

PRODUCT MONOGRAPH

Pr **GELNIQUE**[®]

Oxybutynin Chloride Gel

100 mg oxybutynin chloride per gram of topical gel

Topical Administration Only

Antispasmodic/anticholinergic agent for treatment of overactive bladder

ATC code: G04B D04

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Pr **GELNIQUE**[®]
Oxybutynin Chloride Gel

PART I: HEALTH PROFESSIONAL INFORMATION

SUMMARY PRODUCT INFORMATION

Route of Administration	Dosage Form / Strength	Clinically Relevant Nonmedicinal Ingredients
Transdermal	10% oxybutynin chloride gel	<i>For a complete listing see Dosage Forms, Composition and Packaging sections.</i>

INDICATIONS AND CLINICAL USE

GELNIQUE, (10% oxybutynin chloride gel), is an antispasmodic, anticholinergic agent indicated for:

- The treatment of overactive bladder with symptoms of urge urinary incontinence, urgency, and frequency.

Geriatrics (≥65 years of age): Available data suggest that there are no clinically meaningful differences in the safety or effectiveness between the geriatric subject and younger subjects following administration of GELNIQUE.

Pediatrics (<18 years of age): The safety and effectiveness of GELNIQUE have not been evaluated in individuals younger than 18 years of age (see WARNINGS AND PRECAUTIONS).

CONTRAINDICATIONS

GELNIQUE is contraindicated in patients with urinary retention, gastric retention, severe gastrointestinal condition, myasthenia gravis, or narrow-angle glaucoma and in patients who are at risk for these conditions.

Known serious hypersensitivity reactions to GELNIQUE, oxybutynin, or, to any of the components of GELNIQUE.

WARNINGS AND PRECAUTIONS

Cardiovascular

Caution should be used when prescribing antimuscarinics/anticholinergics to patients with preexisting cardiac diseases.

Renal

The effect of GELNIQUE on patients with renal impairment has not been tested.

Hepatic

The effect of GELNIQUE on patients with hepatic impairment has not been tested.

Angioedema

Angioedema requiring hospitalization and emergency medical treatment has occurred with first or subsequent doses of oral oxybutynin. In the event of angioedema, oxybutynin containing products should be discontinued and appropriate therapy promptly provided.

Skin

Skin areas with eczema, seborrhea or psoriasis should be avoided during application of GELNIQUE because the Oxybutynin Gel has not been tested on patients with these disorders.

Carcinogenesis and Mutagenesis

Carcinogenicity and mutagenicity studies have been performed in animals (see TOXICOLOGY section).

Central Nervous System:

GELNIQUE should be used with caution in patients who have autonomic neuropathy, cognitive impairment or Parkinson's disease.

Gastrointestinal

GELNIQUE should be administered with caution to patients with gastrointestinal obstructive disorders because of the risk of gastric retention.

GELNIQUE, like other anticholinergic drugs, may decrease gastrointestinal motility and should be used with caution in patients with conditions such as ulcerative colitis or intestinal atony. GELNIQUE should be used with caution in patients who have gastroesophageal reflux and/or who are concurrently taking drugs (such as bisphosphonates) that can cause or exacerbate esophagitis.

Genitourinary

GELNIQUE should be administered with caution to patients with clinically significant bladder outflow obstruction because of the risk of urinary retention.

Ophthalmologic

GELNIQUE is contraindicated in patients with uncontrolled narrow-angle glaucoma and in patients at risk of this condition.

Special Populations

Pregnant Women: Reproductive studies with oxybutynin chloride in the mouse, rat, hamster, and rabbit showed no evidence of impaired fertility or harm to the animal fetus. Subcutaneous administration to rats at doses up to 25 mg/kg (approximately 50 times the human exposure based on surface area) and to rabbits at doses up to 0.4 mg/kg (approximately 1 times the human exposure) revealed no evidence of harm to the fetus due to oxybutynin chloride. The safety of GELNIQUE administration to women who are or who may become pregnant has not been established. Therefore, GELNIQUE should not be given to pregnant women unless, in the judgment of the physician, the probable clinical benefits outweigh the possible hazards.

Nursing Women: It is not known whether oxybutynin is excreted in human milk. Because oxybutynin is excreted in the milk of rats, and because many drugs are excreted in human milk, use of GELNIQUE is not recommended during breast-feeding.

Pediatrics (≤ 18 years of age): Safety and effectiveness of GELNIQUE in pediatric patients have not been established.

Geriatrics (≥ 65 years of age): Of the 496 patients exposed to GELNIQUE in the Phase 3 study, 188 patients (38%) were 65 years of age and older. No meaningful differences in safety or effectiveness were observed between these patients and younger patients. An additional study on 153 healthy volunteers [69 – 79 years old] demonstrated that GELNIQUE does not have a clinical meaningful effect on the cognitive function in older adults when compared to placebo.

There is no dose adjustment necessary in this population. GELNIQUE should be used with caution in elderly patients, who may be more sensitive to the effects of centrally acting anticholinergics and may exhibit differences in pharmacokinetics.

Race: Available data suggest that there are no clinically meaningful differences in the pharmacokinetics or treatment outcome of GELNIQUE based on race in healthy volunteers or patients.

ADVERSE REACTIONS

Adverse Drug Reaction Overview

No serious adverse reactions related to treatment were reported. The vast majority of treatment-related adverse reactions were described as mild or moderate in intensity, except for two patients reporting severe headache. The most common treatment-related adverse reactions reported $\geq 2\%$ during the 12-week double blind, placebo controlled Phase 3 study were dry mouth (6.9%) and application site pruritus (2.1%). Other treatment-related adverse reactions observed during the Phase 3, double-blind study, reported in $\geq 1\%$ of GELNIQUE-treated patients included headache, application site dermatitis, constipation, dizziness, and pruritus.

The most common treatment-related adverse reactions reported during the 14-week open-label extension of the Phase 3 study were application site dermatitis (2.3%), application site pruritus (2.3%), application site dryness (1.9%), dry mouth (1.9%) and application site erythema (1.4%).

Clinical Trial Adverse Drug Reactions

Because clinical trials are conducted under very specific conditions the adverse drug reaction rates observed in the clinical trials may not reflect the rates observed in practice and should not be compared to the rates in the clinical trials of another drug. Adverse drug reaction information from clinical trials is useful for identifying drug-related adverse events and for approximating rates.

The safety of GELNIQUE was evaluated in 789 patients during a randomized, placebo-controlled, double-blind, 12-week Phase 3 clinical efficacy and safety study and a 14-week open-label safety extension.

A subset of patients (N=216) participated in an open-label safety extension. One hundred nine of the patients who participated in the safety extension had previously received GELNIQUE in the double-blind period and received GELNIQUE treatment for up to 26 weeks.

No deaths were reported during the Phase 3 study.

Table 1 Treatment-Related Adverse Reactions ($\geq 1\%$ for GELNIQUE) for the Double-Blind Period (Safety Population)

Adverse Event	GELNIQUE (N=389) % of patients	Placebo (N=400) % of patients
Nervous System Disorders		
Headache	1.5	2.8
Dizziness	1.5	0.5
Gastrointestinal Disorders		
Constipation	1.3	1.0
Dry mouth	6.9	2.8

Adverse Event	GELNIQUE (N=389) % of patients	Placebo (N=400) % of patients
General Disorders and Administration Site Conditions		
Application site dermatitis	1.8	0.3
Application site pruritus	2.1	0.8
Skin and Subcutaneous Tissue Disorders		
Pruritus	1.3	1.3

Equal numbers of patients in the active (1.8%) and placebo (1.8%) groups discontinued treatment due to treatment-related adverse events during the double-blind treatment period. No patient discontinued GELNIQUE therapy primarily due to dry mouth. The most common adverse event leading to drug discontinuation was application site reaction (0.8% with GELNIQUE versus 0.3% with placebo). During the double-blind period, no patients discontinued GELNIQUE treatment primarily due to dry mouth, and 0.8% discontinued due to application site reactions.

Post-Market Adverse Drug Reactions

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

Nervous System Disorders: confusion

Psychiatric Disorders: hallucinations

DRUG INTERACTIONS

Overview

Because anticholinergic agents such as oxybutynin may produce drowsiness, somnolence, or blurred vision, patients should be advised to exercise caution. Patients should be informed that alcohol may enhance the drowsiness caused by anticholinergic agents such as oxybutynin. Anticholinergic agents may potentially alter the absorption of some concomitantly administered drugs due to effects on gastrointestinal motility.

Other Anticholinergics:

The concomitant use of oxybutynin chloride with other anticholinergic agents may increase the frequency and/or severity of dry mouth, constipation, blurred vision and other anticholinergic pharmacological effects.

The anticholinergic activity of oxybutynin is increased by concurrent use of other anticholinergics or medicinal products with anticholinergic activity, such as antiparkinsonian medicinal products, antihistamines, antipsychotics, quinidine, tricyclic antidepressants, atropine and related compounds like atropinic antispasmodic drugs and dipyrindamole.

Cytochrome P450 Enzyme Inhibitors:

Pharmacokinetic studies have not been performed with patients concomitantly receiving cytochrome P450 enzyme inhibitors, such as antimycotic agents (e.g. ketoconazole, itraconazole, and miconazole) or macrolide antibiotics (e.g. erythromycin and clarithromycin). No specific drug-drug interaction studies have been performed with GELNIQUE, but interactions cannot be ruled out. Consumption of grapefruit juice may also influence the metabolism of oxybutynin.

Drug-Drug Interactions

Interactions with other drugs have not been established

Drug-Food Interactions

Interactions with food have not been established

Drug-Herb Interactions

Interactions with herbal products have not been established.

Drug-Laboratory Test Interactions

Interactions with laboratory tests have not been established.

DOSAGE AND ADMINISTRATION

Recommended Dose

The contents of one sachet (each gram of gel containing 100 mg oxybutynin chloride) of GELNIQUE should be applied once daily to dry, intact skin on the abdomen, upper arms/shoulders, or thighs. GELNIQUE is intended for topical application only and is not meant to be ingested.

Missed Dose

Daily treatment with GELNIQUE is recommended to maintain therapeutic blood levels of oxybutynin for optimal treatment of symptoms resulting from overactive bladder. If on occasion a daily treatment is missed, the patient should resume treatment with the recommended daily dose, one sachet, the following day.

Administration

GELNIQUE is a topical gel formulation designed for daily application. The gel should be applied immediately after the sachet is opened. Application sites should be rotated. Application of GELNIQUE should not be made to the same site on consecutive days. GELNIQUE should

not be applied to a recently shaved skin surface or skin areas with eczema, seborrhea or psoriasis. Open flames and smoking close to the application site should be avoided.

OVERDOSAGE

Overdosage with oxybutynin has been associated with anticholinergic effects including CNS excitation, flushing, fever, dehydration, cardiac arrhythmia, vomiting, and urinary retention. Oral ingestion of 100 mg oxybutynin chloride in association with alcohol has been reported in a 13-year-old boy who experienced memory loss, and in a 34-year-old woman who developed stupor, followed by disorientation and agitation on awakening, dilated pupils, dry skin, cardiac arrhythmia, and retention of urine. Both patients recovered fully with symptomatic treatment.

Plasma concentrations of oxybutynin begin to decline 24 hours after GELNIQUE application. Patients should be monitored until symptoms resolve.

For management of a suspected overdose, contact a regional Poison Control Centre.

ACTION AND CLINICAL PHARMACOLOGY

Mechanism of Action

Oxybutynin acts as a competitive antagonist of acetylcholine at postganglionic muscarinic receptors, resulting in relaxation of bladder smooth muscle. In patients with conditions characterized by involuntary detrusor contractions, cystometric studies have demonstrated that oxybutynin increases maximum urinary bladder capacity and increases the volume to first detrusor contraction. Oxybutynin thus decreases urinary urgency and the frequency of both incontinence episodes and voluntary urination.

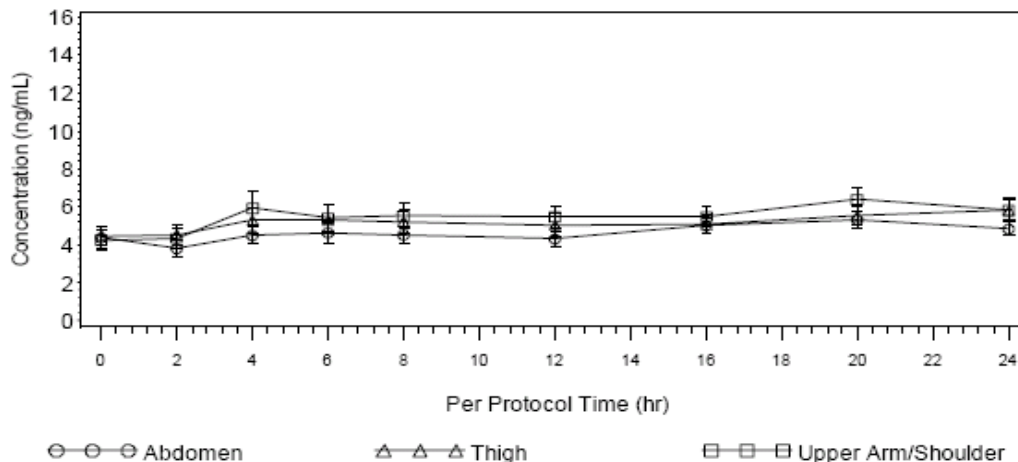
Oxybutynin is a racemic (50:50) mixture of R- and S- isomers. Antimuscarinic activity resides predominantly with the R-isomer. The active metabolite, N-desethyloxybutynin, has pharmacological activity on the human detrusor muscle that is similar to that of oxybutynin in *in-vitro* studies.

Pharmacokinetics

Absorption

Oxybutynin is transported across intact skin and into the systemic circulation by passive diffusion across the stratum corneum. Steady-state concentrations are achieved within 7 days of continuous dosing. Absorption of oxybutynin is similar when GELNIQUE is applied to the abdomen, upper arm/shoulders or thighs. Mean plasma concentrations during a randomized, crossover study of the three recommended application sites in 39 healthy men and women are shown in Figure 1.

Figure 1 Mean (\pm SEM) plasma oxybutynin concentrations during steady-state application of GELNIQUE to the abdomen, upper arm/shoulder and thigh (N=39).



Average steady-state plasma oxybutynin concentrations were 4.7, 5.2, and 5.5 ng/mL for the abdomen, upper arm/shoulder and thigh application sites, respectively (Table 2).

Table 2 Mean (SD) steady-state pharmacokinetic parameters for oxybutynin following GELNIQUE application to the abdomen, upper arm/shoulder and thigh (N=39).

Application Site	AUC ₀₋₂₄ (ng·hr/mL)	C _{max} (ng/mL)	C _{avg} (ng/mL)
Abdomen	112.7 (58.00)	6.8 (3.93)	4.7 (2.39)
Upper Arm/Shoulder	133.8 (81.58)	8.3 (5.97)	5.5 (3.37)
Thigh	125.1 (84.67)	7.0 (4.95)	5.2 (3.50)

Following intravenous administration, the elimination half-life of oxybutynin is approximately 2 hours. After the final steady-state dose of GELNIQUE, oxybutynin and N-desethyloxybutynin [DEO, active metabolite] demonstrated biphasic elimination with plasma concentrations beginning to decrease 24 hours after dosing. Elimination was more rapid between 24 and 48 hours after dosing, during which time plasma concentrations of oxybutynin and N-desethyloxybutynin declined by about one-half. The initial elimination phase was followed by a more prolonged terminal elimination phase. The apparent elimination half-lives including the terminal elimination phase were 64 hours and 82 hours for oxybutynin and DEO, respectively.

A randomized crossover study comparing the steady-state pharmacokinetics of GELNIQUE and 3.9 mg/day Oxytrol® transdermal system confirmed that GELNIQUE provides similar delivery of oxybutynin as Oxytrol (nominal delivery of 4 mg/day) (Table 3).

Table 3 Oxybutynin pharmacokinetic parameters at steady-state for GELNIQUE and Oxytrol.

Parameter	Statistic	GELNIQUE (N=20)	Oxytrol (N=20)
AUC _[0-96] (ng·hr/mL)	Mean (SD)	321.7 (112.3)	312.5 (67.62)
	Min, Max	146.8, 578.5	191.5, 430.0
C _{avg} (ng/mL)	Mean (SD)	3.35 (1.17)	3.26 (0.70)
	Min, Max	1.53, 6.03	1.99, 4.48
C _{max} (ng/mL)	Mean (SD)	5.99 (2.58)	4.82 (1.31)
	Min, Max	2.30, 10.20	2.35, 8.16

Distribution

Oxybutynin is widely distributed in body tissues following systemic absorption. The volume of distribution was estimated to be 193 L after intravenous administration of 5 mg oxybutynin chloride.

Metabolism

Oxybutynin is metabolized primarily by the cytochrome P450 enzyme systems, particularly CYP3A4, found mostly in the liver and gut wall. Metabolites include phenylcyclohexylglycolic acid, which is pharmacologically inactive, and N-desethyloxybutynin, which is pharmacologically active.

Transdermal administration of oxybutynin bypasses the first-pass gastrointestinal and hepatic metabolism, reducing the formation of the N-desethyloxybutynin metabolite. Only small amounts of CYP3A4 are found in skin, limiting pre-systemic metabolism during transdermal absorption. The resulting plasma concentration AUC ratio of N-desethyloxybutynin metabolite to parent compound following multiple transdermal applications is approximately 1:1 for GELNIQUE.

Excretion

Oxybutynin is extensively metabolized by the liver, with less than 0.1% of the administered dose excreted unchanged in the urine. Also, less than 0.1% of the administered dose is excreted as the metabolite N-desethyloxybutynin.

Special Populations and Conditions

Race

Available data suggest that there are no clinically meaningful differences in the pharmacokinetics or treatment outcome of GELNIQUE based on race in healthy volunteers or patients.

Geriatric

Available data suggest that there are no clinically meaningful differences in the pharmacokinetics or treatment outcomes of oxybutynin based on geriatric status in patients following administration of GELNIQUE.

Pediatric

The pharmacokinetics of oxybutynin and N-desethyloxybutynin has not been evaluated in individuals younger than 18 years of age following GELNIQUE application.

Gender

Available data suggest that there are no clinically meaningful differences in the pharmacokinetics or treatment outcomes of oxybutynin based on gender in healthy volunteers or patients following administration of GELNIQUE.

STORAGE AND STABILITY

Store at controlled room temperature (15 to 30°C). Protect from moisture. Apply immediately after the sachets are opened and contents.

SPECIAL HANDLING INSTRUCTIONS

Discard used sachets in household trash in a manner that prevents accidental application or ingestion by children, pets, or others.

DOSAGE FORMS, COMPOSITION AND PACKAGING

GELNIQUE comes in a carton of 30 sachets. Each sachet contains a 1 gram unit dose (1.14 mL) of 100 mg/g oxybutynin chloride gel.

Non-medicinal ingredients: alcohol, glycerin, hydroxypropyl cellulose, sodium hydroxide, and purified water.

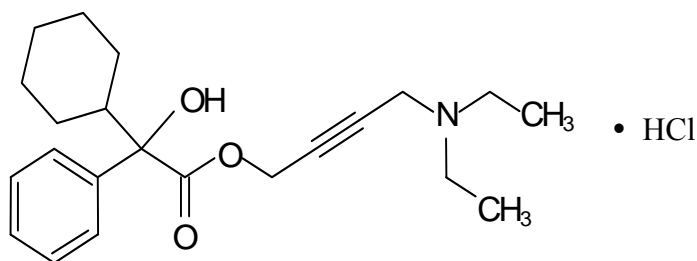
PART II: SCIENTIFIC INFORMATION

PHARMACEUTICAL INFORMATION

Drug Substance

Proper Name:	Oxybutynin chloride
Chemical Name:	4-(Diethylamino)-2-butynyl (±)- α -phenylcyclohexaneglycolate hydrochloride.

Structural Formula:



Molecular Formula: C₂₂H₃₁NO₃ · HCl

Molecular Weight: 393.95

Description: White powder

Physicochemical properties: Oxybutynin chloride is white to off-white crystalline powder with a melting range of 124 -129°C. Oxybutynin chloride is freely soluble in water and in alcohol; very soluble in methanol and in chloroform; soluble in acetone; slightly soluble in ether; very slightly soluble in hexane.

CLINICAL TRIALS

Study Demographics and Trial Design

Phase 3 Study

The efficacy and safety of GELNIQUE were evaluated in patients with urge urinary incontinence in a single Phase 3 study.

The Phase 3 study was a randomized, double-blind, placebo-controlled, parallel group study that included 789 patients. The 12-week double-blind treatment included daily applications of GELNIQUE or matching placebo gel. A 14-week, open-label treatment was available for a subset of patients who completed the double-blind period. The majority of patients were Caucasian (86.3%) and female (89.2%), with a mean age of 59.4 years (range: 18 to 88 years). Approximately 25% of patients were receiving pharmacological treatment prior to starting study. Patients with gastrointestinal obstructive disorders, narrow angle glaucoma, clinically significant bladder outflow obstruction, urinary tract infection, prostatitis, BPH, urethral diverticulum and skin disorders [i.e. eczema, seborrhea, psoriasis] on gel application areas were excluded from the studies.

Study Results

Patients treated with GELNIQUE experienced a highly statistically significant decrease in the number of urinary incontinence episodes per day from baseline to endpoint (the primary efficacy endpoint) compared with placebo ($p < 0.0001$), as well as for the secondary endpoints: a decrease in the average daily urinary frequency ($p = 0.0017$), and an increase in the average urine volume per void ($p = 0.0018$). Significant improvements in the quality of life evaluations measured during the study were also observed with GELNIQUE.

Mean and median change from baseline in daily incontinence episodes, urinary frequency, and urinary void volume between placebo and active treatment groups are summarized in Table 4.

Table 4 Mean and median change from baseline for incontinence episodes, urinary frequency, and urinary void volume at Week 12 (LOCF)

Parameter	GELNIQUE (N=389)		Placebo (N=400)	
	Mean (SD)	Median	Mean (SD)	Median
Daily Incontinence Episodes				
Baseline	5.4 (3.26)	4.7	5.4 (3.28)	4.7
Change from baseline	-3.0 (2.73)	-2.7	-2.5 (3.06)	-2.0
P-value vs. placebo	<0.0001		--	
Daily Urinary Frequency				
Baseline	12.4 (3.34)	11.7	12.2 (3.32)	11.3
Change from baseline	-2.7 (3.21)	-2.7	-2.0 (2.82)	-1.7
P-value vs. placebo	0.0017		--	
Urinary Void Volume (mL)				
Baseline	163.4 (65.85)	160.1	167.9 (68.40)	160.6
Change from baseline	21.0 (65.33)	11.5	3.8 (53.79)	0.0
P-value vs. placebo	0.0018		--	

During the double-blind treatment a significant positive effect on quality of life was seen with GELNIQUE based on the Incontinence Impact Questionnaire (IIQ) and Kings Health Questionnaire (KHQ). These results were evident after the first month of treatment and were maintained throughout double-blind treatment (Table 5).

Table 5 Mean (SD) change from baseline for IIQ total score and subscales at Week 12 (LOCF).

Score	GELNIQUE (N=389)	Placebo (N=400)	P-value (GELNIQUE vs. Placebo)
Total Score	-72.1 (80.01)	-49.5 (76.59)	0.0005
Travel Subscale	-20.9 (25.55)	-15.1 (24.82)	0.0068
Physical Activity Subscale	-18.0 (23.23)	-13.0 (21.68)	0.0078
Social Relationships Subscale	-15.2 (20.07)	-9.7 (19.27)	0.0019
Emotional Health Subscale	-18.1 (21.96)	-11.8 (20.64)	0.0002

Significant positive effects were noted for each subscale domain of the IIQ and for six of ten quality of life domains, including the incontinence impact domain, of the King’s Health Questionnaire (Table 6).

Table 6 Mean (SD) change from baseline in KHQ Domain Scores at Week 12 (LOCF).

Domain	GELNIQUE (N=389)	Placebo (N=400)	P-value (GELNIQUE vs. Placebo)
General Health Perception	0.4 (12.23)	0.1 (11.94)	0.6528
Incontinence Impact	-27.9 (30.02)	-21.3 (27.05)	0.0023
Symptom Severity	-20.6 (22.90)	-15.8 (21.84)	0.0024
Role Limitations	-27.1 (29.24)	-21.3 (27.16)	0.0133
Physical Limitations	-20.2 (30.04)	-16.8 (28.12)	0.1064
Social Limitations	-11.5 (24.40)	-10.3 (23.46)	0.4468
Personal Relationships	-11.2 (24.96)	-6.2 (19.77)	0.0489
Emotions	-11.7 (24.59)	-8.4 (24.89)	0.0649
Sleep and Energy	-15.6 (24.18)	-10.3 (22.42)	0.0061
Severity (Coping) Measures	-15.3 (21.40)	-11.1 (19.16)	0.0058

DETAILED PHARMACOLOGY

Person-to-Person Transference

The potential for dermal transfer of oxybutynin from a treated person to an untreated person was evaluated in a single-dose study where subjects dosed with GELNIQUE engaged in vigorous contact with an untreated partner for 15 minutes, either with (N=14 couples) or without (N=12 couples) clothing covering the application area. The untreated partners not protected by clothing demonstrated detectable plasma concentrations of oxybutynin (mean C_{max} = 0.94 ng/mL). Two of the 14 untreated subjects participating in the clothing-to-skin contact regimen had measurable oxybutynin plasma concentrations ($C_{max} \leq 0.1$ ng/mL) during the 48 hours following contact with treated subjects; oxybutynin was not detectable with the remaining 12 untreated subjects.

Concomitant Use with Sunscreen

The effect of oil-free sunscreen on the absorption of oxybutynin when applied 30 minutes before or 30 minutes after GELNIQUE application was evaluated in a single-dose randomized crossover study (N=16). Concomitant application of oil-free sunscreen, either before or after GELNIQUE application, had no effect on the systemic exposure of oxybutynin. The effect of oil-containing sunscreen on GELNIQUE absorption and systemic exposure as not been tested.

Effects of Showering

The effect of showering on the absorption of oxybutynin was evaluated in a randomized, steady-state crossover study under conditions of no shower, or showering 1, 2 or 6 hours after GELNIQUE application (N=20). The results of the study indicate that showering after one hour does not affect the overall systemic exposure to oxybutynin.

TOXICOLOGY

A 24-month study in rats at dosages of oxybutynin chloride of 20, 80 and 160 mg/kg showed no evidence of carcinogenicity. These doses are approximately 6, 25 and 50 times the maximum exposure in humans taking an oral dose, based on body surface area. Oxybutynin chloride showed no increase of mutagenic activity when tested in *Schizosaccharomyces pompholiciformis*, *Saccharomyces cerevisiae*, and *Salmonella typhimurium* test systems. Reproduction studies with oxybutynin chloride in the mouse, rat, hamster, and rabbit showed no definite evidence of impaired fertility.

PART III: CONSUMER INFORMATION

Pr **GELNIQUE**[®]
Oxybutynin Chloride Gel

This leaflet is Part III of the three-part “Product Monograph” published when GELNIQUE was approved for sale in Canada and is designed specifically for consumers. This leaflet is a summary and will not tell you everything about GELNIQUE. Contact your doctor or pharmacist if you have any questions about the drug.

ABOUT THIS MEDICATION

What the medication is used for:

GELNIQUE is used to relieve symptoms of overactive bladder which include the frequent and urgent need to urinate with or without urine leakage.

What it does:

GELNIQUE works on special areas of the bladder nerves which cause the bladder muscles to stop contracting and become relaxed. The bladder relaxes and is able to hold more urine allowing for longer periods of time between having to urinate. You may not have to urinate as frequently, with as great urgency, and therefore may be able to expel a larger amount of urine when you urinate.

When it should not be used:

Do not use GELNIQUE if you have the following medical conditions:

- Urinary retention. Your bladder does not empty or does not empty completely when you urinate.
- Gastric retention. Your stomach empties slowly or incompletely after a meal.
- Severe stomach problems: Tell your doctor if you have any stomach problems.
- Myasthenia gravis (a condition causing weakness of certain muscles). Tell your doctor if you have this condition.
- Narrow-angle glaucoma (high pressure in your eye). Tell your doctor if you have glaucoma or a family history of glaucoma.
- Allergy (serious hypersensitivity) to oxybutynin chloride or the inactive ingredients in GELNIQUE.

What the medicinal ingredient is:

Oxybutynin chloride

What the nonmedicinal ingredients are:

Alcohol, glycerin, hydroxypropyl cellulose, sodium hydroxide, and purified water.

What dosage form it comes in:

GELNIQUE is gel for topical skin application. Each gram of gel contains 100 mg oxybutynin chloride.

WARNINGS AND PRECAUTIONS

Before you use GELNIQUE, tell your doctor about all your medical conditions, especially if you have any of the following:

- Heart disease
- Liver disease
- Kidney disease
- Difficulty in emptying bladder completely
- Constipation or difficulty in emptying bowels
- Ulcerative colitis (inflamed bowels)
- Gastric reflux disease (heartburn) or esophagitis (inflamed esophagus, the tube between your mouth and stomach), and/or if you are taking drugs that may worsen esophagitis such as bisphosphonates (a type of bone loss preventing drug).
- Skin problems such as eczema, seborrhea, or psoriasis. GELNIQUE has not been tested on patients with these skin disorders.
- Autonomic neuropathy (damage to nerves)
- Cognitive impairment (problems with memory, language, thinking or judgment)
- Parkinson’s disease (movement disorder)
- Pregnant or plan to become pregnant. Tell your doctor immediately if you are pregnant or think you might be pregnant. Your doctor will discuss with you the possible risks of taking GELNIQUE during pregnancy.
- Breastfeeding. It is not known if GELNIQUE passes into your breast milk. Do not take GELNIQUE if you are breastfeeding.
- Elderly. You may be more sensitive to the effects of GELNIQUE.

Angioedema (a swelling on the face, hands, throat, and tongue) required emergency treatment has been reported with the use of oral oxybutynin.

IMPORTANT: PLEASE READ

GELNIQUE may cause sleepiness or blurred vision. Do not driving or operate machinery until you know how GELNIQUE affects you. Drinking alcoholic beverages may increase these effects.

GELNIQUE treatment may decrease sweating. You may overheat or have fever, heat stroke, or heat prostration if you are in warm or hot temperatures.

INTERACTIONS WITH THIS MEDICATION

Tell your doctor about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

The following may interact with GELNIQUE:

- Antiparkinsonian drugs – medicines used to treat Parkinson’s disease
- Antihistamines – medicines often found in cold and allergy remedies
- Antipsychotics – medicines used to treat mental disorders like schizophrenia
- Tricyclic antidepressants – medicines used to treat depression as well as other conditions
- Quinidine – a drug used to treat abnormal heart rhythms
- Atropine – a drug used in many medical situations (e.g., during surgery, to treat eye problems, etc.)
- Atropinic antispasmodic drugs – medicines used to treat muscle spasms
- Dipyridamole – a drug used to prevent blood clots and widen blood vessels

PROPER USE OF THIS MEDICATION

GELNIQUE is a gel which contains alcohol. Gels with alcohol are flammable. Avoid fire, flame or smoking until the gel has dried.

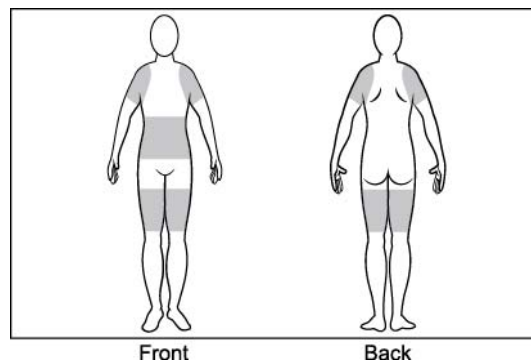
GELNIQUE should be applied to the skin only. GELNIQUE SHOULD NOT BE TAKEN BY MOUTH.

Important: Avoid contact with eyes, nose, open sores, recently shaved skin, and skin with rashes or other areas not approved for the application of GELNIQUE.

Do not apply GELNIQUE to areas of the skin that have been treated with oils, lotions, or powders as that could affect the amount of oxybutynin absorbed through the

skin. However, GELNIQUE may be used with oil-free sunscreen.

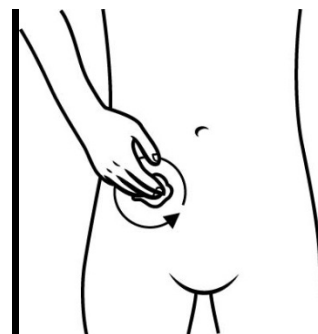
Step 1. The approved application sites for GELNIQUE are the abdomen (stomach), upper arms/shoulder, and thigh. The approved application sites are shown below.



Step 2. Wash your hands with soap and water before applying GELNIQUE.

Step 3. Wash the area where GELNIQUE will be applied with mild soap and water. Allow the area to dry completely.

Step 4. Gently rub GELNIQUE into your skin until it dries. Do not continue rubbing after GELNIQUE has dried. If applying GELNIQUE to the stomach, care should be taken to avoid the area around the navel (belly-button).



Step 5. After applying GELNIQUE, immediately wash your hands thoroughly with soap and water.

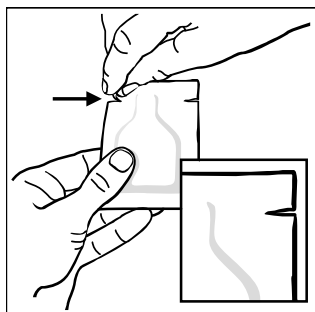
Avoid bathing, swimming, showering, exercising or immersing the application site in water for one hour after application.

IMPORTANT: PLEASE READ

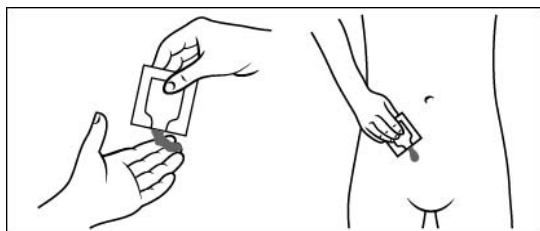
The application site may be covered with clothing once GELNIQUE has dried.

How to use the GELNIQUE packets:

Step 1. Tear the sachet of GELNIQUE open at the indentation just before use.



Squeeze the entire contents of the packet (1.14 mL) into the palm of your hand. Squeeze from the bottom of the packet toward the open end. Repeat until the packet is empty. The contents of the sachet can also be squeezed directly onto the site of application. The amount of gel in each packet is 1.14 mL. It will be about the size of a nickel in your hand.



Step 2. Carefully throw away the open packet of GELNIQUE so that children and pets are not exposed to it.

Overdose:

If you apply more than the recommended dose of GELNIQUE, contact your doctor or the nearest regional Poison Control Centre.

Missed dose:

If you miss a dose, take the next dose the following day. Do not try to make up for the missed dose.

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

You may see mild redness at the site when a patch is removed. This redness should disappear within several hours after removing the patch. If uncomfortable irritation or excessive itchiness continues, tell your doctor.

The most common side effects of GELNIQUE are skin reactions where the patch is put on. These include itching and redness. Other side effects include dry mouth, constipation, abnormal vision and headache. If you take other medicines that cause dry mouth, constipation, or sleepiness, GELNIQUE can increase those effects.

Oxybutynin therapy has been associated with skin rash, painful urination, nausea, abdominal pain, back pain, fatigue, confusion and hallucinations.

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM

Symptom / effect		Talk with your Doctor or pharmacist		Stop taking drug and call your doctor or pharmacist
		Only if severe	In all cases	
Common	Dizziness	√		
	Constipation	√		
Uncommon	Difficulty urinating		√	
	Application site reaction (blisters, numbness, redness, dryness, and/or pain)	√		

This is not a complete list of side effects. For any unexpected effects while taking GELNIQUE, contact your doctor or pharmacist.

HOW TO STORE GELNIQUE

Store at controlled room temperature (15 to 30° C). Protect from moisture. Apply immediately after the sachets are opened. Discard used sachets in household trash in a manner that prevents accidental application or ingestion by children, pets, or others.

REPORTING SUSPECTED SIDE EFFECTS

You can report any suspected adverse reactions associated with the use of health products to the Canada Vigilance Program by one of the following 3 ways:

- Report online at www.healthcanada.gc.ca/medeffect
- Call toll-free at 1-866-234-2345
- Complete a Canada Vigilance Reporting Form and :
 - Fax toll-free to 1-866-678-6789, or
 - Mail to: Canada Vigilance Program
Health Canada
Postal Locator 1908C
Ottawa, Ontario
K1A 0K9

Postage paid labels, Canada Vigilance Reporting Form and the adverse reaction reporting guidelines are available on the MedEffect™ Canada Web site at www.healthcanada.gc.ca/medeffect

Note: Should you require information related to the management of side effects, contact your health professional. The Canada Vigilance Program does not provide medical advice.

MORE INFORMATION

This document plus the full product monograph, prepared for health professionals, can be found at www.allergan.ca or by contacting Allergan Pharma Co. at 1-800-668-6424.

This leaflet was prepared by:
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