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contraceptives and will examine you. The physical examination may be delayed to another time if you request it and the health care provider believes that it is a good medical practice to postpone it. You should be reexamined at least once a year while taking oral contraceptives. The detailed patient information leaflet gives you further information which you should read and discuss with your health care provider.

HOW TO TAKE THE PILL

See full text of *HOW TO TAKE THE PILL* which is printed in full in the ***DETAILED PATIENT LABELING.***

Keep this and all medication out of the reach of children.

Rx only

Revised: Feb. 7, 2000

Address medical inquiries to:
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PO Box 1900
Corona, CA 92878-1149

Mfg. by: Searle & Co.
San Juan, PR 00936
for: WATSON PHARMA, INC.
a subsidiary of Watson Laboratories, Inc.
Corona, CA 92880

Shown in Product Identification Guide, page 339

OXYTROL™ Rx

[ŏks-ē-trōl]

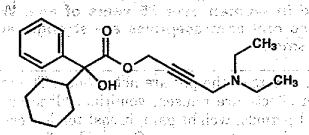
Oxybutynin Transdermal System

Rx only

DESCRIPTION

OXYTROL, oxybutynin transdermal system, is designed to deliver oxybutynin continuously and consistently over a 3- to 4-day interval after application to intact skin. **OXYTROL** is available as a 39 cm^2 system containing 36 mg of oxybutynin. **OXYTROL** has a nominal *in vivo* delivery rate of 3.9 mg oxybutynin per day through skin of average permeability (interindividual variation in skin permeability is approximately 20%).

Oxybutynin is an antispasmodic, anticholinergic agent. Oxybutynin is administered as a racemate of R- and S-isomers. Chemically, oxybutynin is d, l (racemic) 4-diethylamino-2-butynyl phenylcyclohexylglycolate. The empirical formula of oxybutynin is $C_{22}H_{31}NO_3$. Its structural formula is:

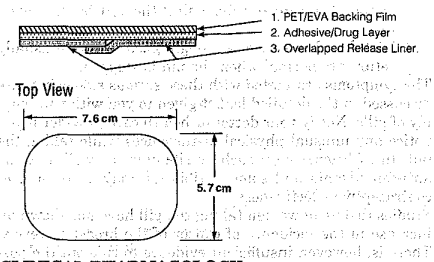


Oxybutynin is a white powder with a molecular weight of 357. It is soluble in alcohol, but relatively insoluble in water.

Transdermal System Components

OXYTROL is a matrix-type transdermal system composed of three layers as illustrated in Figure 1 below. Layer 1 (Backing Film) is a thin flexible polyester/ethylene-vinyl acetate film that provides the matrix system with occlusivity and physical integrity and protects the adhesive/drug layer. Layer 2 (Adhesive/Drug Layer) is a cast film of acrylic adhesive containing oxybutynin and triacetin, USP. Layer 3 (Release Liner) is two overlapped siliconized polyester strips that are peeled off and discarded by the patient prior to applying the matrix system.

Figure 1: Side and top views of the **OXYTROL** system. (Not to scale)



CLINICAL PHARMACOLOGY

The free base form of oxybutynin is pharmacologically equivalent to oxybutynin hydrochloride. 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.

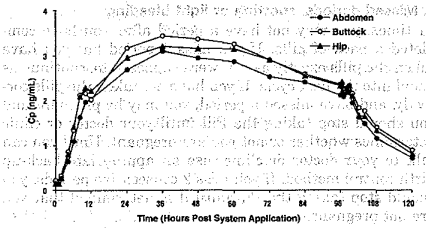
Oxybutynin is a racemic (50:50) mixture of R- and S-isomers. Antimuscarinic activity resides predominantly in

Pharmacokinetics

Absorption

Oxybutynin is transported across intact skin and into the systemic circulation by passive diffusion across the stratum corneum. The average daily dose of oxybutynin absorbed from the 39 cm^2 **OXYTROL** system is 3.9 mg. The average (SD) nominal dose, 0.10 (0.02) mg oxybutynin per cm^2 surface area, was obtained from analysis of residual oxybutynin content of systems worn over a continuous 4-day period during 303 separate occasions in 76 healthy volunteers. Following application of the first **OXYTROL** 3.9 mg/day system, oxybutynin plasma concentration increases for approximately 24 to 48 hours, reaching average maximum concentrations of 3 to 4 ng/mL. Thereafter, steady concentrations are maintained for up to 96 hours. Absorption of oxybutynin is bioequivalent when **OXYTROL** is applied to the abdomen, buttocks, or hip. Average plasma concentrations measured during a randomized, crossover study of the three recommended application sites in 24 healthy men and women are shown in Figure 2.

Figure 2: Average plasma oxybutynin concentrations (Cp) in 24 healthy male and female volunteers during single-dose application of **OXYTROL** 3.9 mg/day to the abdomen, buttock, and hip (System removal at 96 hours).



Steady-state conditions are reached during the second **OXYTROL** application. Average steady-state plasma concentrations were 3.1 ng/mL for oxybutynin and 3.8 ng/mL for N-desethyloxybutynin (Figure 3). Table 1 provides a summary of pharmacokinetic parameters of oxybutynin in healthy volunteers after single and multiple applications of **OXYTROL**.

Figure 3: Average (SEM) steady-state oxybutynin and N-desethyloxybutynin plasma concentrations (Cp) measured in 13 healthy volunteers following the second transdermal system application in a multiple-dose, randomized, crossover study.

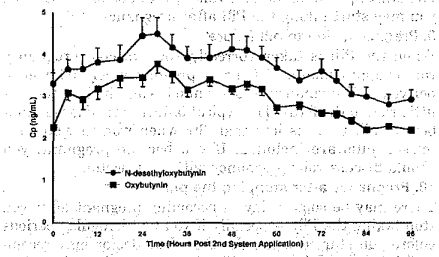


Table 1: Mean (SD) oxybutynin pharmacokinetic parameters from single and multiple dose studies in healthy men and women volunteers after application of **OXYTROL** on the abdomen.

Dosing	Oxybutynin			
	C_{max}(SD) (ng/mL)	T_{max}[1] (hr)	C_{avg} (SD) (ng/mL)	AUC (SD) (ng/mLxh)
Single	3.0 (0.8)	48	—	245 (59)[2]
	3.4 (1.1)	36	—	279 (99)[2]
Multiple	6.6 (2.4)	10	4.2 (1.1)	408 (108)[3]
	4.2 (1.0)	28	3.1 (0.7)	259 (57)[4]

[1] T_{max} given as median
[2] AUC_{inf}
[3] AUC_{0-96}
[4] AUC_{0-84}

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.

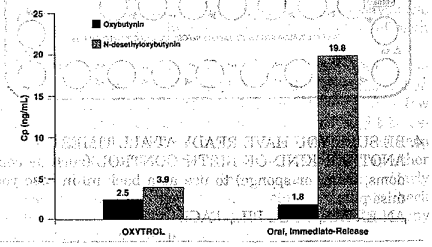
Metabolism

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.

ethyl metabolite compared to oxybutynin (see Figure 4). The plasma concentration AUC ratio of N-desethyl metabolite to parent compound following a single 5 mg oral dose of oxybutynin chloride was 11.9:1.

Transdermal administration of oxybutynin bypasses the first-pass gastrointestinal and hepatic metabolism, reducing the formation of the N-desethyl metabolite (see Figure 4). Only small amounts of CYP3A4 are found in skin, limiting pre-systemic metabolism during transdermal absorption. The resulting plasma concentration AUC ratio of N-desethyl metabolite to parent compound following multiple **OXYTROL** applications was 1.3:1.

Figure 4: Average plasma concentrations (Cp) measured after a single, 96-hour application of the **OXYTROL** 3.9 mg/day system (AUC_{inf}/96) and a single, 5 mg, oral immediate-release dose of oxybutynin chloride (AUC_{inf}/8) in 16 healthy male and female volunteers.



Following intravenous administration, the elimination half-life of oxybutynin is approximately 2 hours. Following removal of **OXYTROL**, plasma concentrations of oxybutynin and N-desethyloxybutynin decline with an apparent half-life of approximately 7 to 8 hours.

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

Geriatric: The pharmacokinetics of oxybutynin and N-desethyloxybutynin were similar in all patients studied.

Pediatric: The pharmacokinetics of oxybutynin and N-desethyloxybutynin were not evaluated in individuals younger than 18 years of age. See **PRECAUTIONS: Pediatric Use**.

Gender: There were no significant differences in the pharmacokinetics of oxybutynin in healthy male and female volunteers following application of **OXYTROL**.

Race: Available data suggest that there are no significant differences in the pharmacokinetics of oxybutynin based on race in healthy volunteers following administration of **OXYTROL**. Japanese volunteers demonstrated a somewhat lower metabolism of oxybutynin to N-desethyloxybutynin compared to Caucasian volunteers.

Renal Insufficiency: There is no experience with the use of **OXYTROL** in patients with renal insufficiency.

Hepatic Insufficiency: There is no experience with the use of **OXYTROL** in patients with hepatic insufficiency.

Drug-Drug Interactions: See **PRECAUTIONS: Drug Interactions**.

Adhesion

Adhesion was periodically evaluated during the Phase 3 studies. Of the 4,746 **OXYTROL** evaluations in the Phase 3 trials, 20 (0.4%) were observed at clinic visits to have become completely detached and 35 (0.7%) became partially detached during routine clinic use. Similar to the pharmacokinetic studies, > 98% of the systems evaluated in the Phase 3 studies were assessed as being ≥ 75% attached and thus would be expected to perform as anticipated.

Clinical Studies

The efficacy and safety of **OXYTROL** were evaluated in patients with urge urinary incontinence in two Phase 3 controlled studies and one open-label extension. Study 1 was a Phase 3, placebo controlled study, comparing the safety and efficacy of **OXYTROL** at dose levels of 1.3, 2.6, and 3.9 mg/day to placebo in 520 patients. Open-label treatment was available for patients completing the study. Study 2 was a Phase 3 study, comparing the safety and efficacy of **OXYTROL** 3.9 mg/day versus active and placebo controls in 361 patients.

Study 1 was a randomized, double-blind, placebo-controlled, parallel group study of three dose levels of **OXYTROL** conducted in 520 patients. The 12-week double-blind treatment included **OXYTROL** doses of 1.3, 2.6, and 3.9 mg/day with matching placebo. An open-label, dose titration treatment extension allowed continued treatment for up to an additional 40 weeks for patients completing the double-blind period. The majority of patients were Caucasian (91%) and female (92%) with a mean age of 61 years (range, 20 to 88 years). Entry criteria required that patients have urge or mixed incontinence (with a predominance of urge), urge incontinence episodes of ≥ 10 per week, and ≥ 8 micturitions per day. The patient's medical history and a urinary diary during the treatment-free baseline period confirmed the diagnosis of urge incontinence. Approximately 80% of patients had no prior pharmacological treatment for incontinence.

Table 2: Mean and median change from baseline to end of treatment (Week 12 or last observation carried forward) in incontinence episodes, urinary frequency, and urinary void volume in patients treated with **OXYTROL** 3.9 mg/day or placebo for 12 weeks (Study 1).

Parameter	Placebo (N=127)		OXYTROL 3.9 mg/day (N=120)	
	Mean (SD)	Median	Mean (SD)	Median
Weekly Incontinence Episodes				
Baseline	37.7 (24.0)	30	34.3 (18.2)	31
Reduction	19.2 (21.4)	15	21.0 (17.1)	19
p value vs. placebo	—		0.0265*	
Daily Urinary Frequency				
Baseline	12.3 (3.5)	11	11.8 (3.1)	11
Reduction	1.6 (3.0)	1	2.2 (2.5)	2
p value vs. placebo	—		0.0313*	
Urinary Void Volume (mL)				
Baseline	175.9 (69.5)	166.5	171.6 (65.1)	168
Increase	10.5 (56.9)	5.5	31.6 (65.6)	26
p value vs. placebo	—		0.0009**	

*Comparison significant if $p < 0.05$
**Comparison significant if $p \leq 0.0167$

Study 2 was a randomized, double-blind, double-dummy, study of **OXYTROL** 3.9 mg/day versus active and placebo controls conducted in 361 patients. The 12-week double-blind treatment included an **OXYTROL** dose of 3.9 mg/day, an active comparator, and placebo. The majority of patients were Caucasian (95%) and female (93%) with a mean age of 64 years (range, 18 to 89 years). Entry criteria required that all patients have urge or mixed incontinence (with a predominance of urge) and had achieved a beneficial response from the anticholinergic treatment they were using at the time of study entry. The average duration of prior pharmacological treatment was greater than 2 years. The patient's medical history and a urinary diary during the treatment-free baseline period confirmed the diagnosis of urge incontinence. Reductions in daily incontinence episodes, urinary frequency, and urinary void volume between placebo and active treatment groups are summarized in Table 3.

Table 3: Mean and median change from baseline to end of treatment (Week 12 or last observation carried forward) in incontinence episodes, urinary frequency, and urinary void volume in patients treated with **OXYTROL** 3.9 mg/day or placebo for 12 weeks (Study 2).

Parameter	Placebo (N=117)		OXYTROL 3.9 mg/day (N=121)	
	Mean (SD)	Median	Mean (SD)	Median
Daily Incontinence Episodes				
Baseline	5.0 (3.2)	4	4.7 (2.9)	4
Reduction	2.1 (3.0)	2	2.9 (3.0)	3
p value vs. placebo	—		0.0137*	
Daily Urinary Frequency				
Baseline	12.3 (3.3)	12	12.4 (2.9)	12
Reduction	1.4 (2.7)	1	1.9 (2.7)	2
p value vs. placebo	—		0.1010*	
Urinary Void Volume (mL)				
Baseline	175.0 (68.0)	171.0	164.8 (62.3)	160
p value vs. placebo	—		0.0010*	

*Comparison significant if $p < 0.05$

INDICATIONS AND USAGE

OXYTROL is indicated for the treatment of overactive bladder with symptoms of urge urinary incontinence, urgency, and frequency.

CONTRAINDICATIONS

OXYTROL is contraindicated in patients with urinary retention, gastric retention, or uncontrolled narrow-angle glaucoma and in patients who are at risk for these conditions. **OXYTROL** is also contraindicated in patients who have demonstrated hypersensitivity to oxybutynin or other components of the product.

PRECAUTIONS

General

OXYTROL should be used with caution in patients with hepatic or renal impairment.

Urinary Retention: **OXYTROL** should be administered with caution to patients with clinically significant bladder outflow obstruction because of the risk of urinary retention (see **CONTRAINDICATIONS**).

Gastrointestinal Disorders: OXYTROL should be administered with caution to patients with gastrointestinal obstructive disorders because of the risk of gastric retention (see **CONTRAINDICATIONS**).

OXYTROL, like other anticholinergic drugs, may decrease gastrointestinal motility and should be used with caution in patients with conditions such as ulcerative colitis, intestinal atony, and myasthenia gravis. **OXYTROL** 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.

Information for Patients

Patients should be informed that heat prostration (fever and heat stroke due to decreased sweating) can occur when anticholinergics such as oxybutynin are used in a hot environment. 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.

OXYTROL should be applied to dry, intact skin on the abdomen, hip, or buttock. A new application site should be selected with each new system to avoid re-application to the same site within 7 days. Details on use of the system are explained in the patient information leaflet that should be dispensed with the product.

Drug Interactions

The concomitant use of oxybutynin with other anticholinergic drugs or with other agents that produce dry mouth, constipation, somnolence, 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. 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 **OXYTROL**.

Carcinogenesis, Mutagenesis, Impairment of Fertility

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.

Pregnancy: Teratogenic Effects

Pregnancy Category B

Reproduction studies with oxybutynin chloride in the mouse, rat, hamster, and rabbit showed no definite 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 **OXYTROL** administration to women who are or who may become pregnant has not been established. Therefore, **OXYTROL** should not be given to pregnant women unless, in the judgment of the physician, the probable clinical benefits outweigh the possible hazards.

Nursing Mothers

It is not known whether oxybutynin is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when **OXYTROL** is administered to a nursing woman.

Geriatric Use

Of the total number of patients in the clinical studies of **OXYTROL**, 49% were 65 and over. No overall differences in safety or effectiveness were observed between these subjects and younger subjects, and other reported clinical experience has not identified differences in response between elderly and younger patients, but greater sensitivity of some older individuals cannot be ruled out (see **CLINICAL PHARMACOLOGY, Pharmacokinetics, *Special Populations: Geriatric***).

ADVERSE REACTIONS

The safety of **OXYTROL** was evaluated in a total of 417 patients who participated in two Phase 3 clinical efficacy and safety studies and an open-label extension. Additional safety information was collected in Phase 1 and Phase 2 trials. In the two pivotal studies, a total of 246 patients received **OXYTROL** during the 12-week treatment periods. A total of 411 patients entered the open-label extension and of those, 65 patients and 52 patients received **OXYTROL** for at least 24 weeks and at least 36 weeks, respectively.

No deaths were reported during treatment. No serious adverse events related to treatment were reported.

Adverse events reported in the pivotal trials are summarized in Tables 4 and 5 below.

Table 4: Number (%) of adverse events occurring in ≥ 2% of **OXYTROL**-treated patients and greater in **OXYTROL** group than in placebo group (Study 1).

Adverse Event*	Placebo (N=132)		OXYTROL (3.9 mg/day) (N=125)	
	N	%	N	%
Application site pruritus	8	6.1%	21	16.8%
Dry mouth	11	8.3%	12	9.6%
Application site erythema	3	2.3%	7	5.6%
Application site vesicles	0	0.0%	4	3.2%
Diarrhea	3	2.3%	4	3.2%
Dysuria	0	0.0%	3	2.4%

*includes adverse events judged by the investigator as possibly, probably or definitely treatment-related.

Table 5: Number (%) of adverse events occurring in ≥ 2% of **OXYTROL**-treated patients and greater in **OXYTROL** group than in placebo group (Study 2).

Adverse Event*	Placebo (N=117)		OXYTROL (3.9 mg/day) (N=121)	
	N	%	N	%
Application site pruritus	5	4.3%	17	14.0%
Application site erythema	2	1.7%	10	8.3%
Dry mouth	2	1.7%	5	4.1%
Constipation	0	0.0%	4	3.3%
Application site rash	1	0.9%	4	3.3%
Application site macules	0	0.0%	3	2.5%
Abnormal vision	0	0.0%	3	2.5%

*includes adverse events judged by the investigator as possibly, probably or definitely treatment-related.

Other adverse events reported by > 1% of **OXYTROL**-treated patients, and judged by the investigator to be possibly, probably or definitely related to treatment include: abdominal pain, nausea, flatulence, fatigue, somnolence, headache, flushing, rash, application site burning and back pain.

Most treatment-related adverse events were described as mild or moderate in intensity. Severe application site reactions were reported by 6.4% of **OXYTROL**-treated patients in Study 1 and by 5.0% of **OXYTROL**-treated patients in Study 2.

Treatment-related adverse events that resulted in discontinuation were reported by 11.2% of **OXYTROL**-treated patients in Study 1 and 10.7% of **OXYTROL**-treated patients in Study 2. Most of these were secondary to application site reaction. In the two pivotal studies, no patient discontinued **OXYTROL** treatment due to dry mouth.

In the open-label extension, the most common treatment-related adverse events were: application site pruritus, application site erythema and dry mouth.

Continued on next page

OVERDOSAGE

Plasma concentration of oxybutynin declines within 1 to 2 hours after removal of transdermal system(s). Patients should be monitored until symptoms resolve. Overdosage with oxybutynin has been associated with anticholinergic effects including CNS excitation, flushing, fever, dehydration, cardiac arrhythmia, vomiting, and urinary retention. Ingestion of 100 mg oral 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.

DOSAGE AND ADMINISTRATION

OXYTROL should be applied to dry, intact skin on the abdomen, hip, or buttock. A new application site should be selected with each new system to avoid re-application to the same site within 7 days.

The dose of **OXYTROL** is one 3.9 mg/day system applied twice weekly (every 3 to 4 days).

HOW SUPPLIED

OXYTROL 3.9 mg/day (oxybutynin transdermal system). Each 39 cm^2 system imprinted with **OXYTROL** 3.9 mg/day contains 36 mg oxybutynin for nominal delivery of 3.9 mg oxybutynin per day when dosed in a twice weekly regimen.

NDC 52544-920-08 Patient Calendar Box of 8 Systems

Storage

Store at 25°C (77°F); excursions permitted to 15–30°C (59–86°F). Protect from moisture and humidity. Do not store outside the sealed pouch. Apply immediately after removal from the protective pouch. Discard used **OXYTROL** in household trash in a manner that prevents accidental application or ingestion by children, pets, or others.

WATSON Pharma, Inc.
A Subsidiary of Watson Pharmaceuticals, Inc.
Corona, CA 92880 USA

DATE OF ISSUANCE: FEBRUARY 2003
U.S. Patent Nos. 5,601,839 and 5,834,010

Shown in Product Identification Guide, page 339

TRI-NORINYL®-28 ℞

(norethindrone and ethinyl estradiol)

℞ only

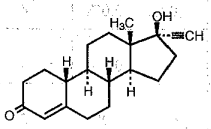
Patients should be counseled that this product does not protect against HIV infection (AIDS) and other sexually transmitted diseases.

ORAL CONTRACEPTIVE AGENTS

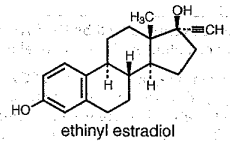
DESCRIPTION

Tri-Norinyl-28 provides a continuous oral contraceptive regimen of 7 blue tablets, 9 yellow-green tablets, 5 more blue tablets, and then 7 orange tablets. Each blue tablet contains norethindrone 0.5 mg and ethinyl estradiol 0.035 mg, each yellow-green tablet contains norethindrone 1 mg and ethinyl estradiol 0.035 mg, and each orange tablet contains inert ingredients.

Norethindrone is a potent progestational agent with the chemical name 17-Hydroxy-19-nor-17α-pregn-4-en-20-yn-3-one. Ethinyl estradiol is an estrogen with the chemical name 19-Nor-17α-pregna-1,3,5(10)-trien-20-yne-3,17-diol. Their structural formulae follow:



norethindrone



ethinyl estradiol

The yellow-green TRI-NORINYL tablets contain the following inactive ingredients: D&C Green No. 5, D&C Yellow No. 10, lactose, magnesium stearate, povidone, and starch.

The blue TRI-NORINYL tablets contain the following inactive ingredients: FD&C Blue No. 1, lactose, magnesium stearate, povidone, and starch.

The inactive orange tablets in the 28-day regimen contain the following inactive ingredients: FD&C Yellow No. 6, lactose, magnesium stearate, povidone, and starch.

CLINICAL PHARMACOLOGY

Combination oral contraceptives act by suppression of gonadotrophins. Although the primary mechanism of this action is inhibition of ovulation, other alterations include changes in the cervical mucus (which increase the difficulty of sperm entry into the uterus) and the endometrium (which may reduce the likelihood of implantation).

Table 1— Percentage of women experiencing an unintended pregnancy during the first year of typical use and the first year of perfect use of contraception and the percentage continuing use at the end of the first year. United States.

Method (1)	% of Women Experiencing an Unintended Pregnancy within the First Year of Use: Typical use[1] (2)	Perfect use[2] (3)	% of Women Continuing Use at One Year[3] (4)
Chance[4]	85	85	
Spermicides[5]	26	6	40
Periodic abstinence	25		63
Calendar		9	
Ovulation method		3	
Sympto-thermal[6]		2	
Post-ovulation		1	
Withdrawal	19	4	
Cap[7]			
Parous women	40	26	42
Nulliparous women	20	9	56
Sponge			
Parous women	40	20	42
Nulliparous women	20	9	56
Diaphragm[7]	20	6	56
Condom[8]			
Female (Reality)	21	5	56
Male	14	3	61
Pill	5		71
Progestin only		0.5	
Combined		0.1	
IUD			
Progesterone T	2.0	1.5	81
Copper T 380A	0.8	0.6	78
LNg 20	0.1	0.1	81
Depo-Provera	0.3	0.3	70
Norplant and Norplant-2	0.05	0.05	88
Female sterilization	0.5	0.5	100
Male sterilization	0.15	0.10	100

Emergency Contraceptive Pills: Treatment initiated within 72 hours after unprotected intercourse reduces the risk of pregnancy by at least 75%.[9]

Lactational Amenorrhea Method: LAM is a highly effective, *temporary* method of contraception.[10]

Source: Trussell J. Contraceptive Efficacy Table from Hatcher R.A., Trussell J. Stewart F, Cates W, Stewart GK, Kowal D, Guest F, in Contraceptive Technology: Seventeenth Revised Edition. New York, NY: Irvington Publishers, 1998.

[1] Among *typical* couples who initiate use of a method (not necessarily for the first time), the percentage who experience an accidental pregnancy during the first year if they do not stop use for any other reason.

[2] Among couples who initiate use of a method (not necessarily for the first time) and who use it *perfectly* (both consistently and correctly), the percentage who experience an accidental pregnancy during the first year if they do not stop use for any other reason.

[3] Among couples attempting to avoid pregnancy, the percentage who continue to use a method for one year.

[4] The percentage becoming pregnant in columns (2) and (3) are based on data from populations where contraception is not used and from women who cease using contraception in order to become pregnant. Among such populations, about 89% become pregnant within one year. This estimate was lowered slightly (to 85%) to represent the percent who would become pregnant within one year among women now relying on reversible methods of contraception if they abandoned contraception altogether.

[5] Foams, creams, gels, vaginal suppositories, and vaginal film.

[6] Cervical mucus (ovulation) method supplemented by calendar in the pre-ovulatory and basal body temperature in the post-ovulatory phases.

[7] With spermicidal cream or jelly.

[8] Without spermicides.

[9] The treatment schedule is one dose within 72 hours after unprotected intercourse and a second dose 12 hours after the first dose. The Food and Drug Administration has declared the following brands of oral contraceptives to be safe and effective for emergency contraception: Ovral (1 dose is 2 white pills), Aleese (1 dose is 5 pink pills), Nordette or Levlen (1 dose is 2 light-orange pills), Lo/Ovral (1 dose is 4 white pills), Triphasil or Tri-Levlen (1 dose is 4 yellow pills).

[10] However, to maintain effective protection against pregnancy, another method of contraception must be used as soon as menstruation resumes, the frequency or duration of breastfeeds is reduced, bottle feeds are introduced, or the baby reaches six months of age.

INDICATIONS AND USAGE

Oral contraceptives are indicated for the prevention of pregnancy in women who elect to use this product as a method of contraception.

Oral contraceptive products such as Norinyl, which contain 50 mcg of estrogen, should not be used unless medically indicated.

Oral contraceptives are highly effective. Table 1 lists the typical accidental pregnancy rates for users of combination oral contraceptives and other methods of contraception.[1] The efficacy of these contraceptive methods, except sterilization, depends upon the reliability with which they are used. Correct and consistent use of methods can result in lower failure rates.

[See table 1 above]

CONTRAINDICATIONS

Oral contraceptives should not be used in women who have the following conditions:

- Thrombophlebitis or thromboembolic disorders
- A past history of deep vein thrombophlebitis or thromboembolic disorders
- Cerebral vascular or coronary artery disease
- Known or suspected carcinoma of the breast
- Carcinoma of the endometrium or other known or suspected estrogen-dependent neoplasia
- Undiagnosed abnormal genital bleeding
- Cholestatic jaundice of pregnancy or jaundice with prior pill use
- Hepatic adenomas, carcinomas or benign liver tumors
- Known or suspected pregnancy

WARNINGS

Cigarette smoking increases the risk of serious cardiovascular side effects from oral contraceptive use. This risk increases with age and with heavy smoking (15 or more cigarettes per day) and is quite marked in women over 35 years of age. Women who use oral contraceptives should be strongly advised not to smoke.

The use of oral contraceptives is associated with increased risks of several serious conditions including myocardial infarction, thromboembolism, stroke, hepatic neoplasia, and gallbladder disease, although the risk of serious morbidity or mortality is very small in healthy women without underlying risk factors. The risk of morbidity and mortality increases significantly in the presence of other underlying risk factors such as hypertension, hyperlipidemias, hypercholesterolemia, obesity and diabetes.[2-5]

Practitioners prescribing oral contraceptives should be familiar with the following information relating to these risks.

The information contained in this package insert is principally based on studies carried out in patients who used oral contraceptives with higher formulations of both estrogens and progestogens than those in common use today.[6-11] The effect of long-term use of the oral contraceptives with lower formulations of both estrogens and progestogens remains to be determined.

Throughout this labeling, epidemiological studies reported are of two types: retrospective or case control studies and prospective or cohort studies. Case control studies provide a measure of the relative risk of a disease. Relative risk, the *ratio* of the incidence of a disease among oral contraceptive