PRODUCT MONOGRAPH

[Pr]Teva-Oxybutynin

oxybutynin chloride tablets, USP, 5 mg

Anticholinergic/Antispasmodic Agent

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PART I: HEALTH PROFESSIONAL INFORMATION

SUMMARY PRODUCT INFORMATION

Route of Administration	Dosage Form / Strength	Clinically Relevant Nonmedicinal Ingredients
oral	tablet, 5 mg	Lactose *For a complete listing of nonmedicinal ingredients, see* **DOSAGE FORMS, COMPOSITION AND PACKAGING** *section.*

INDICATIONS AND CLINICAL USE

Teva-Oxybutynin (oxybutynin chloride) is indicated for the relief of symptoms associated with voiding in patients with uninhibited neurogenic bladder and reflex neurogenic bladder (i.e., urgency, frequency, urinary leakage, urge incontinence, dysuria).

Geriatrics (> 65 years of age):
Clinical studies of oxybutynin chloride did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger patients. Other reported clinical experience has not identified differences in responses between healthy elderly and younger patients.

Pediatrics (< 5 years of age):
The safety and effectiveness of Teva-Oxybutynin in pediatric patients under 5 years of age have not been established.

CONTRAINDICATIONS

Teva-Oxybutynin is contraindicated in patients with urinary retention, gastric retention and other severe decreased gastrointestinal motility conditions, uncontrolled narrow-angle glaucoma, and in patients who are at risk for these conditions.

Teva-Oxybutynin is contraindicated in patients who have demonstrated hypersensitivity to the drug substance or other components of the product. For a complete listing of the nonmedicinal ingredients, see the **DOSAGE FORMS, COMPOSITION AND PACKAGING** section of the Product Monograph.

WARNINGS AND PRECAUTIONS

General

Anticholinergics, such as Teva-Oxybutynin can cause heat prostration (fever and heat stroke due to decreased sweating) when administered in the presence of high environmental temperature.

Because anticholinergic agents, such as Teva-Oxybutynin, may produce drowsiness or blurred vision, the patient should be cautioned regarding activities requiring mental alertness, such as operating a motor vehicle or other machinery or performing hazardous work while taking this drug.

Alcohol or other sedative drugs may enhance the drowsiness caused by anticholinergic agents such as Teva-Oxybutynin.

Pretreatment examinations should include cystometry and other appropriate diagnostic procedures. Cystometry should be repeated at appropriate intervals to evaluate response to therapy. The appropriate antibiotic therapy should be instituted in the presence of infection.

Carcinogenesis and Mutagenesis

See ***Product Monograph Part II*: TOXICOLOGY, Carcinogenesis and Mutagenesis**, for discussion on animal data.

Cardiovascular

The symptoms of coronary heart disease, congestive heart failure, cardiac arrhythmias, tachycardia and hypertension may be aggravated following administration of Teva-Oxybutynin.

Endocrine and Metabolism

The symptoms of hyperthyroidism and prostatic hypertrophy may be aggravated following administration of Teva-Oxybutynin.

Gastrointestinal

Teva-Oxybutynin should be administered with caution to patients with gastrointestinal obstructive disorders because of the risk of gastric retention (see **CONTRAINDICATIONS**).

Administration of oxybutynin chloride to patients with severe ulcerative colitis may precipitate toxic megacolon.

Teva-Oxybutynin, like other anticholinergic drugs, may decrease gastrointestinal motility and should be used with caution in patients with conditions such as ulcerative colitis and intestinal atony (see **CONTRAINDICATIONS**).

Teva-Oxybutynin 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
Teva-Oxybutynin should be administered with caution to patients with clinically significant bladder obstruction because of the risk of urinary retention (see **CONTRAINDICATIONS**).

Hepatic
Teva-Oxybutynin should be used with caution in patients with hepatic disease.

Neurologic
Teva-Oxybutynin, like other anticholinergic drugs, should be used with caution in patients with pre-existing dementia treated with cholinesterase inhibitors due to the risk of aggravation of symptoms.

Teva-Oxybutynin should be used with caution in patients with myasthenia gravis.

Renal
Teva-Oxybutynin should be used with caution in patients with renal disease.

Special Populations

Pregnant Women: The safety of oxybutynin chloride in pregnancy has not been established. Therefore, Teva-Oxybutynin should not be used in women of child-bearing potential, unless, in the opinion of the physician, the expected benefit to the patient outweighs the possible risk to the fetus.

Nursing Women: It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when Teva-Oxybutynin is administered to a nursing woman.

Pediatrics (< 5 years of age): Because the safety of oxybutynin chloride in children under the age of 5 has not been established, use of the drug in this age group is not recommended.

Geriatrics (> 65 years of age): Teva-Oxybutynin should be used with caution in the frail elderly.

ADVERSE REACTIONS

Adverse Drug Reaction Overview

The most common adverse events reported were the expected side effects of anticholinergic agents which include but are not limited to dry mouth, constipation and blurred vision. The incidence of dry mouth was dose related.

Clinical Trial Adverse Drug Reactions

Because clinical trials are conducted under very specific conditions the adverse 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 and efficacy of oxybutynin chloride were evaluated in a total of 199 patients in three clinical trials comparing oxybutynin chloride with oxybutynin chloride XL (see Table 1.1). These participants were treated with oxybutynin chloride 5-20 mg/day for up to 6 weeks. Table 1.1 shows the incidence of adverse events judged by investigators to be at least possibly related to treatment and reported by at least 1% of patients.

Table 1.1: Incidence (%) of Adverse Events Reported by ≥1% of Patients Using Oxybutynin chloride (5-20 mg/day)

Body System	Adverse Event	Oxybutynin chloride (5-20 mg/day) (n=199)
Infections and Infestations	Urinary tract infection	6.5%
	Nasopharyngitis	1.5%
	Upper respiratory tract infection	2.5%
	Bronchitis	2.0%
	Cystitis	1.0%
	Fungal infection	1.0%
Metabolism and Nutrition Disorders	Fluid retention	1.0%
Psychiatric Disorders	Insomnia	5.5%
	Nervousness	6.5%
	Confusional state	2.5%
Nervous System Disorders	Headache	7.5%
	Somnolence	14.1%
	Dizziness	16.6%
	Dysgeusia	1.5%
	Sinus headache	2.0%
Eye Disorders	Keratoconjunctivitis sicca	2.5%
	Vision blurred	9.6%
	Eye irritation	1.0%
Cardiac Disorders	Palpitations	4.5%
	Sinus arrhythmia	1.0%
Vascular Disorders	Flushing	1.0%

Table 1.1: Incidence (%) of Adverse Events Reported by ≥1% of Patients Using oxybutynin chloride (5-20 mg/day) (cont'd)

Body System	Adverse Event	oxybutynin chloride (5-20 mg/day) (n=199)
Respiratory, Thoracic and Mediastinal Disorders	Nasal drying	4.5%
	Cough	3.0%
	Pharyngolaryngeal pain	1.5%
	Dry throat	2.5%
	Sinus congestion	2.0%
	Hoarseness	1.0%
	Asthma	1.0%
	Nasal congestion	2.0%
Gastrointestinal Disorders	Dry mouth	71.4%
	Constipation	15.1%
	Diarrhea	3.5%
	Nausea	11.6%
	Dyspepsia	6.0%
	Abdominal pain	2.5%
	Loose stools	3.0%
	Flatulence	2.5%
	Vomiting	1.5%
	Abdominal pain upper	3.0%
	Dysphagia	1.5%
	Aptyalism	1.0%
	Eructation	1.0%
	Tongue coated	1.0%
Skin and Subcutaneous Tissue Disorders	Dry skin	3.0%
	Pruritus	1.5%
Musculoskeletal and Connective Tissue Disorders	Back pain	2.0%
	Arthralgia	2.0%
	Pain in extremity	1.0%
	Flank pain	1.0%
Renal and Urinary Disorders	Urinary retention	6.0%
	Urinary hesitation	8.5%
	Dysuria	2.5%
	Pollakiuria	1.0%
General Disorders and Administration Site Conditions	Fatigue	3.0%
	Edema peripheral	4.0%
	Asthenia	2.5%
	Pain	1.0%
	Thirst	1.0%
	Edema	1.0%
Investigations	Blood pressure increased	1.5%
	Blood glucose increased	1.5%
	Blood pressure decreased	1.0%
Injury, Poisoning and Procedural Complications	Fall	1.0%

In addition, the following adverse events were reported by <1% of patients using oxybutynin chloride (5-20 mg/day) in all studies:

Gastrointestinal Disorders: gastroesophageal reflux disease; *General Disorders and Administration Site Conditions:* chest pain; *Infections and Infestations:* sinusitis.

Other adverse events that have been reported include: tachycardia, hallucinations, cycloplegia, mydriasis, impotence, suppression of lactation, rash, decreased gastrointestinal motility, convulsions, decreased sweating, difficulty swallowing, increased ocular tension, chest pain, syncope, nose bleed, weakness, mood changes, anorexia, bloated feeling, interference with normal heat regulation, severe allergic reactions or drug idiosyncrasies including urticaria and other dermal manifestations.

DRUG INTERACTIONS

Overview

The concomitant use of oxybutynin with other anticholinergic drugs or with other agents which produce dry mouth, constipation, somnolence (drowsiness), and/or other anticholinergic-like effects may increase the frequency and/or severity of such effects.

Anticholinergic agents may potentially alter the absorption of some concomitantly administered drugs due to anticholinergic effects on gastrointestinal motility. This may be of concern for drugs with a narrow therapeutic index.

Drug-Drug Interactions

Mean oxybutynin plasma concentrations were approximately 3- to 4-fold higher when oxybutynin chloride was administered with ketoconazole, a potent CYP3A4 inhibitor.

Other inhibitors of the cytochrome P450 3A4 enzyme system, such as antimycotic agents (e.g., itraconazole and miconazole) or macrolide antibiotics (e.g., erythromycin and clarithromycin), may alter oxybutynin mean pharmacokinetic parameters (i.e., C_{max} and AUC). The clinical relevance of such potential interactions is not known. Caution should be used when such drugs are co-administered.

Drug-Food Interactions

Oxybutynin solution co-administered with food resulted in a slight delay in absorption and an increase in its bioavailability by 25%.

Drug-Herb Interactions

Interactions with herbal products have not been established.

Drug-Lifestyle Interactions

Alcohol may enhance the drowsiness caused by anticholinergic agents such as oxybutynin.

DOSAGE AND ADMINISTRATION

Dosing Considerations

In elderly and debilitated patients, it is advisable to initiate treatment at the lowest recommended dosage and to increase the dosage carefully according to tolerance and response.

Recommended Dose and Dosage Adjustment

Adults

The usual dose is one 5 mg tablet two or three times a day. The maximum recommended dose is one 5 mg tablet four times a day.

Children Over 5 Years of Age

The usual dose is one 5 mg tablet two times a day. The maximum recommended dose is one 5 mg tablet three times a day.

Missed Dose

The missed dose should be taken as soon as possible. If it is almost time for the next dose, the missed dose should not be taken. Instead, the next scheduled dose should be taken. Doses should not be doubled.

OVERDOSAGE

The symptoms of overdosage with Teva-Oxybutynin may be any of those seen with other anticholinergic agents. Symptoms may include signs of central nervous system excitation (e.g., convulsions, restlessness, tremor, irritability, delirium, hallucinations), flushing, fever, nausea, vomiting, tachycardia, hypotension or hypertension, respiratory failure, paralysis, dehydration, cardiac arrhythmia, urinary retention and coma.

In the event of an overdose or exaggerated response, treatment should be symptomatic and supportive. Induce emesis or perform gastric lavage (emesis is contraindicated in precomatose, convulsive, or psychotic state) and maintain respiration. Activated charcoal may be administered as well as magnesium sulphate. Physostigmine may be considered to reverse symptoms of anticholinergic intoxication. Hyperpyrexia may be treated symptomatically with ice bags or other cold applications and alcohol sponges.

Ingestion of 100 mg oxybutynin chloride in association with alcohol has been reported in a 13-year-old boy who experienced memory loss, and 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 fully recovered with symptomatic treatment.

ACTION AND CLINICAL PHARMACOLOGY

Mechanism of Action

Teva-Oxybutynin is a tertiary amine anticholinergic agent which exerts antimuscarinic as well as direct antispasmodic action on smooth muscle. *In vitro* studies have shown that its anticholinergic effects are weaker than those of atropine, but it possesses greater antispasmodic activity. No blocking effects occur at skeletal neuromuscular junctions or in autonomic ganglia (no antinicotinic effects).

In addition to its smooth muscle relaxing effects, Oxybutynin chloride exerts an analgesic and a local anesthetic effect. In animal studies, the central nervous system and cardiovascular actions of oxybutynin chloride were shown to be similar to but weaker than those of atropine.

Oxybutynin chloride relaxes bladder smooth muscle. In patients with uninhibited neurogenic and reflex neurogenic bladder, cystometric studies have demonstrated that oxybutynin chloride increases bladder (vesical) capacity, diminishes the frequency of uninhibited contractions of the detrusor muscle, and delays the initial desire to void. Oxybutynin chloride thus decreases urgency and frequency of both incontinent episodes and voluntary urination. These effects are more consistently improved in patients with uninhibited neurogenic bladder.

Pharmacokinetics

Absorption: Following oral administration of oxybutynin chloride, oxybutynin is rapidly absorbed achieving C_{max} within an hour, following which plasma concentration decreases with an effective half-life of approximately 2 to 3 hours. The absolute bioavailability of oxybutynin is reported to be about 6% (range 1.6% to 10.9%) for the tablet. Wide interindividual variation in pharmacokinetic parameters is evident following oral administration of oxybutynin.

The mean pharmacokinetic parameters for R- and S-oxybutynin are summarized in Table 1.2.

Table 1.2: Mean (SD) R- and S-Oxybutynin Pharmacokinetic Parameters Following Three Doses of oxybutynin chloride 5 mg Administered Every 8 Hours (n = 23)

Parameters (units)	R-Oxybutynin	S-Oxybutynin
C_{max} (ng/mL)	3.6 (2.2)	7.8 (4.1)
T_{max} (h)	0.89 (0.34)	0.65 (0.32)
AUC_t (ng•h/mL)	22.6 (11.3)	35.0 (17.3)
AUC_{inf} (ng•h/mL)	24.3 (12.3)	37.3 (18.7)

Data in the literature suggests that oxybutynin solution co-administered with food resulted in a slight delay in absorption and an increase in its bioavailability by 25% (n=18).

Distribution: Plasma concentrations of oxybutynin decline biexponentially following intravenous or oral administration. The volume of distribution is 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. Its metabolic products include phenylcyclohexylglycolic acid, which is pharmacologically inactive, and desethyloxybutynin, which is pharmacologically active.

Excretion: Oxybutynin is extensively metabolized by the liver, with less than 0.1% of the administered dose excreted unchanged in the urine.

STORAGE AND STABILITY

Store at 15° to 30°C in tight, light-resistant containers.

DOSAGE FORMS, COMPOSITION AND PACKAGING

Dosage Forms and Packaging

Teva–Oxybutynin (oxybutynin chloride) 5 mg is available as blue coloured round bi-convex compressed tablets, engraved modified N | N on one side and 5 on the reverse.
Each tablet contains 5 mg of oxybutynin chloride. Supplied in bottles of 100 and 500.

Composition

Inactive Ingredients: Each tablet contains calcium stearate, FD & C Blue #1 lake, lactose and microcrystalline cellulose.

PART II: SCIENTIFIC INFORMATION

PHARMACEUTICAL INFORMATION

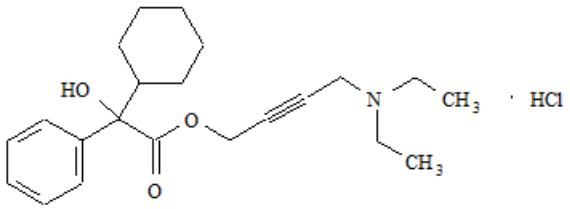
Drug Substance

Proper name: oxybutynin chloride

Chemical name: Benzeneacetic acid, a-cyclohexyl-a-hydroxy-, 4-(diethylamino)-2-butynyl ester hydrochloride, (±)-

Molecular formula and molecular mass: $C_{22}H_{31}NO_3$•HCl and 393.96

Structural formula:



Physicochemical properties: Oxybutynin chloride is a white crystalline practically odorless powder. The melting range is 124°C–129°C. Freely soluble in water and alcohol, very soluble in methanol and chloroform, soluble in acetone, slightly soluble in ether, very slightly soluble in hexane.

CLINICAL TRIALS

Comparative Bioavailability Studies

A randomized, single dose (2 x 5 mg), crossover comparative bioavailability study of Teva-Oxybutynin (Teva Canada Limited) and Ditropan (Norwich Eaton Pharmaceutical Inc.) was conducted in healthy, adult, male subjects under fasting conditions. The results obtained from the 20 subjects that were included in the statistical analysis are presented in the following table.

SUMMARY TABLE OF THE COMPARATIVE BIOAVAILABILITY DATA

Oxybutynin (2 x 5 mg) Geometric Mean Arithmetic Mean (CV%)				
Parameter	Test[1]	Reference[2]	% Ratio of Geometric Means	90% Confidence Interval
AUC_T (ng•h/mL)	13.58 17.39 (86)	13.24 18.08 (61)	102.6	90.4 – 116.4
AUC_I (ng•h/mL)	17.25 21.27 (76)	18.01 21.18 (53)	96	Data unavailable
C_{max} (ng/mL)	7.60 10.84 (96)	7.37 10.89 (72)	103.1	90.5 – 117.4
T_{max}[3] (h)	0.67 (0.5 – 1.5)	0.75 (0.5 – 2.0)		
$T_{1/2}$[4] (h)	Data unavailable	Data unavailable		

[1] Teva-Oxybutynin (oxybutynin chloride) tablets 5 mg (Teva Canada Limited)
[2] Ditropan (oxybutynin chloride) tablets 5 mg (Norwich Eaton Pharmaceutical Inc.), purchased in Canada
[3] Expressed as the median (range)
[4] Expressed as the arithmetic mean (CV%) only

Oxybutynin chloride was well tolerated in patients administered the drug in controlled studies of 30 days duration. Oxybutynin chloride has been used clinically for more than 20 years and has proven to be effective and relatively well tolerated for the relief of symptoms associated with overactive bladder.

DETAILED PHARMACOLOGY

Animal Pharmacology

In Vitro

In a series of *in vitro* tests, oxybutynin chloride was found to be more effective than propantheline, methantheline and atropine in inhibiting barium chloride-induced contractions in rabbit bladder detrusor muscle. It was, however, less active than the other drugs in inhibiting contractions caused by histamine and carbamylcholine.

In Vivo

Oxybutynin chloride was more effective than atropine in relieving morphine-induced spasm in the anesthetized dog. Atropine had a partial effect, presumably due to the musculotropic component of its action, while methscopolamine, a neurotropic compound, was ineffective. Against neostigmine-induced spasm, oxybutynin chloride showed about 15% of the potency of atropine. These results suggest that the major antispasmodic activity of oxybutynin chloride is musculotropic rather than neurotropic.

Oxybutynin chloride was less potent than atropine in producing mydriasis in the mouse and in inhibiting the sialogogic response in dogs.

In tests for analgesic activity, oxybutynin chloride was shown to be 35% as potent as codeine in the mouse tail-clip test and approximately equal to acetylsalicylic acid in the acetic acid stretch test. It was approximately twice as potent as lidocaine in producing local anesthesia in the rabbit cornea.

Oxybutynin chloride was less potent than atropine but similar in potency to methscopolamine in producing characteristic anticholinergic CNS effects in dogs. The cardiovascular actions of oxybutynin chloride in the anesthetized dog were also relatively weak.

Using oxybutynin chloride doses at least seven times greater than the maximum recommended therapeutic dosage, the following results were obtained in various drug interaction tests: Dicumarol effects were potentiated; hexobarbital sleep time was not significantly affected; zoxazolamine paralysis time was not significantly affected; there were no effects on aniline or hexobarbital hydroxylation; O-demethylation of codeine was possibly inhibited; the nitro-reduction of codeine was possibly inhibited; the nitro-reduction of p-aminobenzoic acid was stimulated; and oxphenbutazone metabolism was not affected.

TOXICOLOGY

Acute Toxicity

A summary of the acute toxicity studies performed with oxybutynin chloride is presented in Table 2.1.

Table 2.1: Single-dose toxicity studies with oxybutynin chloride

Species	Route	LD_{50} (95% C.L.)*	Slope (95% C.L.)*
Mouse	P.O.	1550 mg/kg (1372-1751)	1.69 (1.48-1.93)
Mouse	I.P.	260 mg/kg (186-346)	2.2 (1.6-3.1)
Mouse	I.V.	40 mg/kg (36-45)	1.25 (1.1–1.4)
Rat	P.O.	1600 mg/kg (1176-2176)	1.94 (1.39-2.72)
Rat	I.P.	430 mg/kg (371-499)	1.32 (1.21-1.4)

Newborn Rat	P.O.	560 mg/kg (528-594)	1.07 (0.82-1.39)
Approximate Minimum Lethal Dose			
Dog	I.V.	> 25 but < 50 mg/kg	
Dog	P.O.	> 750 but < 1000 mg/kg	

* 95% confidence limits

Signs and symptoms of toxicity in mice and rats were exophthalmos, CNS stimulation, ataxia and convulsions. In rats receiving the drug orally, intraocular tension was increased in some animals at each dose level. Females were more susceptible to toxicity and mortality than males. In newborn rats, laboured respiration and decreased activity were the only toxic symptoms noted, with most deaths occurring on day 2. Mydriasis, hyperventilation, ataxia, emesis, muscular weakness of hind limbs and convulsions were commonly seen in dogs.

Subacute and Chronic Toxicity

In a three-month study, 0, 50, 100, and 150 mg/kg/day of oxybutynin chloride were administered orally to groups of 20 rats. At the highest dose, mortality was approximately 50%, while at lower doses it did not differ significantly from the control rate. Other effects observed at high dosage were ataxia, depression, hypersensitivity to stimulation and pilomotor erection.

In a six-month rat study, 20-200 mg/kg/day p.o. was administered 6 days per week. At the lowest dose, no significant toxic effects were observed, while rats receiving 63-200 mg/kg/day showed signs of continuous acute pharmacologic effects, decreased food consumption with suppression of weight gain, and somewhat dose-related pathological changes consisting primarily of irregular and enlarged hepatic cells and of degenerative changes in kidney tubules.

In a two-year oral study in rats, 0, 20, 80 and 160 mg/kg/day were given to 50 animals of each sex per group. No high-dose and only a few mid-dose animals survived beyond 90 weeks. A dose-related reduction in weight gain was observed at all dose levels. Slight mydriasis was noted in a few rats at 20 mg/kg/day and mydriasis, tenseness, hyperactivity and excessive salivation in the higher dose groups. Serum alkaline phosphatase values for most high-dose rats were slightly higher than those of controls at most intervals of analysis. Microscopic examination of the urine showed an increase in the number of red and white blood cells in mid-dose males and in the number of red cells in high-dose males at termination. No other drug-related changes were observed in hematology, ophthalmologic examinations, organ weights, gross pathology or histopathology. Tumour incidence was similar in the control and experimental groups.

A six-month study in dogs showed no toxic effects following administration of 3 and 6 mg/kg/day of oxybutynin chloride 6 days per week, while higher doses produced anorexia, tremors and nervousness during the first weeks. These signs of toxicity diminished during the remainder of the study and no other abnormalities were observed.

Groups of 4 male and 4 female beagle dogs received 0, 4, 8 and 16 mg/kg/day p.o. for one year. Dogs in the 16 mg/kg/day group were initiated at 4 mg/kg b.i.d. and the dose was gradually increased over 8 weeks to 8 mg/kg b.i.d. There were no mortalities. Dry oral mucous membranes and mydriasis were noted in all treated dogs. Some animals at 8 and 16 mg/kg/day had a dry nose, and at the highest dose level occasional increased activity, purulent ocular or nasal discharge, emaciation and/or dehydration were also observed. A dose-related decrease in body weight was seen at all dose levels, although food consumption did not differ significantly from

control values.

Slightly microcytic normochromic erythrocytes were noted in a few treated dogs after one month only. Slight decreases in erythrocyte count, hemoglobin concentration and hematocrit values were noted in the 16 mg/kg/day group at all intervals of analysis. No other drug-related changes were seen in hematologic, biochemical or urinalysis values, in ophthalmoscopic examinations, or in electrocardiograms, and no gross or microscopic pathologic lesions or significant variations in organ weight were observed in any treated dogs.

Reproductive Studies

Twenty female rats per group were administered 0, 20, and 160 mg/kg/day orally from day 6 to 16 of gestation. Dams were sacrificed on day 20 and fetuses examined. One dam in the 20 mg/kg/day group died during the gestation period. Slight mydriasis was noted at the low dose and slight to marked mydriasis and occasional tenseness at the high dose. No drug-related effects on any fetal parameters evaluated were observed at either dose level.

The teratogenic potential of oxybutynin chloride has also been studied in mice, hamsters and rabbits at doses of up to 180 mg/kg/day. No abnormalities were observed.

Carcinogenesis and Mutagenesis

A 24-month study in rats at dosages of oxybutynin chloride of 20, 80, and 160 mg/kg/day showed no evidence of carcinogenicity. These doses are approximately 6, 25, and 50 times the maximum human exposure, based on surface area.

Oxybutynin chloride showed no increase of mutagenic activity when tested in *Schizosaccharomyces pompholiciformis*, *Saccharomyces cerevisiae*, and *Salmonella typhimurium* test systems.

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17. Bioequivalence study of Novopharm and Norwich Eaton (PrDITROPAN®) 5 mg oxybutynin chloride tablets. August 1993. Data on file at Teva Canada Limited.

PART III: CONSUMER INFORMATION

[Pr]Teva-Oxybutynin
oxybutynin chloride tablets, USP, 5 mg

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

ABOUT THIS MEDICATION

What the medication is used for:
Teva-Oxybutynin is used to relieve the symptoms of overactive bladder which include the frequent and urgent need to urinate with or without urine leakage.

What it does:
Teva-Oxybutynin decreases the urgency and frequency of both incontinent episodes and voluntary urination.

When it should not be used:
You should **not** take Teva-Oxybutynin if:
- you have difficulty urinating, passing and digesting food, or suffer from glaucoma (high pressure and pain in the eyes), or if you are at risk for these conditions;
- you are allergic to oxybutynin chloride or any of the other ingredients in Teva-Oxybutynin (see **What the nonmedicinal ingredients are**).

What the medicinal ingredient is:
oxybutynin chloride

What the nonmedicinal ingredients are:
calcium stearate, FD & C Blue #1 lake, lactose and microcrystalline cellulose.

What dosage forms it comes in:
Tablets: 5 mg

WARNINGS AND PRECAUTIONS

BEFORE you use Teva-Oxybutynin talk to your doctor or pharmacist if:
- you suffer from stomach problems affecting passage and digestion of food;
- you suffer from glaucoma (high pressure and pain in the eyes);
- you suffer from gastroesophageal reflux or are taking drugs (such as bisphosphonates which are used to prevent bone thinning and fractures caused by osteoporosis) that can worsen esophagitis (inflammation of the tube that connects the mouth and the stomach);
- you suffer from ulcerative colitis (inflammatory bowel disease);
- you suffer from myasthenia gravis (a muscle weakening disease);
- you suffer from kidney and liver problems;
- you are taking certain drugs for treatment of dementia (such as Alzheimer's disease);
- you have difficulty urinating;
- you have had a reaction to oxybutynin chloride or any of the other ingredients;
- you are pregnant or trying to become pregnant;
- you are breast-feeding;
- you are taking or have recently taken any other medication including medications bought without a prescription.

You should be informed of the following information when taking Teva-Oxybutynin:
- When administered in high environmental temperature, Teva-Oxybutynin can cause heat prostration (fever and heat stroke due to decreased sweating).
- Teva-Oxybutynin may produce drowsiness or blurred vision. You should exercise caution while driving or operating machinery.
- Alcohol may enhance the drowsiness caused by anticholinergic agents such as Teva-Oxybutynin.

INTERACTIONS WITH THIS MEDICATION

Always tell your doctor about all medicines you are taking. Your doctor will decide if it is safe for you to use Teva-Oxybutynin with other medicines. If you take any of the following medicines with Teva-Oxybutynin, it may affect how well they work or increase the likelihood of side effects:

- drugs that could result in serious adverse effects if small changes in dosage occur (such as digoxin for heart problems)
- other anticholinergic drugs, used to treat a number of different medical conditions (a few examples are atropine for glaucoma or hyoscine for nausea), or drugs with similar undesired effects (such as dry mouth, constipation, drowsiness, and blurred vision)
- certain antibiotics (such as erythromycin and clarithromycin)
- certain medicines for the treatment of fungal infections (such as oral ketoconazole, itraconazole, and miconazole)

PROPER USE OF THIS MEDICATION

Usual dose:

Adults

The usual dose is one 5 mg tablet two or three times a day. The maximum recommended dose is one 5 mg tablet four times a day.

Children Over 5 Years of Age

The usual dose is one 5 mg tablet two times a day. The maximum recommended dose is one 5 mg tablet three times a day.

Overdose:

If you take more tablets than your doctor prescribed, call your doctor or regional Poison Control Centre immediately.

Missed dose:

If you miss a dose, take it as soon as you remember. If it is almost time for the next dose, do not take the missed dose. Instead, take the next scheduled dose. Do not try to make up for the missed dose by taking a double dose next time.

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

In clinical studies with oxybutynin chloride, the most common side effects reported by patients were dry mouth, constipation, nausea, drowsiness and dizziness.

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

HOW TO STORE IT

Store at 15° to 30°C in tight, light-resistant containers.

Reporting Side Effects

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada/adverse-reaction-reporting.html) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

MORE INFORMATION

If you want more information about Teva-Oxybutynin:

- Talk to your healthcare professional.
- Find the full Product Monograph that is prepared for healthcare professionals and includes this Consumer Information by visiting the Health Canada website (https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/drug-product-database.html); the manufacturer's website www.tevacanada.com, or by contacting Teva Canada Limited by:

  Phone: 1-800-268-4127 ext. 3;
  Email: druginfo@tevacanada.com; or
  Fax: 1-416-335-4472

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