OXYBUTYNIN CHLORIDE- oxybutynin chloride tablet, extended release
Coupler LLC

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use OXYBUTYNIN CHLORIDE EXTENDED-RELEASE TABLETS safely and effectively. See full prescribing information for OXYBUTYNIN CHLORIDE EXTENDED-RELEASE TABLETS.
OXYBUTYNIN CHLORIDE extended-release tablets for oral use
Initial U.S. Approval: 1975

INDICATIONS AND USAGE

- Oxybutynin chloride is a muscarinic antagonist indicated for the treatment of overactive bladder with symptoms of urge urinary incontinence, urgency, and frequency. (1)
- Oxybutynin chloride extended-release tablets are also indicated for the treatment of pediatric patients aged 6 years and older with symptoms of detrusor overactivity associated with a neurological condition (e.g., spina bifida). (1)

DOSAGE AND ADMINISTRATION

Oxybutynin chloride extended-release tablets must be swallowed whole with the aid of liquids, and must not be chewed, divided, or crushed. Oxybutynin chloride extended-release tablets may be administered with or without food. (2)

- **Adults:**Start with 5 mg or 10 mg, once daily at approximately the same time every day. Dose should not exceed 30 mg per day. (2.1)
- **Pediatric patients (6 years of age or older):**Start with 5 mg, once daily at approximately the same time every day. Dose should not exceed 20 mg per day. (2.2)

DOSAGE FORMS AND STRENGTHS

Extended release tablets 5 mg, 10 mg and 15 mg (3)

CONTRAINDICATIONS

- Urinary retention (4)
- Gastric Retention (4)
- Uncontrolled narrow angle glaucoma (4)
- Known hypersensitivity to oxybutynin chloride extended-release tablets, oxybutynin or any component of oxybutynin chloride extended-release tablets (4)

WARNINGS AND PRECAUTIONS

- Angioedema: Angioedema has been reported with oxybutynin. If symptoms of angioedema occur, discontinue oxybutynin chloride extended-release tablets immediately and initiate appropriate therapy. (5.1)
- Central Nervous System (CNS) effects: CNS effects have been reported with oxybutynin. If patient experiences anticholinergic CNS effects, consider dose adjustment or discontinuation of oxybutynin chloride extended-release tablets. (5.2)
- Use with caution due to aggravation of symptoms:
  - Pre-existing dementia in patients treated with cholinesterase inhibitors (5.2),
  - Parkinson’s disease (5.2),
  - Myasthenia gravis (5.3), and
  - Decreased gastrointestinal motility in patients with autonomic neuropathy. (5.4).
- Urinary Retention: Use with caution in patients with clinically significant bladder outflow obstruction because of the risk of urinary retention (5.5)
- Gastrointestinal Adverse Reactions: Use with caution in patients with gastrointestinal obstructive disorders or decreased intestinal motility due to risk of gastric retention. Use with caution in patients with gastroesophageal reflux or in patients concurrently taking drugs that can exacerbate esophagitis. (5.6)

ADVERSE REACTIONS

The most common (incidence greater than or equal to 5%) adverse reactions were dry mouth, constipation, diarrhea, headache, somnolence, and dizziness. (6)

To report SUSPECTED ADVERSE REACTIONS, contact Ajanta Pharma USA Inc. at 1-855-664-

7744 or FDA at 1-800-FDA-1088 or *www.fda.gov/medwatch.*

DRUG INTERACTIONS

- Co-administration with other anticholinergic drugs may increase the frequency and/or severity of anticholinergic-like effects. (7)
- Co-administration with strong cytochrome P450 (CYP) 3A4 inhibitors (e.g., ketoconazole) increases the systemic exposure of oxybutynin. (7)

USE IN SPECIFIC POPULATIONS

- Pediatric Use: Oxybutynin chloride extended-release tablets are not recommended in pediatric patients who cannot swallow the tablet whole without chewing, dividing or crushing, or in children under the age of 6 years. (8.4)
- Renal or Hepatic Impairment: There have been no studies conducted in patients with renal or hepatic impairment. (8.6, 8.7)

See 17 for PATIENT COUNSELING INFORMATION.

Revised: 5/2023

FULL PRESCRIBING INFORMATION: CONTENTS*

* Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

Oxybutynin chloride is a muscarinic antagonist indicated for the treatment of overactive bladder with symptoms of urge urinary incontinence, urgency, and frequency.

Oxybutynin chloride extended-release tablets is also indicated for the treatment of pediatric patients aged 6 years and older with symptoms of detrusor overactivity associated with a neurological condition (e.g., spina bifida).

2 DOSAGE AND ADMINISTRATION

Oxybutynin chloride extended-release tablets must be swallowed whole with the aid of liquids, and must not be chewed, divided, or crushed.

Oxybutynin chloride extended-release tablets may be administered with or without food.

2.1 Adults

The recommended starting dose of oxybutynin chloride extended-release tablets is 5 mg or 10 mg once daily at approximately the same time each day. Dosage may be adjusted in 5-mg increments to achieve a balance of efficacy and tolerability (up to a maximum of 30 mg/day). In general, dosage adjustment may proceed at approximately weekly intervals.

2.2 Pediatric Patients Aged 6 Years of Age and Older

The recommended starting dose of oxybutynin chloride extended-release tablets is 5 mg once daily at approximately the same time each day. Dosage may be adjusted in 5-mg increments to achieve a balance of efficacy and tolerability (up to a maximum of 20 mg/day).

3 DOSAGE FORMS AND STRENGTHS

Oxybutynin chloride extended-release tablets, USP are available as 5 mg, 10 mg and 15 mg tablets for oral use:

5 mg: Light yellow to yellow colored, round, enteric coated tablets with “0B1” imprinted

on one side with black ink.

10 mg: Light pink to pink colored, round, enteric coated tablets with “0B2” imprinted on one side with black ink.

15 mg: Light grey to grey colored, round, enteric coated tablets with “0B3” imprinted on one side with black ink.

4 CONTRAINDICATIONS

Oxybutynin chloride extended-release tablets are contraindicated in patients with urinary retention, gastric retention and other severe decreased gastrointestinal motility conditions, uncontrolled narrow-angle glaucoma.

Oxybutynin chloride extended-release tablets are also contraindicated in patients who have demonstrated hypersensitivity to the drug substance or other components of the product. There have been reports of hypersensitivity reactions, including anaphylaxis and angioedema.

5 WARNINGS AND PRECAUTIONS

5.1 Angioedema

Angioedema of the face, lips, tongue and/or larynx has been reported with oxybutynin. In some cases, angioedema occurred after the first dose. Angioedema associated with upper airway swelling may be life-threatening. If involvement of the tongue, hypopharynx, or larynx occurs, oxybutynin should be promptly discontinued and appropriate therapy and/or measures necessary to ensure a patent airway should be promptly provided.

5.2 Central Nervous System Effects

Oxybutynin is associated with anticholinergic central nervous system (CNS) effects *[see Adverse Reactions (6)].*A variety of CNS anticholinergic effects have been reported, including hallucinations, agitation, confusion and somnolence. Patients should be monitored for signs of anticholinergic CNS effects, particularly in the first few months after beginning treatment or increasing the dose. Advise patients not to drive or operate heavy machinery until they know how oxybutynin chloride extended-release tablets affects them. If a patient experiences anticholinergic CNS effects, dose reduction or drug discontinuation should be considered.

Oxybutynin chloride extended-release tablets should be used with caution in patients with preexisting dementia treated with cholinesterase inhibitors due to the risk of aggravation of symptoms.

Oxybutynin chloride extended-release tablets should be used with caution in patients with Parkinson’s disease due to the risk of aggravation of symptoms.

5.3 Worsening of Symptoms of Myasthenia Gravis

Oxybutynin chloride extended-release tablets should be used with caution in patients with myasthenia gravis due to the risk of aggravation of symptoms.

5.4 Worsening of Symptoms of Decreased Gastrointestinal Motility in Patients with Autonomic Neuropathy

Oxybutynin chloride extended-release tablets should be used with caution in patients with autonomic neuropathy due to the risk of aggravation of symptoms of decreased gastrointestinal motility.

5.5 Urinary Retention

Oxybutynin chloride extended-release tablets should be administered with caution to patients with clinically significant bladder outflow obstruction because of the risk of urinary retention *[see Contraindications (4)].*

5.6 Gastrointestinal Adverse Reactions

Oxybutynin chloride extended-release tablets should be administered with caution to patients with gastrointestinal obstructive disorders because of the risk of gastric retention *[see Contraindications (4)].*

Oxybutynin chloride extended-release tablets, 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.

Oxybutynin chloride extended-release tablets 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.

As with any other nondeformable material, caution should be used when administering oxybutynin chloride extended-release tablets to patients with preexisting severe gastrointestinal narrowing (pathologic or iatrogenic). There have been rare reports of obstructive symptoms in patients with known strictures in association with the ingestion of other drugs in nondeformable controlled-release formulations.

6 ADVERSE REACTIONS

6.1 Clinical Trials Experience

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

The safety and efficacy of oxybutynin chloride extended-release tablets (5 mg/day to 30 mg/day) was evaluated in 774 adult subjects who participated in five double-blind, controlled clinical trials. In four of the five studies, oxybutynin chloride tablets (5 mg/day to 20 mg/day in 199 subjects) was an active comparator. Adverse reactions reported by

greater than or equal to 1% of subjects are shown in Table 1.

Table 1: Adverse Drug Reactions Reported by greater than or equal to 1% of Oxybutynin Chloride Extended-Release Tablets- treated Adult Subjects in Five Double-blind, Controlled Clinical Trials of Oxybutynin Chloride Extended-Release Tablets.

System/Organ Class Preferred Term	Oxybutynin Chloride Extended-Release Tablets 5 to 30 mg/day n=774 %	Oxybutynin Chloride Tablets [1] 5 to 20 mg/day n=199 %
Psychiatric Disorders		
Insomnia	3.0	5.5
Nervous System Disorders		
Headache	7.5	8.0
Somnolence	5.6	14.1
Dizziness	5.0	16.6
Dysgeusia	1.6	1.5
Eye Disorders		
Vision blurred	4.3	9.6
Dry eye	3.1	2.5
Respiratory, Thoracic and Mediastinal Disorders		
Cough	1.9	3.0
Oropharyngeal pain	1.9	1.5
Dry throat	1.7	2.5
Nasal dryness	1.7	4.5
Gastrointestinal Disorders		
Dry mouth	34.9	72.4
Constipation	8.7	15.1
Diarrhea	7.9	6.5
Dyspepsia	4.5	6.0
Nausea	4.5	11.6
Abdominal pain	1.6	2.0
Vomiting	1.3	1.5
Flatulence	1.2	2.5
Gastro-esophageal reflux disease	1.0	0.5
Skin and Subcutaneous Tissue Disorders		
Dry skin	1.8	2.5
Pruritus	1.3	1.5
Renal and Urinary Disorders		
Dysuria	1.9	2.0
Urinary hesitation	1.9	8.5
Urinary retention	1.2	3.0
General Disorders and Administration Site Conditions		
Fatigue	2.6	3.0
Investigations		

Residual urine volume [2]	2.3	3.5

[1] Immediate-release formulation
[2] The bundled term residual urine volume consists of the preferred terms residual urine volume and residual urine volume increased.

The discontinuation rate due to adverse reactions was 4.4% with oxybutynin chloride extended-release tablets compared to 0% with oxybutynin chloride tablets. The most frequent adverse reaction causing discontinuation of study medication was dry mouth (0.7%).

The following adverse reactions were reported by less than 1% of oxybutynin chloride extended-release tablets-treated patients and at a higher incidence than placebo in clinical trials: *Metabolism and Nutrition Disorders:*anorexia, fluid retention; *Vascular disorders:*hot flush; *Respiratory, thoracic and mediastinal disorders:*dysphonia; *Gastrointestinal Disorders:*dysphagia, frequent bowel movements; *General disorders and administration site conditions:*chest discomfort, thirst.

6.2 Postmarketing Experience

The following additional adverse reactions have been reported from worldwide postmarketing experience with oxybutynin chloride extended-release tablets. Because postmarketing reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

*Infections and Infestations:*Urinary tract infection; *Psychiatric Disorders:*psychotic disorder, agitation, confusional state, hallucinations, memory impairment, abnormal behavior; *Nervous System Disorders:*convulsions; *Eye Disorders:*glaucoma; *Respiratory, Thoracic and Mediastinal Disorders:*nasal congestion; *Cardiac Disorders:*arrhythmia, tachycardia, palpitations; QT interval prolongation;

*Vascular Disorders:*flushing, hypertension; *Skin and Subcutaneous Tissue Disorders:*rash; *Renal and Urinary Disorders*: impotence; *General Disorders and Administration Site Conditions:*hypersensitivity reactions, including angioedema with airway obstruction, urticaria, and face edema; anaphylactic reactions requiring hospitalization for emergency treatment; *Injury, poisoning and procedural complications:*fall.

Additional adverse events reported with some other oxybutynin chloride formulations include: cycloplegia, mydriasis, and suppression of lactation. In one reported case, concomitant use of oxybutynin with carbamazepine and dantrolene was associated with adverse events of vomiting, drowsiness, confusion, unsteadiness, slurred speech and nystagmus, suggestive of carbamazepine toxicity.

7 DRUG INTERACTIONS

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. Anticholinergic agents may also antagonize the effects of prokinetic agents, such as metoclopramide.

Mean oxybutynin plasma concentrations were approximately 2 fold higher when oxybutynin chloride extended-release tablets 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.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

There are no adequate data on oxybutynin chloride extended-release tablets use in pregnant women to evaluate for a drug-associated risk of major birth defects, miscarriage or adverse maternal or fetal outcomes.

In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively. The background risk of major birth defects and miscarriage for the indicated population is unknown.

8.2 Lactation

Risk Summary

There are no data on the presence of oxybutynin in human milk, the effects on the breastfed infant, or the effects of oxybutynin chloride extended-release tablets on milk production. The developmental and health benefits of breastfeeding should be considered along with the mother’s clinical need for oxybutynin chloride extended-release tablets and any potential adverse effects on the breastfed child from oxybutynin chloride extended-release tablets or from the underlying maternal condition.

8.4 Pediatric Use

The safety and efficacy of oxybutynin chloride extended-release tablets were studied in 60 children in a 24-week, open-label, non-randomized trial. Patients were aged 6-15 years, all had symptoms of detrusor overactivity in association with a neurological condition (e.g., spina bifida), all used clean intermittent catheterization, and all were current users of oxybutynin chloride. Study results demonstrated that administration of oxybutynin chloride extended-release tablets 5 mg/day to 20 mg/day was associated with an increase from baseline in mean urine volume per catheterization from 108 mL to 136 mL, an increase from baseline in mean urine volume after morning awakening from 148 mL to 189 mL, and an increase from baseline in the mean percentage of catheterizations without a leaking episode from 34% to 51%.

Urodynamic results were consistent with clinical results. Administration of oxybutynin chloride extended-release tablets resulted in an increase from baseline in mean maximum cystometric capacity from 185 mL to 254 mL, a decrease from baseline in mean detrusor pressure at maximum cystometric capacity from 44 cm H_2O to 33 cm H_2O, and a reduction in the percentage of patients demonstrating uninhibited detrusor contractions (of at least 15 cm H_2O) from 60% to 28%.

The pharmacokinetics of oxybutynin chloride extended-release tablets in these patients were consistent with those reported for adults *[see Clinical Pharmacology (12.3)].*

Oxybutynin chloride extended-release tablets are not recommended in pediatric patients who cannot swallow the tablet whole without chewing, dividing, or crushing, or in children under the age of 6.

8.5 Geriatric Use

The rate and severity of anticholinergic effects reported by patients less than 65 years old and those 65 years and older were similar. The pharmacokinetics of oxybutynin chloride extended-release tablets were similar in all patients studied (up to 78 years of age).

8.6 Renal Impairment

There were no studies conducted with oxybutynin chloride extended-release tablets in patients with renal impairment.

8.7 Hepatic Impairment

There were no studies conducted with oxybutynin chloride extended-release tablets in patients with hepatic impairment.

10 OVERDOSAGE

The continuous release of oxybutynin from oxybutynin chloride extended-release tablets should be considered in the treatment of overdosage. Patients should be monitored for at least 24 hours. Treatment should be symptomatic and supportive. A cathartic may be administered.

Overdosage with oxybutynin chloride has been associated with anticholinergic effects including central nervous system excitation, flushing, fever, dehydration, cardiac arrhythmia, vomiting, and urinary retention.

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.

11 DESCRIPTION

Oxybutynin chloride, USP is an antispasmodic, muscarinic antagonist. Each oxybutynin chloride extended-release tablet, USP contains 5 mg, 10 mg, or 15 mg of oxybutynin chloride USP, formulated as a once-a-day controlled-release tablet for oral administration. Oxybutynin chloride, USP is administered as a racemate of R- and S-enantiomers.

Chemically, oxybutynin chloride, USP is 4(diethylamino-but-2-ynyl (RS) 2-cyclohexyl-2-hydroxy 2 phenyl acetate hydrochloride. The molecular formula of oxybutynin chloride, USP is $C_{22}H_{31}NO_3 \cdot HCl$.

Its structural formula is:

Oxybutynin chloride, USP is a white crystalline powder with a molecular weight of 393.95. It 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.

Oxybutynin chloride extended-release tablets, USP also contains the following inert ingredients: anhydrous dibasic calcium phosphate, povidone, hypromellose, colloidal silicon dioxide, magnesium stearate, polyethylene glycol, methacrylic acid copolymer type c, talc, titanium dioxide, triethyl citrate, sodium bicarbonate, sodium lauryl sulfate, ferrosoferric oxide, ferric oxide red (in 10 mg only) and iron oxide yellow (in 5 mg and 15 mg only).

The imprinting material contains: shellac glaze, black iron oxide, propylene glycol and ammonium hydroxide.

Meets USP Dissolution Test 9.

System Components and Performance

Oxybutynin chloride extended-release tablets, USP are formulated to deliver oxybutynin chloride at a controlled rate over approximately 24 hours. The dosage form is comprised of a hydrophilic cellulose polymer matrix tablet surrounded by an enteric coating system. The enteric coat is insoluble in the low pH environment of the stomach. As the tablet passes through the stomach and enters the higher pH environment of the small intestine, the enteric coating dissolves and/or erodes to expose the polymer matrix tablet which swells and releases drug at a controlled rate via diffusion and/or erosion.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Oxybutynin relaxes bladder smooth muscle. Oxybutynin chloride exerts a direct antispasmodic effect on smooth muscle and inhibits the muscarinic action of acetylcholine on smooth muscle. No blocking effects occur at skeletal neuromuscular junctions or autonomic ganglia (antinicotinic effects).

Antimuscarinic activity resides predominantly in the R-isomer. A metabolite, desethyloxybutynin, has pharmacological activity similar to that of oxybutynin in *in*

*vitro*studies.

12.2 Pharmacodynamics

In patients with conditions characterized by involuntary bladder contractions, cystometric studies have demonstrated that oxybutynin increases bladder (vesical) capacity, diminishes the frequency of uninhibited contractions of the detrusor muscle, and delays the initial desire to void.

12.3 Pharmacokinetics

Absorption

Following the first dose of oxybutynin chloride extended-release tablets, oxybutynin plasma concentrations rise for 4 to 6 hours; thereafter steady concentrations are maintained for up to 24 hours, minimizing fluctuations between peak and trough concentrations associated with oxybutynin.

The relative bioavailabilities of R- and S-oxybutynin from oxybutynin chloride extended-release tablets are 156% and 187%, respectively, compared with oxybutynin. The mean pharmacokinetic parameters for R and S-oxybutynin are summarized in Table 2. The plasma concentration-time profiles for R- and S-oxybutynin are similar in shape; Figure 1 shows the profile for R-oxybutynin.

Table 2: Mean (SD) R- and S-Oxybutynin Pharmacokinetic Parameters Following a Single Dose of Oxybutynin Chloride Extended-Release Tablets10 mg (n=43)

Parameters (units)	**R-Oxybutynin**		**S-Oxybutynin**	
C_{max}(ng/mL)	1.0	(0.6)	1.8	(1.0)
T_{max}(h)	12.7	(5.4)	11.8	(5.3)
$t_{1/2}$(h)	13.2	(6.2)	12.4	(6.1)
$AUC_{(0-48)}$(ng•h/mL)	18.4	(10.3)	34.2	(16.9)
AUC_{inf}(ng•h/mL)	21.3	(12.2)	39.5	(21.2)

Figure 1:Mean R-oxybutynin plasma concentrations following a single dose of Oxybutynin Chloride Extended-Release Tablets10 mg and oxybutynin 5 mg administered every 8 hours (n=23 for each treatment).

Steady state oxybutynin plasma concentrations are achieved by Day 3 of repeated oxybutynin chloride extended-release tablets dosing, with no observed drug accumulation or change in oxybutynin and desethyloxybutynin pharmacokinetic parameters.

Oxybutynin chloride extended-release tablets steady state pharmacokinetics were studied in 19 children aged 5 to15 years with detrusor overactivity associated with a neurological condition (e.g., spina bifida). The children were on oxybutynin chloride extended-release tablets total daily dose ranging from 5 mg to 20 mg (0.10 mg/kg to 0.77 mg/kg). Sparse sampling technique was used to obtain serum samples. When all available data are normalized to an equivalent of 5 mg per day of oxybutynin chloride extended-release tablets the mean pharmacokinetic parameters derived for R- and S-

oxybutynin and R- and S-desethyloxybutynin are summarized in Table 3. The plasma-time concentration profiles for R- and S-oxybutynin are similar in shape; Figure 2 shows the profile for R-oxybutynin when all available data are normalized to an equivalent of 5 mg per day.

Table 3: Mean ± SD R- and S-Oxybutynin and R- and S-Desethyloxybutynin Pharmacokinetic Parameters in Children Aged 5 to 15 Following Administration of 5 to 20 mg Oxybutynin Chloride Extended-Release Tablets Once Daily (n=19), All Available Data Normalized to an Equivalent of Oxybutynin Chloride Extended-Release Tablets 5 mg Once Daily

	R-Oxybutynin	S-Oxybutynin	R- Desethyl oxybutynin	S-Desethyl oxybutynin
C_{max}(ng/mL)	0.7 ± 0.4	1.3 ± 0.8	7.8 ± 3.7	4.2 ± 2.3
T_{max}(h)	5.0	5.0	5.0	5.0
AUC (ng•h/mL)	12.8 ± 7.0	23.7 ± 14.4	125.1 ± 66.7	73.6 ± 47.7

Figure 2: Mean steady state (± SD) R-oxybutynin plasma concentrations following administration of 5 to 20 mg Oxybutynin Chloride Extended-Release Tablets once daily in children aged 5 to 15. Plot represents all available data normalized to an equivalent of Oxybutynin Chloride Extended-Release Tablets 5 mg once daily.

Food Effects

The rate and extent of absorption and metabolism of oxybutynin are similar under fed and fasted conditions.

Distribution

Oxybutynin is widely distributed in body tissues following systemic absorption. The volume of distribution is 193 L after intravenous administration of 5 mg oxybutynin chloride. Both enantiomers of oxybutynin are highly bound (greater than 99%) to plasma proteins. Both enantiomers of N-desethyloxybutynin are also highly bound (greater than 97%) to plasma proteins. The major binding protein is alpha-1 acid glycoprotein.

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. Following oxybutynin chloride extended-release tablets administration, plasma concentrations of R- and S-desethyloxybutynin are 73% and 92%, respectively, of concentrations observed with oxybutynin.

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 desethyloxybutynin.

Dose Proportionality

Pharmacokinetic parameters of oxybutynin and desethyloxybutynin (C_{max} and AUC) following administration of 5 mg - 20 mg of oxybutynin chloride extended-release tablets are dose proportional.

Use in Specific Populations

Pediatric

The pharmacokinetics of oxybutynin chloride extended-release tablets were evaluated in 19 children aged 5-15 years with detrusor overactivity associated with a neurological condition (e.g., spina bifida). The pharmacokinetics of oxybutynin chloride extended-release tablets in these pediatric patients were consistent with those reported for adults (see Tables 2 and 3, and Figures 1 and 2 above).

Gender

There are no significant differences in the pharmacokinetics of oxybutynin in healthy male and female volunteers following administration of oxybutynin chloride extended-release tablets.

Race

Available data suggest that there are no significant differences in the pharmacokinetics of oxybutynin based on race in healthy volunteers following administration of oxybutynin chloride extended-release tablets.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenesis

A 24-month study in rats at dosages of oxybutynin chloride of 20 mg/kg/day, 80 mg/kg/day, 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 a human equivalent dose taking into account normalization of body surface area.

Mutagenesis

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

Impairment of Fertility

No impairment of fertility was seen in rats at dosages up to 75 mg/kg/day (24 times the MRHD on a mg/m2 basis) when administered for 2 weeks prior to mating in females and for 9 weeks prior to mating in males.

14 CLINICAL STUDIES

Oxybutynin chloride extended-release tablets were evaluated for the treatment of patients with overactive bladder with symptoms of urge urinary incontinence, urgency, and frequency in three controlled efficacy studies. The majority of patients were Caucasian (89.0%) and female (91.9%) with a mean age of 59 years

(range, 18 to 98 years). Entry criteria required that patients have urge or mixed incontinence (with a predominance of urge) as evidenced by greater than or equal to 6 urge incontinence episodes per week and greater than or equal to 10 micturitions per day. Study 1 was a fixed-dose escalation design, whereas the

other two studies used a dose-adjustment design in which each patient's final dose was adjusted to a balance between improvement of incontinence symptoms and tolerability of side effects. All three studies included patients known to be responsive to oxybutynin or other anticholinergic medications, and

these patients were maintained on a final dose for up to 2 weeks.

The efficacy results for the three controlled trials are presented in the following Tables 4, 5, and 6 and Figures 3, 4, and 5.

Table 4: Number of Urge Urinary Incontinence Episodes Per Week (Study 1)

Study 1	**n**	**Oxybutynin Chloride Extended-Release Tablets**	**n**	**Placebo**
Mean Baseline	34	15.9	16	20.9
Mean (SD) Change from Baseline †	34	-15.8 (8.9)	16	-7.6 (8.6)
95% Confidence Interval for Difference (Oxybutynin Chloride Extended-Release Tablets - Placebo)	(-13.6, -2.8) *			

*The difference between oxybutynin chloride extended-release tablets and placebo was statistically significant.

†Covariate adjusted mean with missing observations set to baseline values

Figure 3: Mean Change (±SD) in Urge Urinary Incontinence Episodes Per Week from Baseline (Study 1)

* The difference between oxybutynin chloride extended-release tablets and placebo was statistically significant.

Table 5: Number of Urge Urinary Incontinence Episodes Per Week (Study 2)

Study 2	**n**	**Oxybutynin Chloride Extended-Release Tablets**	**n**	**oxybutynin**
Mean Baseline	53	27.6	52	23.0
Mean (SD) Change from Baseline †	53	-17.6 (11.9)	52	-19.4 (11.9)
95% Confidence Interval for Difference (Oxybutynin Chloride Extended-Release Tablets - Oxybutynin)	(-2.8, 6.5)			

†Covariate adjusted mean with missing observations set to baseline values

Figure 4: Mean Change (±SD) in Urge Urinary Incontinence Episodes Per Week from Baseline (Study 2)

Table 6: Number of Urge Urinary Incontinence Episodes Per Week (Study 3)

Study 3	**n**	**Oxybutynin Chloride Extended-Release Tablets**	**n**	**oxybutynin**
Mean Baseline	111	18.9	115	19.5
Mean (SD) Change from Baseline †	111	-14.5 (8.7)	115	-13.8 (8.6)
95% Confidence Interval for Difference (Oxybutynin Chloride Extended-Release Tablets - Oxybutynin)	(-3.0, 1.6) **			

**The difference between oxybutynin chloride extended-release tablets and oxybutynin fulfilled the criteria for comparable efficacy.

†Covariate adjusted mean with missing observations set to baseline values

Figure 5: Mean Change (±SD) in Urge Urinary Incontinence Episodes Per Week from Baseline (Study 3)

** The difference between oxybutynin chloride extended-release tablets and oxybutynin fulfilled the criteria for comparable efficacy.

16 HOW SUPPLIED/STORAGE AND HANDLING

Oxybutynin chloride extended-release tablets, USP are available in three dosage strengths, 5 mg (light yellow to yellow), 10 mg (light pink to pink), and 15 mg (light grey to grey) and are imprinted on one side with "0B1", "0B2", or "0B3" with black ink. Oxybutynin chloride extended-release tablets, USP are supplied in bottles of 100 tablets and 500 tablets.

5 mg	100 count bottle with child resistant closures	NDC 27241-155-04
	500 count bottle	NDC 27241-155-08
10 mg	100 count bottle with child resistant closures	NDC 27241-156-04
	500 count bottle	NDC 27241-156-08
15 mg	100 count bottle with child resistant closures	NDC 27241-157-04
	500 count bottle	NDC 27241-157-08

Storage

Store at 20°C to 25°C (68°F to 77°F); excursions permitted to 15°C to 30°C (59°F to 86°F). [see USP Controlled Room Temperature]. Protect from moisture and humidity.

Keep out of reach of children.

17 PATIENT COUNSELING INFORMATION

- Patients should be informed that oxybutynin may produce angioedema that could result in life threatening airway obstruction. Patients should be advised to promptly discontinue oxybutynin therapy and seek immediate medical attention if they experience swelling of the tongue, edema of the laryngopharynx, or difficulty breathing.
- Patients should be informed that anticholinergic (antimuscarinic) agents such as oxybutynin chloride extended-release tablets, may produce clinically significant adverse reactions related to anticholinergic activity such as:
  - Urinary retention and constipation
  - Heat prostration due to decreased sweating. Heat prostration can occur when anticholinergic medicines are administered in the presence of high environmental temperature.
- Patients should be informed that anticholinergic medicines such as oxybutynin chloride extended-release tablets may produce drowsiness (somnolence), dizziness or blurred vision. Patients should be advised to exercise caution in decisions to engage in potentially dangerous activities until oxybutynin chloride extended-release tablets effects have been determined.
- Patients should be informed that alcohol may enhance the drowsiness caused by anticholinergic agents such as oxybutynin chloride extended-release tablets.
- Patients should be informed that oxybutynin chloride extended-release tablets should be swallowed whole with the aid of liquids. Patients should not chew, divide, or crush tablets.
- Oxybutynin chloride extended-release tablets should be taken at approximately the same time each day.

For more information call 1-855-664-7744.

Product of INDIA

Marketed by:

Ajanta Pharma USA Inc.

Bridgewater, NJ 08807.

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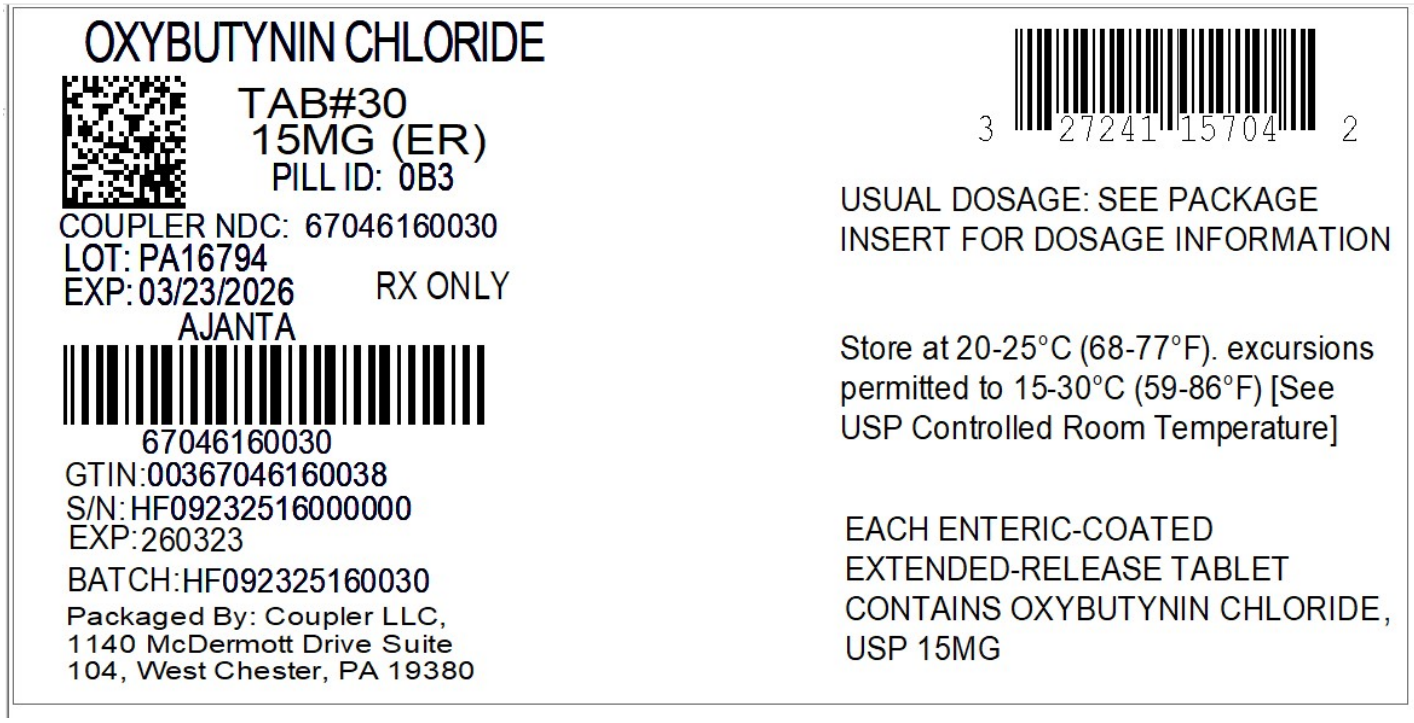
Revised: 05/2021



OXYBUTYNIN CHLORIDE

oxybutynin chloride tablet, extended release

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:67046-1600(NDC:27241-157)
Route of Administration	ORAL		

Active Ingredient/Active Moiety		
Ingredient Name	**Basis of Strength**	**Strength**
OXYBUTYNIN CHLORIDE (UNII: L9F3D9RENQ) (OXYBUTYNIN - UNII:K9P6MC7092)	OXYBUTYNIN CHLORIDE	15 mg

Inactive Ingredients	
Ingredient Name	**Strength**
CALCIUM PHOSPHATE, UNSPECIFIED FORM (UNII: 97Z1WI3NDX)	
POVIDONE K30 (UNII: U725QWY32X)	
HYPROMELLOSE 2208 (100 MPA.S) (UNII: B1QE5P712K)	
SILICON DIOXIDE (UNII: ETJ7Z6XBU4)	
MAGNESIUM STEARATE (UNII: 70097M6I30)	
POLYETHYLENE GLYCOL, UNSPECIFIED (UNII: 3WQ0SDW1A)	
METHACRYLIC ACID (UNII: 1CS02G8656)	
TALC (UNII: 7SEV7J4R1U)	
TITANIUM DIOXIDE (UNII: 15FIX9V2JP)	
TRIETHYL CITRATE (UNII: 8Z96QXD6UM)	
SODIUM BICARBONATE (UNII: 8MDF5V39QO)	
SODIUM LAURYL SULFATE (UNII: 368GB5141J)	

FERROSOFERRIC OXIDE (UNII: XM0M87F357)	
FERRIC OXIDE YELLOW (UNII: EX438O2MRT)	
SHELLAC (UNII: 46N107B71O)	
PROPYLENE GLYCOL (UNII: 6DC9Q167V3)	
AMMONIA (UNII: 5138Q19F1X)	

Product Characteristics

Color	gray (light gray to gray)	**Score**	no score
Shape	ROUND	**Size**	8mm
Flavor		**Imprint Code**	0B3
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:67046-1600-3	30 in 1 BLISTER PACK; Type 0: Not a Combination Product	09/23/2025	

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA211655	09/23/2025	

Labeler - Coupler LLC (119003108)

Registrant - Ajanta Pharma Limited (918594859)

Establishment

Name	Address	ID/FEI	Business Operations
Coupler LLC		119003108	repack(67046-1600)

Revised: 12/2025 Coupler LLC