-term studies in animals have been conducted to evaluate the carcinogenic potential of scopolamine. The mutagenic potential of scopolamine has not been evaluated.

Fertility studies were performed in female rats and revealed no evidence of impaired fertility or harm to the fetus due to scopolamine hydrobromide administered by daily subcutaneous injection. Maternal body weights were reduced in the highest-dose group (plasma level approximately 500 times the level achieved in humans using a transdermal system). However, fertility studies in male animals were not performed.

14 CLINICAL STUDIES

14.1 Prevention of Motion Sickness

In 195 adult subjects of different racial origins who participated in clinical efficacy studies at sea or in a controlled motion environment, there was a 75% reduction in the incidence of motion-induced nausea and vomiting. TRANSDERM SCŌP was applied from 4 to 16 hours prior to the onset of motion in these studies.

14.2 Prevention of Post-Operative Nausea and Vomiting

A clinical efficacy study evaluated 168 adult female patients undergoing gynecological surgery with anesthesia and opiate analgesia. Patients received TRANSDERM SCŌP or placebo applied approximately 11 hours before anesthesia/opiate analgesia. No retching/vomiting during the 24-hour post-operative period was reported in 79% of those treated with TRANSDERM SCŌP compared to 72% of those receiving placebo. When the need for additional antiemetic medication was assessed during the same period, there was no need for medication in 89% of patients treated with TRANSDERM SCŌP as compared to 72% of placebo-treated patients.

16 HOW SUPPLIED/STORAGE AND HANDLING

TRANSDERM SCŌP (scopolamine transdermal system) 1 mg/3 days is available as the following:

Cartons of 4, 10, and 24 transdermal systems, packaged into individual foil pouches.

- Carton of 4 transdermal systems. NDC 10019-553-06
- Carton of 10 transdermal systems. NDC 10019-553-03
- Carton of 24 transdermal systems. NDC 10019-553-04

Store at controlled room temperature between 68°F to 77°F (20°C to 25°C).

Store pouch(es) in an upright position.

Do not bend or roll pouch(es).

Wash hands thoroughly with soap and water immediately after handling the transdermal system. Do not touch the system during the treatment. Upon removal, fold the used transdermal system in half with the sticky side together, and discard in household trash in a manner that prevents accidental contact or ingestion by children, pets or others. Wash the application site after transdermal system removal *[see Dosage and Administration (2.1), Warnings and Precautions (5.7)]*.

17 PATIENT COUNSELING INFORMATION

Advise the patient to read the FDA-approved patient labeling (Patient Information and Instructions for Use).

Administration Instructions
Counsel patients on how to apply and remove the transdermal system *[see Dosage and Administration (2.1)]*:

- Only wear one transdermal system at any time.
- Do not cut the transdermal system.
- Apply the transdermal system to the skin in the postauricular (hairless area behind one ear) area.
- After the transdermal system is applied on the dry skin behind the ear, wash hands thoroughly with soap and water and dry hands.
- If the transdermal system becomes displaced, discard the transdermal system, and apply a new transdermal system on the hairless area behind the other ear.
- Once the transdermal system has been affixed, it should not be touched again while it is being worn, since pressure exerted on it may cause scopolamine to ooze out at the edge.
- Upon removal, fold the used transdermal system in half with the sticky side together, and discard in household trash in a manner that prevents accidental contact or ingestion by children, pets or others.
- Wash the hands and application site after transdermal system removal.

Patients with Open-Angle Glaucoma
Advise patients with open-angle glaucoma to remove the TRANSDERM SCŌP transdermal system immediately and contact their healthcare provider if they experience symptoms of acute angle closure glaucoma, including pain and reddening of the eyes, accompanied by dilated pupils, blurred vision and/or seeing halos around lights *[see Warnings and Precautions (5.1)]*.

Neuropsychiatric Adverse Reactions

- Advise patients that psychiatric adverse reactions may occur, especially in patients with a past psychiatric history or in those receiving other drugs also associated with psychiatric effects, and to report to their healthcare provider any new or worsening psychiatric symptoms.
- Advise patients to discontinue TRANSDERM SCŌP and contact a healthcare provider immediately if they experience a seizure.
- Advise patients, especially elderly patients, that cognitive impairment may occur during treatment with TRANSDERM SCŌP, especially in those receiving other drugs also associated with CNS effects, and to report to their healthcare provider if they develop signs or symptoms of cognitive impairment such as hallucinations, confusion or dizziness.
- Inform patients not to operate motor vehicles or other dangerous machinery or participate in underwater sports until they are reasonably certain that TRANSDERM SCŌP does not affect them adversely *[see Warnings and Precautions (5.2)]*.

Idiosyncratic Reactions

Instruct patients that idiosyncratic reactions may occur with ordinary therapeutic doses of scopolamine *[see Warnings and Precautions (5.3)]*.

Decreased Gastrointestinal Motility and Urinary Retention

Instruct patients to remove the transdermal system if they develop symptoms of intestinal obstruction (abdominal pain, nausea or vomiting) or any difficulties in urinating *[see Warnings and Precautions (5.5)]*.

Drug Withdrawal/Post-Removal Symptoms

Inform patients that if they remove the TRANSDERM SCŌP transdermal system before treatment is complete, withdrawal symptoms may occur and to seek immediate medical care if they develop severe symptoms after removing TRANSDERM SCŌP *[see Warnings and Precautions (5.6)]*.

Blurred Vision

Inform patients that temporary dilation of the pupils and blurred vision may occur if TRANSDERM SCŌP comes in contact with the eyes. Instruct patients to wash their hands thoroughly with soap and water immediately after handling the transdermal system, do not touch the system while wearing it, and wash the application site after transdermal system removal *[see Dosage and Administration (2.1), Warnings and Precautions (5.7)]*.

MRI Skin Burns

Instruct patients to remove the TRANSDERM SCŌP transdermal system before undergoing an MRI *[see Warnings and Precautions (5.8)]*.

Pregnancy

Advise a female patient to inform the prescriber if she is pregnant or planning to become pregnant *[see Use in Specific Populations (8.1)]*.

Lactation

Advise a female patient to inform the prescriber if she is breastfeeding *[see Use in Specific Populations (8.2)]*.

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