HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use SANCTURA XR™ safely and effectively. See full prescribing information for SANCTURA XR™.

SANCTURA XR™ (trospium chloride extended release capsules)
Initial U.S. Approval: May 2004

---------- **INDICATIONS AND USAGE** ----------
SANCTURA XR™ is an anticholinergic indicated for the treatment of overactive bladder (OAB) with symptoms of urge urinary incontinence, urgency, and urinary frequency. (1)

-------- **DOSAGE AND ADMINISTRATION** --------
The recommended dosage of **SANCTURA XR™** is one 60 mg capsule daily in the morning.
SANCTURA XR™ should be dosed with water on an empty stomach, at least one hour before a meal. (2)
SANCTURA XR™ is not recommended for use in patients with severe renal impairment (creatinine clearance < 30 mL/minute). (2)

------- **DOSAGE FORMS AND STRENGTHS** -------
• 60 mg capsules (white opaque body and orange opaque cap, printed with SAN 60) (3)

---------- **CONTRAINDICATIONS** ----------
SANCTURA XR™ is contraindicated in patients with urinary retention, gastric retention, or uncontrolled narrow-angle glaucoma, and in patients who are at risk for these conditions. (4)

-------- **WARNINGS AND PRECAUTIONS** ---------
SANCTURA XR™ should be administered with caution to patients with clinically significant bladder outflow obstruction or gastrointestinal obstructive disorders due to risk of urinary or gastric retention. (5.1, 5.2)
In patients with narrow angle glaucoma **SANCTURA XR™** should be used only with careful monitoring. (5.3)
SANCTURA XR™ is not recommended for use in patients with severe renal impairment (creatinine clearance < 30 mL/minute). (5.4)
Alcohol should not be consumed within 2 hours of **SANCTURA XR™** administration. (5.5)

---------- **ADVERSE REACTIONS** ----------
The most common adverse reactions with **SANCTURA XR™** were dry mouth (10.7%) and constipation (8.5%). (6.1)
To report SUSPECTED ADVERSE REACTIONS, contact Allergan, Inc. at 1-800-433-8871 or FDA at 1-800-FDA-1088 or *www.fda.gov/medwatch*.

---------- **DRUG INTERACTIONS** ----------
Trospium is metabolized by ester hydrolysis and excreted by the kidneys through a combination of tubular secretion and glomerular filtration. (7)
Based on *in vitro* data, no clinically relevant metabolic drug-drug interactions are anticipated with **SANCTURA XR™**. (7)
Some drugs which are actively secreted by the kidney may interact with **SANCTURA XR™** by competing for renal tubular secretion. (7)
• Concomitant use with digoxin did not affect the pharmacokinetics of either drug (7.1)
• Exposure to trospium on average was comparable in the presence of and without antacid, however, some individuals demonstrated increases or decreases in trospium exposure in the presence of antacid. The clinical relevance of these findings is not known. (7.2)
• The oral bioavailability was reduced following a high fat-content meal (7.3)

-------- **USE IN SPECIFIC POPULATIONS** --------
• PREGNANCY CATEGORY C
• In post-parturition animal studies trospium chloride was excreted to a limited extent into the milk (8.3)
• The safety and effectiveness of **SANCTURA XR™** in pediatric patients have not been established. (8.4)
• **SANCTURA XR™** is not recommended for use in patients with severe renal impairment (8.6)
• Caution is advised when **SANCTURA XR™** is used in patients with moderate to severe hepatic impairment (8.7)

See 17 for PATIENT COUNSELING INFORMATION

Revised: 11/2008

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FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

SANCTURA XR™ is indicated for the treatment of overactive bladder (OAB) with symptoms of urge urinary incontinence, urgency, and urinary frequency.

2 DOSAGE AND ADMINISTRATION

The recommended dosage of **SANCTURA XR™** is one 60 mg capsule daily in the morning.
SANCTURA XR™ capsules should be dosed with water on an empty stomach, at least one hour before a meal.
SANCTURA XR™ is not recommended for use in patients with severe renal impairment (creatinine clearance < 30 mL/minute) (see *Warnings and Precautions (5), Use in Specific Populations (8), and Clinical Pharmacology (12)).*

3 DOSAGE FORMS AND STRENGTHS

SANCTURA XR™ is supplied as 60 mg capsules (white opaque body and orange opaque cap, printed with SAN 60).

4 CONTRAINDICATIONS

SANCTURA XR™ is contraindicated in patients with urinary retention, gastric retention, or uncontrolled narrow-angle glaucoma and in patients who are at risk for these conditions. **SANCTURA XR™** is also contraindicated in patients who have demonstrated hypersensitivity to the drug or any of its ingredients.

5 WARNINGS AND PRECAUTIONS

5.1 Risk of Urinary Retention

SANCTURA XR™ capsules should be administered with caution to patients with clinically significant bladder outflow obstruction because of the risk of urinary retention (see *Contraindications (4)*).

5.2 Decreased Gastrointestinal Motility

SANCTURA XR™ should be administered with caution to patients with gastrointestinal obstructive disorders because of the risk of gastric retention. **SANCTURA XR™**, like other antimuscarinic agents, may decrease gastrointestinal motility and should be used with caution in patients with conditions such as ulcerative colitis, intestinal atony and myasthenia gravis (see *Contraindications (4)*).

5.3 Controlled Narrow-angle Glaucoma

In patients being treated for narrow-angle glaucoma, **SANCTURA XR™** should only be used if the potential benefits outweigh the risks, and in that circumstance only with careful monitoring (see *Contraindications (4)*).

5.4 Patients with Severe Renal Impairment

SANCTURA XR™ is not recommended for use in patients with severe renal impairment (creatinine clearance < 30 mL/minute) (see Dosage and Administration (2), Use in Specific Populations (8), and Clinical Pharmacology (12)).

5.5 Alcohol Interaction

Alcohol should not be consumed within 2 hours of **SANCTURA XR™** administration. In addition, patients should be informed that alcohol may enhance the drowsiness caused by anticholinergic agents.

6 ADVERSE REACTIONS

6.1 Adverse Reactions in Clinical Trials

The data described below reflect exposure to **SANCTURA XR™** capsules in 578 patients for 12 weeks in two Phase 3 double-blind, placebo controlled trials (n = 1165). These studies included overactive bladder patients of ages 21 to 90 years, of which 86% were female and 85% were Caucasian. Patients received 60 mg daily doses of **SANCTURA XR™**. Patients in these studies were eligible to continue treatment with **SANCTURA XR™** 60 mg for up to one year. From both these controlled trials combined, 769 and 238 patients received treatment with **SANCTURA XR™** for at least 24 and 52 weeks, respectively.

There were 157 (27.2%) **SANCTURA XR™** patients and 98 (16.7%) placebo patients who experienced one or more double-blind treatment-emergent adverse events (TEAEs) that were assessed by the investigator as at least possibly related to study medication. The most common TEAEs were dry mouth and constipation which, when reported, commonly occurred early in treatment (often within the first week). In the two Phase 3 studies, constipation, dry mouth, and urinary retention led to discontinuation in 1%, 0.7%, and 0.5% of patients treated with **SANCTURA XR™** 60 mg daily, respectively. In the placebo group, there were no discontinuations due to dry mouth or urinary retention and one due to constipation.

The incidence of serious adverse events was similar among patients receiving **SANCTURA XR™** and patients receiving placebo. No treatment-emergent serious adverse events in either treatment group were judged by the investigators as being possibly related to the study medication.

Table 1 lists those treatment-emergent adverse events from the trials that were assessed by the investigator as possibly related to study medication, reported in at least 1% of **SANCTURA XR™** patients, and were more common for the **SANCTURA XR™** group than for placebo.

Table 1: Incidence of treatment-emergent adverse events reported in at least 1% of patients judged by the investigator as at least possibly related to treatment and more common for the SANCTURA XR™ group than for placebo.

MedDRA Preferred term	Number of patients (%)	
	Placebo N = 587	SANCTURA XR™ N = 578
Dry Mouth	22 (3.7)	62 (10.7)
Constipation	9 (1.5)	49 (8.5)
Dry eye	1 (0.2)	9 (1.6)
Flatulence	3 (0.5)	9 (1.6)
Nausea	2 (0.3)	8 (1.4)
Abdominal Pain	2 (0.3)	8 (1.4)
Dyspepsia	4 (0.7)	7 (1.2)
Urinary tract infection	5 (0.9)	7 (1.2)
Constipation aggravated	3 (0.5)	7 (1.2)
Abdominal distension	2 (0.3)	6 (1.0)
Nasal dryness	0 (0.0)	6 (1.0)

Additional adverse events reported in less than 1% of **SANCTURA XR™**-treated patients and more common for **SANCTURA XR™** than placebo, judged by the investigator at least possibly related to treatment were: vision blurred, feces hard, back pain, somnolence, urinary retention, and dry skin.

Table 2 lists all treatment-emergent adverse events for the trials reported in at least 2% of all **SANCTURA XR™** patients and more common for the **SANCTURA XR™** group than for placebo without regard to the investigator's judgment on drug relatedness.

Table 2: Incidence of treatment-emergent adverse events reported in at least 2% of patients regardless of reported relationship to treatment and more common for the SANCTURA XR™ group than for placebo.

MedDRA Preferred term	Number of patients (%)	
	Placebo N = 587	SANCTURA XR™ N = 578
Dry Mouth	22 (3.7)	64 (11.1)
Constipation	10 (1.7)	52 (9.0)
Urinary tract infection	29 (4.9)	42 (7.3)
Nasopharyngitis	10 (1.7)	17 (2.9)
Influenza	9 (1.5)	13 (2.2)

Additional adverse events reported in less than 2% of **SANCTURA XR™**-treated patients and twice as frequent for **SANCTURA XR™** compared to placebo, regardless of reported relationship to treatment were: tachycardia, dry eyes, abdominal pain, dyspepsia, abdominal distension, constipation aggravated, nasal dryness, and rash.

In the open-label treatment phase, the most common TEAEs reported in the 769 patients with at least 6 months exposure to **SANCTURA XR™** were: constipation, and dry mouth. Urinary tract infection and rash was also reported in several patients, including one of each judged by the investigator to be possibly related to treatment. Several adverse events were reported as severe in the open-label treatment phase, including one urinary tract infection, two urinary retention events, and one aggravated constipation.

Electrophysiology
The effect of 20 mg BID and up to 100 mg BID of an immediate-release formulation of trospium chloride on QT interval was evaluated in a single-blind, randomized, placebo and active (moxifloxacin 400 mg daily) controlled, 5-day parallel trial in 170 male and female healthy volunteer subjects aged 18 to 45 years. The QT interval was measured over a 24-hour period at steady state. Trospium chloride was not associated with an increase in individual corrected (QTcI) or Fridericia corrected (QTcF) QT interval at any time during steady state measurement, while moxifloxacin was associated with a 6.4 msec increase in QTcF.

In this study, asymptomatic, non-specific T-wave inversions were observed more often in subjects receiving trospium chloride than in subjects receiving moxifloxacin or placebo following five days of treatment. The clinical significance of T-wave inversion in this study is unknown. This finding was not observed during routine safety monitoring in overactive bladder patients from 2 placebo-controlled clinical trials in 591 patients treated with 20 mg BID of immediate-release trospium chloride, nor was it observed in 2 placebo-controlled clinical trials in 578 patients treated with **SANCTURA XR™** capsules.

Also in this study, the immediate-release formulation of trospium chloride was associated with an increase in heart rate that correlated with increasing plasma concentration, with a mean elevation in heart rate compared to placebo of 9 beats per minute for the 20 mg dose and of 18 beats per minute for the 100 mg dose. In the two Phase 3 **SANCTURA XR™** trials the mean increase in heart rate compared to placebo was approximately 3 beats per minute in both studies.

6.2 Post-marketing Experience
The following adverse reactions have been identified during European and US postapproval use of trospium chloride 20 mg BID. Reported events have included: Gastrointestinal – gastritis; Cardiovascular – palpitations, supraventricular tachycardia, chest pain, syncope, “hypertensive crisis”; Immunological – Stevens-Johnson syndrome, anaphylactic reaction; Nervous System – vision abnormal, hallucinations and delirium; Musculoskeletal – rhabdomyolysis; General – rash.

7 DRUG INTERACTIONS
Trospium is metabolized by ester hydrolysis and excreted by the kidneys through a combination of tubular secretion and glomerular filtration. Based on *in vitro* data, no clinically relevant metabolic drug-drug interactions are anticipated with **SANCTURA XR™**. However, some drugs which are actively secreted by the kidney may interact with **SANCTURA XR™** by competing for renal tubular secretion.

The concomitant use of **SANCTURA XR™** with other antimuscarinic agents that produce dry mouth and constipation and other anticholinergic effects may increase the frequency and/or severity of such effects. **SANCTURA XR™** capsules may potentially alter the absorption of some concomitantly administered drugs due to anticholinergic effects on GI motility.

7.1 Digoxin
Concomitant use of trospium chloride 20mg BID and digoxin did not affect the pharmacokinetics of either drug.

7.2 Antacid
A drug interaction study was conducted to evaluate the effect of an antacid containing aluminum hydroxide and magnesium carbonate on the PK of **SANCTURA XR™** (n =11). While the systemic exposure of trospium on average was comparable with and without antacid, 5 individuals demonstrated either an increase or decrease in trospium exposure, in presence of antacid. The clinical relevance of these findings is not known.

7.3 Food Interaction
Administration of **SANCTURA XR™** immediately after a high fat-content meal reduced the oral bioavailability of trospium chloride by 35% for $AU_{(0\text{-}Tlast)}$ and by 60% for C_{max}. It is therefore recommended that **SANCTURA XR™** be taken on an empty stomach at least one hour before a meal.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Pregnancy Category C: Trospium chloride was not teratogenic at statistically significant levels in rats or rabbits at doses up to 200 mg/kg/day (approximately 16 and 32 times the maximum expected clinical dose, respectively). However, in rabbits, one fetus in each of the low, medium and high dose groups (1, 1, and 32 times, respectively) demonstrated multiple malformations, including umbilical hernia and skeletal malformations. At 200 mg/kg/day trospium chloride, maternal toxicity was observed in rats and rabbits. At 20 mg/kg/day in rats and rabbits, no maternal or fetal toxicity was observed (approximately equivalent to the expected clinical dose via AUC). No developmental toxicity was observed in rats up to 200 mg/kg/day. There are no adequate and well-controlled studies in pregnant women. **SANCTURA XR™** should be used during pregnancy only if the potential benefit justifies the potential risk.

8.2 Labor and delivery

The effect of **SANCTURA XR™** capsules on labor and delivery is unknown.

8.3 Nursing mothers

Trospium chloride (2 mg/kg PO and 50 µg/kg IV) was excreted, to a limited extent (<1%), into the milk of lactating rats (primarily parent compound). It is not known whether this drug is excreted into human milk. Because many drugs are excreted into human milk, **SANCTURA XR™** should be used during lactation only if the potential benefit justifies the potential risk.

8.4 Pediatric use

The safety and effectiveness of **SANCTURA XR™** in pediatric patients have not been established.

8.5 Geriatric use

Of 1165 patients in Phase 3 clinical studies of **SANCTURA XR™**, 37% (n=428) were ages 65 and over, while 12% (n=143) were ages 75 and over.

No overall differences in effectiveness were observed between those subjects aged 65 and over and younger subjects. In **SANCTURA XR™** subjects ages 65 and over compared to younger subjects, the following adverse reactions were reported at a higher incidence: dry mouth, constipation, abdominal pain, dyspepsia, urinary tract infection and urinary retention. In subjects ages 75 and over, three reported a fall and in one of them a relationship to the event could not be excluded.

8.6 Renal Impairment

Severe renal impairment (creatinine clearance < 30 mL/minute) may significantly alter the disposition of **SANCTURA XR™**. In a study of immediate-release trospium chloride, 4.5-fold and 2-fold increases in mean AUC and C_{max}, respectively, were detected in patients with severe renal impairment. Use of **SANCTURA XR™** is not recommended in patients with severe renal impairment (see *Clinical Pharmacology (12)*). The pharmacokinetics of trospium chloride have not been studied in people with moderate or mild renal impairment (CLcr ranging from 30-80 mL/min).

Trospium is known to be substantially excreted by the kidney, and the risk of adverse reactions may be greater in patients with impaired renal function.

8.7 Hepatic Impairment

There is no information regarding the effect of moderate to severe hepatic impairment on exposure to **SANCTURA XR™**. Caution is advised when administering **SANCTURA XR™** to patients with moderate to severe hepatic impairment.

10 OVERDOSAGE

Overdosage with antimuscarinic agents, including **SANCTURA XR™**, can result in severe antimuscarinic effects. Supportive treatment should be provided according to symptoms. In the event of overdosage, ECG monitoring is recommended.

11 DESCRIPTION

SANCTURA XR™ is an extended-release formulation of trospium chloride, a quaternary ammonium compound with the chemical name of spiro[8-azoniabicyclo[3,2,1]octane-8,1'-pyrrolidinium]-3-[(hydroxydiphenyl-acetyl)-oxy] chloride(1α,3β,5α)-(9Cl). The empirical formula of trospium chloride is C25H30ClNO3 and its molecular weight is 427.97. The structural formula of trospium chloride is represented below:

Trospium chloride is a fine, colorless to slightly yellow, crystalline solid. The compound's solubility in water is approximately 1 g/2 mL.

SANCTURA XR™ capsules contain 60 mg of trospium chloride to be given orally. Each capsule also contains the following inactive ingredients: sugar spheres, methacrylic acid copolymer, ethyl cellulose, hydroxypropyl methylcellulose, triethyl citrate, talc, and *Opadry*® white.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of action

Trospium chloride is an antispasmodic, antimuscarinic agent.

Trospium chloride antagonizes the effect of acetylcholine on muscarinic receptors in cholinergically innervated organs including the bladder. Its parasympatholytic action reduces the tonus of smooth muscle in the bladder.

In vitro receptor binding studies have demonstrated the selectivity of trospium chloride for muscarinic over nicotinic receptors, and similar affinity for the M_2 and M_3 muscarinic receptor subtypes. M_2 and M_3 receptors are found in the bladder and may play a role in the pathogenesis of overactive bladder.

12.2 Pharmacodynamics

Placebo-controlled studies assessing the impact on urodynamic variables of an immediate-release formulation of trospium chloride were conducted in patients with conditions characterized by involuntary detrusor contractions. The results demonstrated that trospium chloride increases maximum cystometric bladder capacity and volume at first detrusor contraction.

12.3 Pharmacokinetics

Absorption: Mean absolute bioavailability of a 20 mg immediate-release dose is 9.6% (range 4.0-16.1%). Following a single 60 mg dose of **SANCTURA XR™**, peak plasma concentration (C_{max}) of 2.0 ng/mL occurred 5.0 hours post dose. By contrast, following a single 20 mg dose of an immediate-release formulation of trospium chloride, C_{max} was 2.7 ng/mL.

A summary of mean (± standard deviation) pharmacokinetic parameters for a single dose of 60 mg **SANCTURA XR™** is provided in Table 3.

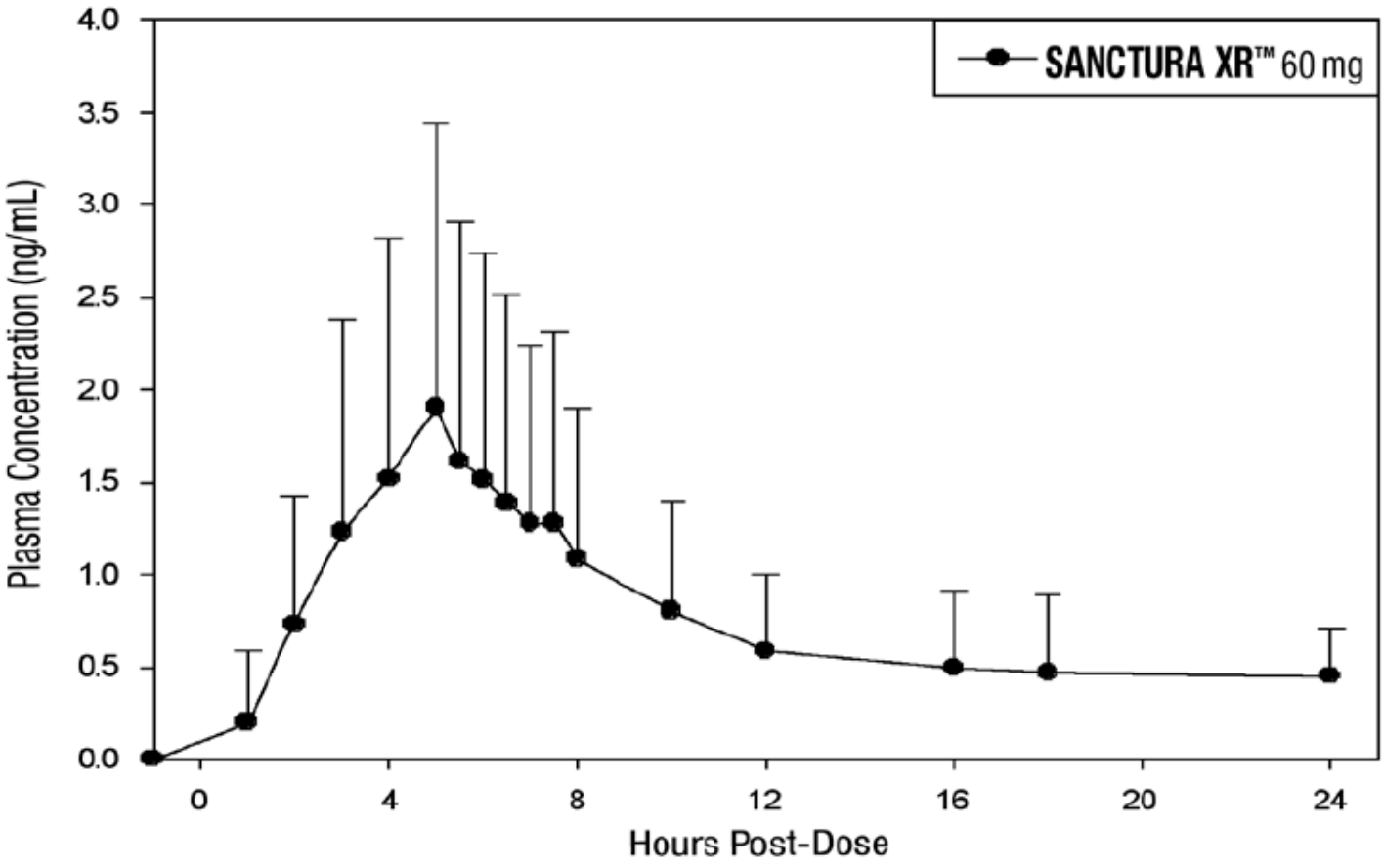
Table 3: Mean (±SD) Pharmacokinetic Parameter Estimates for a Single 60 mg Oral Dose of SANCTURA XR™ in Healthy Volunteers

Treatment	$AUC_{(0-24)}$ (ng•h/mL)	C_{max} (ng/mL)	T_{max} [a] (h)	$t_{½}$ [b] (h)
SANCTURA XR™ 60 mg	18.0 ± 13.4	2.0 ± 1.5	5.0 (3.0-7.5)	36 ± 22

a T_{max} expressed as median (range).
b $t_{½}$ was determined following multiple (10) doses.

The mean sample concentration-time (+ standard deviation) profile for **SANCTURA XR™** is shown in Figure 1.

Figure 1: Mean (+SD) Concentration-Time Profile for a Single 60 mg Oral Dose of SANCTURA XR™ in Healthy Volunteers



Administration of **SANCTURA XR™** capsules immediately after a high (50%) fat-content meal reduced the oral bioavailability of trospium chloride by 35% for $AUC_{(0-Tlast)}$ and by 60% for C_{max}. Other pharmacokinetic parameters such as T_{max} and $t_{½}$ were unchanged in the presence of food. Coadministration with antacid had inconsistent effects on the oral bioavailability of **SANCTURA XR™**.

Distribution: Protein binding ranged from 48 to 78%, depending upon the assessment method used, when a range of concentration levels of trospium chloride (0.5-100 µg/L) were incubated *in vitro* with human serum.

The ratio of ^{3}H-trospium chloride in plasma to whole blood was 1.6:1. This ratio indicates that the majority of ^{3}H- trospium chloride is distributed in plasma.

Trospium chloride is widely distributed, with an apparent volume of distribution >600 L.

Metabolism: The metabolic pathway of trospium in humans has not been fully defined. Of the dose absorbed following oral administration, metabolites account for approximately 40% of the excreted dose. The major metabolic pathway of trospium is hypothesized as ester hydrolysis with subsequent conjugation of benzylic acid to form azoniaspironortropanol with glucuronic acid. Cytochrome P450 does not contribute significantly to the elimination of trospium. Data taken from *in vitro* studies of human liver microsomes, investigating the inhibitory effect of trospium on seven cytochrome P450 isoenzyme substrates (CYP1A2, 2A6, 2C9, 2C19, 2D6, 2E1, and 3A4), suggest a lack of inhibition at clinically relevant concentrations.

Excretion: The plasma half-life for trospium following oral administration of **SANCTURA XR™** is approximately 35 hours. After oral administration of an immediate-release formulation of ^{14}C-labeled trospium chloride, a majority of the dose (85.2%) was recovered in feces and a smaller amount (5.8% of the dose) was recovered in urine. Of the radioactivity excreted into the urine, 60% was unchanged trospium.

The mean renal clearance for trospium (29.07 L/hour) is 4-fold higher than average glomerular filtration rate, indicating that active tubular secretion is a major route of elimination. There may be competition for elimination with other compounds that are also renally eliminated (see *Drug Interactions (7)*).

Pharmacokinetics in Specific Populations
Age: In a phase 3 clinical trial of **SANCTURA XR™**, the observed plasma trospium concentrations were similar in older (≥ 65 years) and younger (< 65 years) OAB patients.

Pediatric: The pharmacokinetics of **SANCTURA XR™** were not evaluated in pediatric patients.

Race: Pharmacokinetic differences due to race have not been studied.

Gender: Gender differences in pharmacokinetics of **SANCTURA XR™** have not been formally assessed. Data from healthy subjects suggests lower exposure in males compared to females.

Hepatic: There is no information regarding the effect of moderate to severe hepatic impairment on exposure to **SANCTURA XR™**.

Renal Impairment: The pharmacokinetics of **SANCTURA XR™** in patients with severe renal impairment has not been evaluated.

In a study of an immediate-release formulation of trospium chloride, 4.5-fold and 2-fold increases in mean $AUC_{(0-\infty)}$ and C_{max}, respectively, were detected in patients with severe renal impairment (creatinine clearance < 30 mL/minute), compared with healthy subjects, along with the appearance of an additional elimination phase with a long half-life (~33 hours vs. 18 hours). Use of **SANCTURA XR™** is not recommended in patients with severe renal impairment (see *Dosage and Administration (2)*). The pharmacokinetics of trospium chloride have not been studied in people with mild or moderate renal impairment (CLcr ranging from 30-80 mL/min).

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, mutagenesis, impairment of fertility

Carcinogenicity studies with trospium chloride were conducted in mice and rats for 78 weeks and 104 weeks, respectively, at maximally tolerated doses. No evidence of a carcinogenic effect was found in either mice or rats administered up to 200 mg/kg/day (approximately 1 and 16 times the expected clinical exposure levels, respectively, via AUC).

Trospium chloride was not mutagenic nor genotoxic in tests *in vitro* in bacteria (Ames test) and mammalian cells (L5178Y mouse lymphoma and CHO cells) or *in vivo* in the mouse micronucleus test.

No evidence of impaired fertility was observed in rats administered doses up to 200 mg/kg/day (about 16 times the expected clinical exposure via AUC).

14 CLINICAL STUDIES

SANCTURA XR™ was evaluated for the treatment of patients with overactive bladder who had symptoms of urinary frequency, urgency and urge urinary incontinence in two 12-week, randomized, double-blind, placebo-controlled studies. For both studies, entry criteria required the presence of urge incontinence (predominance of urge), at least one incontinence episode per day, and 10 or more micturitions (voids) per day (assessed by 3-day urinary diary). Medical history and data from the baseline urinary diary confirmed the diagnosis. Approximately 88% of the patients enrolled completed the 12-week studies. The mean age was 60 years, and the majority of patients were female (84%) and Caucasian (86%).

The co-primary endpoints in the trials were the mean change from baseline to Week 12 in number of voids/24 hours (reductions in urinary frequency) and the mean change from baseline to Week 12 in number of incontinence episodes/24 hours. Secondary endpoints included mean change from baseline to Week 12 in volume per void.

Study 1 included 592 patients in both **SANCTURA XR™** 60 mg and placebo groups. As illustrated in Table 4 and Figures 2 and 3, **SANCTURA XR™** demonstrated statistically significantly ($p<0.01$) greater reductions in the urinary frequency and incontinence episodes, and increases in void volume when compared to placebo starting at Week 1 and maintained through Weeks 4 and 12.

Table 4: Mean (SE) Change from Baseline in Urinary Frequency, Urge Incontinence Episodes and Void Volume in Study 1

Efficacy Endpoint [a]	**Week**	**Placebo**	**SANCTURA XR™**	**P-Value**
Urinary frequency / 24 hours		(N = 300)	(N = 292)	
Mean Baseline	0	12.7 (0.2)	12.8 (0.2)	
Mean Change from Baseline	1	-1.2 (0.1)	-1.7 (0.1)	0.0092
	4	-1.6 (0.2)	-2.4 (0.2)	<0.0001
	12	-2.0 (0.2)	-2.8 (0.2)	<0.0001
Urge incontinence episodes / week		(N = 300)	(N = 292)	
Mean Baseline	0	29.0 (1.3)	28.8 (1.3)	
Mean Change from Baseline	1	-8.7 (1.0)	-13.0 (0.9)	0.0003
	4	-12.2 (1.1)	-16.5 (1.2)	0.0054
	12	-13.5 (1.1)	-17.3 (1.2)	0.0024
Urinary volume / void (mL)		(N = 300)	(N = 290)	
Mean Baseline	0	155.9 (3.0)	151.0 (2.9)	
Mean Change from Baseline	1	12.1 (2.1)	21.6 (2.8)	0.0036
	4	17.2 (2.5)	30.0 (3.1)	0.0007
	12	18.9 (2.8)	29.8 (3.2)	0.0039

[a] treatment differences assessed by rank ANOVA for intent-to-treat population, last observation carried forward (ITT:LOCF) data set

Figure 2: Mean Change from Baseline in Urinary Frequency/24 hours by Visit: Study 1

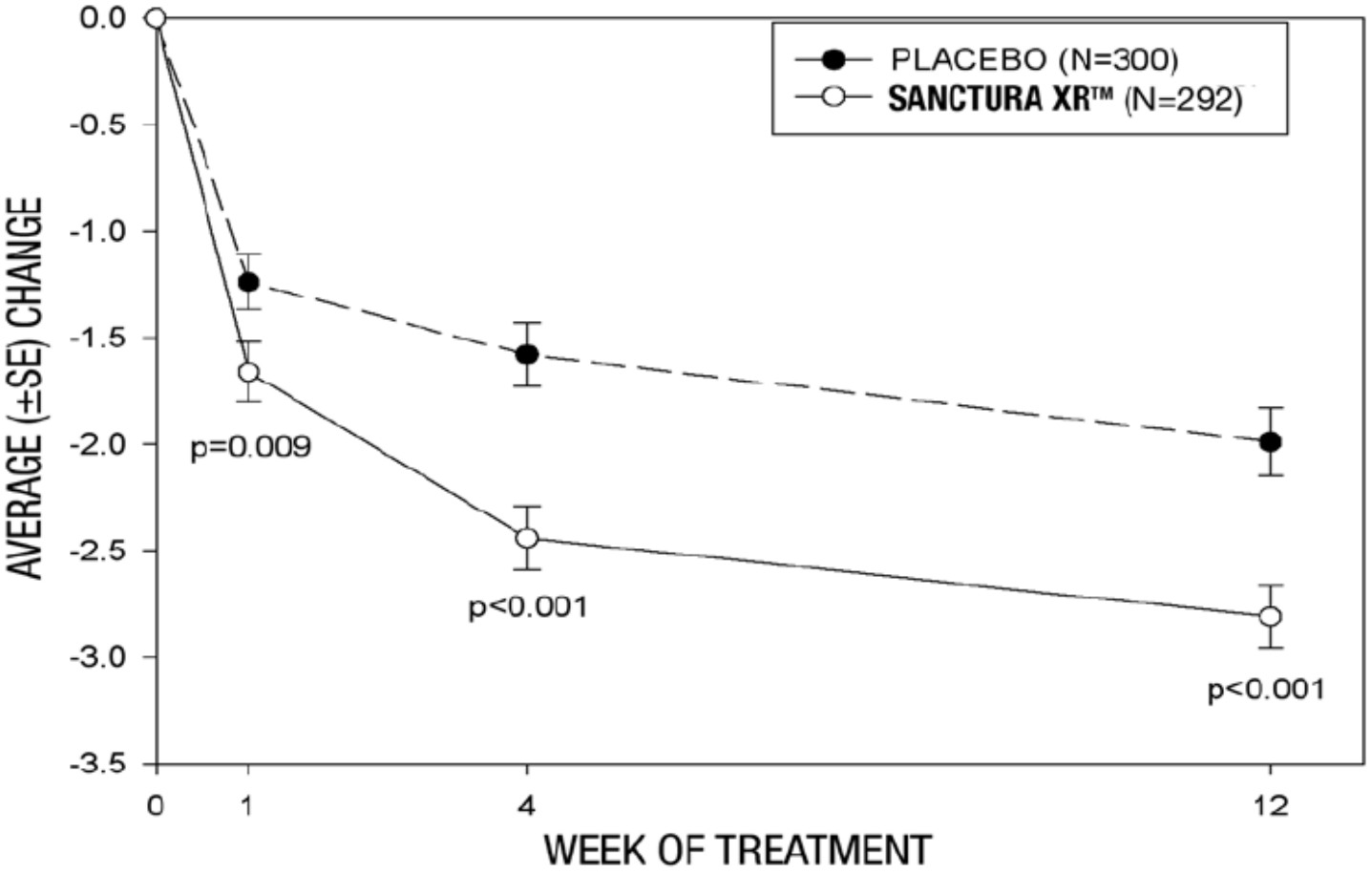
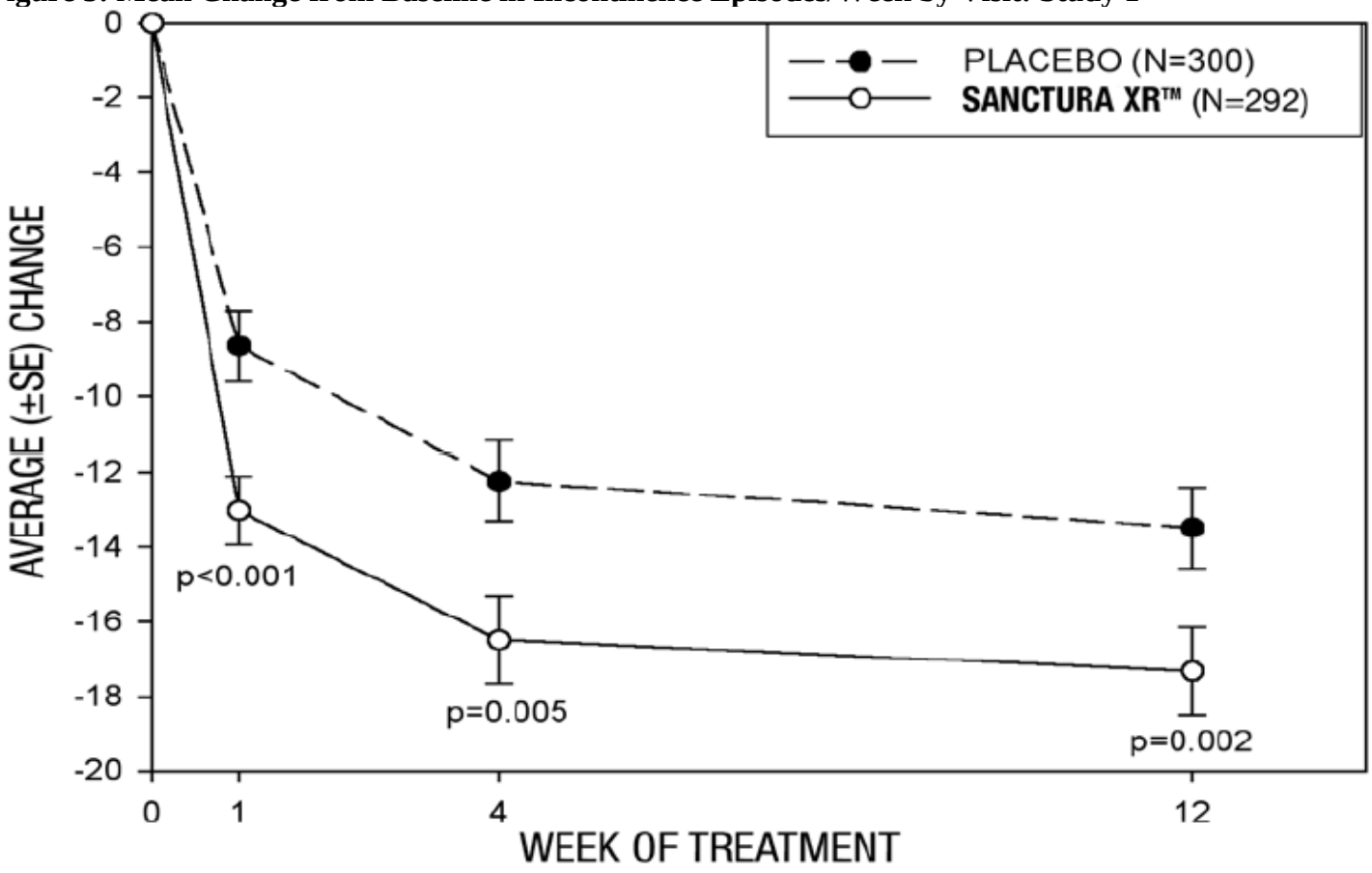


Figure 3: Mean Change from Baseline in Incontinence Episodes/Week by Visit: Study 1



Study 2 included 543 patients in both **SANCTURA XR™** 60 mg and placebo groups and was identical in design to Study 1. As illustrated in Table 5 and Figures 4 and 5, **SANCTURA XR™** capsules demonstrated statistically significantly ($p<0.01$) greater reductions in urinary frequency and incontinence episodes, and increases in void volume when compared to placebo at Weeks 4 and 12. However, at Week 1, statistically significant reductions were seen in urinary incontinence episodes and volume void only.

Table 5: Mean (SE) Change from Baseline in Urinary Frequency, Urge Incontinence Episodes and Void Volume in Study 2

Efficacy Endpoint [a]	Week	Placebo	SANCTURA XR™	P-Value
Urinary frequency / 24 hours		(N = 276)	(N = 267)	
Mean Baseline	0	12.9 (0.2)	12.8 (0.2)	
Mean Change from Baseline	1	-1.2 (0.1)	-1.4 (0.2)	0.0759
	4	-1.7 (0.2)	-2.3 (0.2)	0.0047
	12	-1.8 (0.2)	-2.5 (0.2)	0.0009
Urge incontinence episodes / week		(N = 276)	(N = 267)	
Mean Baseline	0	28.3 (1.4)	28.2 (1.2)	
Mean Change from Baseline	1	-7.3 (1.0)	-11.9 (1.0)	<0.0001
	4	-10.6 (1.1)	-15.8 (1.1)	<0.0001
	12	-11.3 (1.2)	-16.4 (1.3)	<0.0001
Urinary volume / void (mL)		(N = 276)	(N = 266)	
Mean Baseline	0	151.8 (2.8)	149.6 (2.9)	
Mean Change from Baseline	1	11.9 (2.5)	24.1 (2.4)	<0.0001
	4	19.6 (3.1)	29.3 (3.0)	0.0020
	12	17.8 (3.3)	31.5 (3.4)	0.0014

[a] treatment differences assessed by rank ANOVA for intent-to-treat population, last observation carried forward (ITT:LOCF) data set

Figure 4: Mean Change from Baseline in Urinary Frequency/24 hours by Visit: Study 2

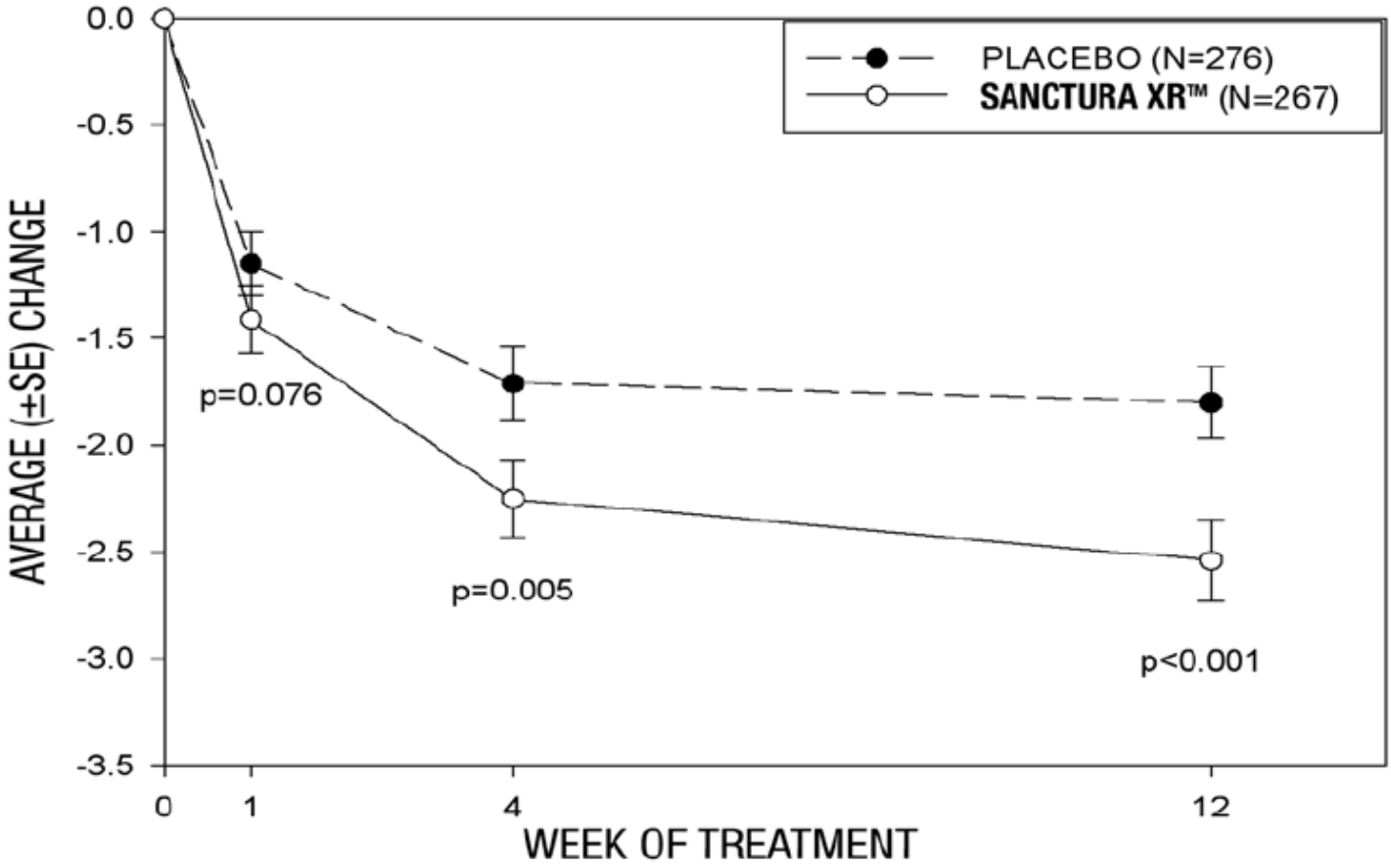
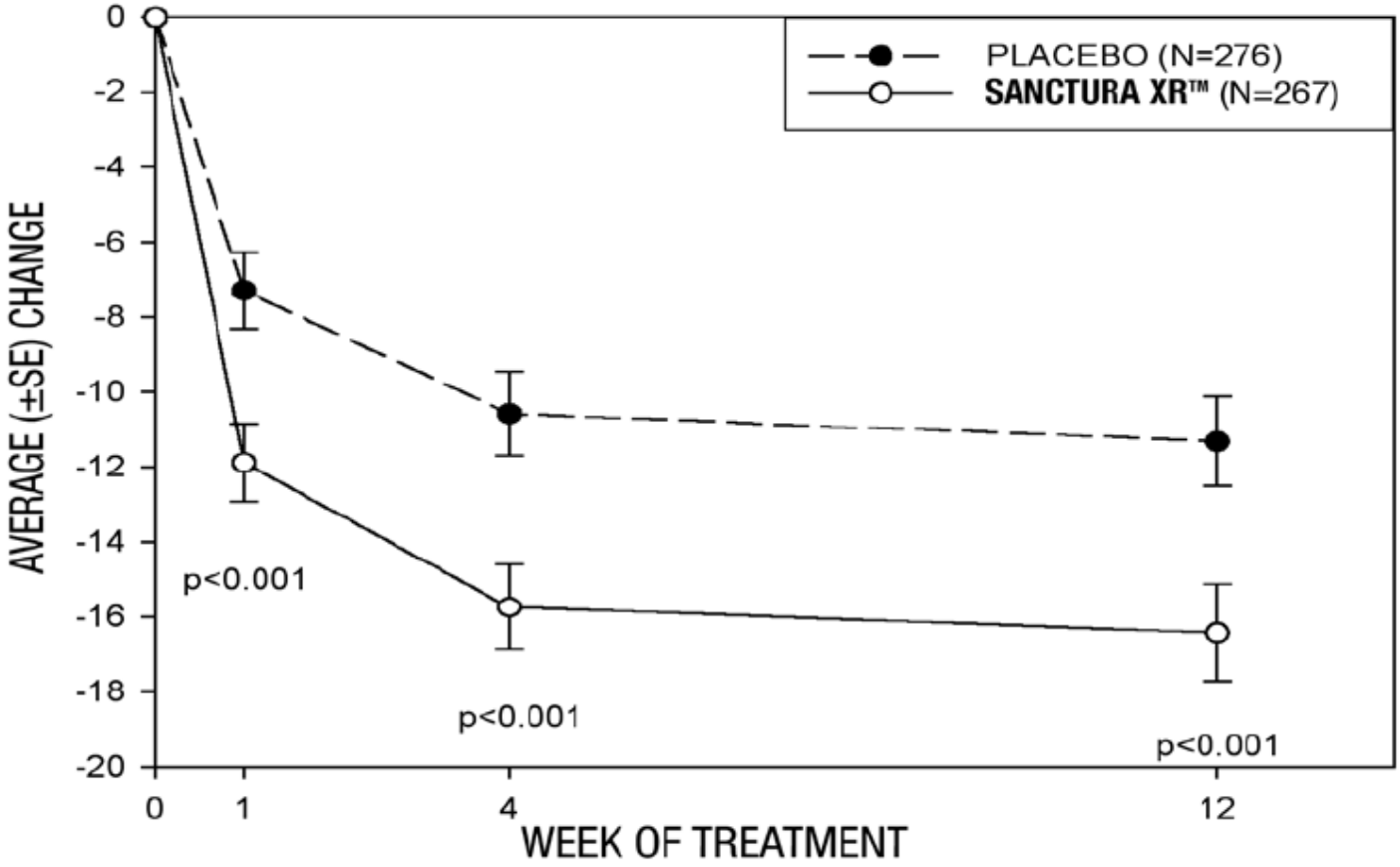


Figure 5: Mean Change from Baseline in Incontinence Episodes/Week by Visit: Study 2



16 HOW SUPPLIED/STORAGE AND HANDLING

SANCTURA XR™ is supplied as 60 mg capsules (white opaque body and orange opaque cap, printed with SAN 60): 60 mg capsule, 30 count, HDPE bottle: NDC 0023-9350-30

Store at controlled room temperature 20° to 25°C (68° to 77°F). Excursion permitted at 15° to 30°C (see USP).

17 PATIENT COUNSELING INFORMATION

See Patient Information Sheet for additional details

Prior to treatment, patients should fully understand the risks and benefits of **SANCTURA XR™** . In particular, patients should be informed not to take **SANCTURA XR™** capsules if they:

- have urinary retention;
- gastric retention;
- uncontrolled narrow-angle glaucoma;
- are allergic to any component of **SANCTURA XR™**

Patients should be instructed regarding the recommended dosing and administration of **SANCTURA XR™**:

- Take one **SANCTURA XR™** capsule daily in the morning with water.
- Take **SANCTURA XR™** on an empty stomach or at least 1 hour before a meal.
- Use of alcoholic beverages within 2 hours of dosing with **SANCTURA XR™** is not recommended.

Patients should be informed that the most common side effects with **SANCTURA XR™** are dry mouth and constipation and that other less common side effects include trouble emptying the bladder, blurred vision, and heat prostration. Patients should be informed that alcohol may enhance the drowsiness caused by anticholinergic agents.

Manufactured for:
Allergan, Inc.

Irvine, CA 92612, U.S.A.

Manufactured by:
Catalent Pharma Solutions, Inc.
Somerset, NJ 08873, U.S.A.

71966US12X

Patient Information
SANCTURA XR™ [SANK-TOUR-AH EKS-AHR]
(trospium chloride extended release capsules)
Read the Patient Information that comes with **SANCTURA XR™** before you start taking it and each time you get a refill. There may be new information. This leaflet does not take the place of talking with your doctor about your medical condition or your treatment.

What is **SANCTURA XR™**?
SANCTURA XR™ is a prescription medicine used to treat adults with overactive bladder who have the following symptoms:
• a strong need to urinate right away;
• leaking or wetting accidents due to a strong need to urinate right away
• a need to urinate often.

Who should not take SANCTURA XR™?
Do not take **SANCTURA XR™** if you:
• have trouble emptying your bladder;
• have delayed or slow emptying of your stomach;
• have an eye problem called “uncontrolled narrow-angle glaucoma”;
• are allergic to **SANCTURA XR™** or any of its ingredients. See the end of this leaflet for a complete list of ingredients.

SANCTURA XR™ has not been studied in children under the age of 18 years.

What should I tell my doctor before starting SANCTURA XR™?
Tell your doctor about all of your medical conditions including if you:
• have any stomach or intestinal problems or problems with constipation;
• have trouble emptying your bladder or have a weak urine stream;
• have an eye problem called narrow-angle glaucoma;
• have kidney problems;
• have liver problems;
• are pregnant or planning to become pregnant. It is not known if **SANCTURA XR™** can harm your unborn baby.
• are breastfeeding. It is not known if **SANCTURA XR™** passes into breast milk and if it can harm your baby. You should talk to your doctor about the best way to feed your baby if you are taking **SANCTURA XR™**.

Tell your doctor about all the medicines you take including prescription and nonprescription medicines, vitamins and herbal supplements. **SANCTURA XR™** and certain other medicines can interact and make some side effects worse. **SANCTURA XR™** can affect how other medicines are handled by the body.

Know all the medicines you take. Keep a list of them with you to show your doctor and pharmacist each time you get a new medicine.

How should I take SANCTURA XR™?
Take **SANCTURA XR™** exactly as prescribed.
• Take one **SANCTURA XR™** capsule daily in the morning with water.
• Take **SANCTURA XR™** on an empty stomach or at least 1 hour before a meal.
• Do not take alcohol within 2 hours of taking **SANCTURA XR™**.
• If you take too much **SANCTURA XR™**, call your local Poison Control Center or go to an emergency room right away.

What are the possible side effects of SANCTURA XR™?
The most common side effects with **SANCTURA XR™** are:
• dry mouth;
• constipation.

SANCTURA XR™ may cause other less common side effects, including:
• trouble emptying the bladder;
• blurred vision;
• heat prostration. Due to decreased sweating, heat prostration can occur when drugs such as **SANCTURA XR™** are used in a hot environment.

Tell your doctor if you have any side effects that bother you or that do not go away. These are not all possible side effects of **SANCTURA XR™**. For more information, ask your doctor, healthcare professional or pharmacist.

How should I store SANCTURA XR™?
• Keep **SANCTURA XR™** and all other medicines out of the reach of children.
• Store **SANCTURA XR™** at room temperature, 68° to 77°F (20° to 25°C).

• Safely dispose of **SANCTURA XR™** capsules that are out of date or that you no longer need.

General information about SANCTURA XR™
Medicines are sometimes prescribed for conditions that are not mentioned in patient information leaflets. Do not use **SANCTURA XR™** for a condition for which it was not prescribed. Do not give **SANCTURA XR™** to other people, even if they have the same symptoms you have. It may harm them.

This leaflet summarizes the most important information about **SANCTURA XR™**. If you would like more information, talk with your doctor. You can ask your doctor or pharmacist for information about **SANCTURA XR™** that is written for health professionals. You can also call Allergan's product information department at 1-800-433-8871.

What are the ingredients in SANCTURA XR™?
Active Ingredient: trospium chloride.
Inactive Ingredients: sugar spheres, methacrylic acid copolymer, ethyl cellulose, hydroxypropyl methylcellulose, triethyl citrate, talc, and ***Opadry***® white.