

HIGHLIGHTS OF PRESCRIBING INFORMATION

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

EVOXAC® (cevimeline hydrochloride) capsules, for oral use

EVOXAC (cevimeline hydrochloride) oral solution

Initial U.S. Approval: 2000

INDICATIONS AND USAGE

EVOXAC is a cholinergic agonist indicated for the treatment of symptoms of dry mouth in adults with Sjögren's disease. (1)

DOSAGE AND ADMINISTRATION

EVOXAC Capsules:

The recommended dosage of EVOXAC capsules is 30 mg (1 capsule) orally three times a day with or without food. (2)

EVOXAC Oral Solution:

The recommended dosage of EVOXAC oral solution is 30 mg (5 mL) three times a day taken with a glass of water. EVOXAC oral solution may be taken with or without food. (2)

DOSAGE FORMS AND STRENGTHS

- Capsules: 30 mg of cevimeline hydrochloride. (3)
- Oral Solution: 30 mg of cevimeline hydrochloride per 5 mL. (3)

CONTRAINDICATIONS

EVOXAC is contraindicated in patients:

- when miosis is undesirable, e.g., in acute iritis and in narrow-angle (angle-closure) glaucoma. (4)
- with known hypersensitivity to cevimeline. (4)
- with uncontrolled asthma. (4)

WARNINGS AND PRECAUTIONS

Cardiovascular Adverse Reactions: EVOXAC can alter cardiac conduction and/or heart rate. Monitor patients with a history of atrial fibrillation or cardiovascular disease. (5.1)

Pulmonary Adverse Reactions: EVOXAC can increase airway resistance, bronchial smooth muscle tone, and bronchial secretions. Monitor patients with controlled asthma, chronic bronchitis, or chronic obstructive pulmonary disease. (5.2)

Ophthalmic Adverse Reactions: Advise caution while driving or performing hazardous activities. (5.3)

Cholinergic Adverse Reactions: Monitor patients for adverse reactions related to EVOXAC's cholinergic effects. Closely monitor patients with a history of nephrolithiasis or cholelithiasis. (5.4)

ADVERSE REACTIONS

The most common (incidence $\geq 3\%$) adverse reactions observed with EVOXAC capsules having equal or greater incidence than placebo are excessive sweating, nausea, sinusitis, upper respiratory tract infection, rhinitis, abdominal pain, urinary tract infection, coughing, vomiting, injury, back pain, bronchitis, arthralgia, and fatigue. (6)

To report SUSPECTED ADVERSE REACTIONS, contact Cosette Pharmaceuticals, Inc. at 1-800-922-1038 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

DRUG INTERACTIONS

Beta-adrenergic Antagonists: Closely monitor patients who concomitantly use beta adrenergic antagonists for cardiac conduction disturbances. (7)

Muscarinic Antagonists: Closely monitor patients who concomitantly use muscarinic antagonists. Concomitant use may interfere with antimuscarinic drugs effects. (7)

Cholinergic Agonists: Closely monitor patients who concomitantly use cholinergic agonists. Concomitant use may increase the risk of EVOXAC-associated adverse reactions. (7)

CYP2D6 and CYP3A3/4 Inhibitors: Closely monitor patients who concomitantly use CYP2D6 and CYP3A3/4 inhibitors. Concomitant use may increase the risk of EVOXAC-associated adverse reactions. (7)

USE IN SPECIFIC POPULATIONS

Lactation: Breastfeeding not recommended during EVOXAC treatment and for one day after the last dose. (8.2)

CYP2D6 Poor Metabolizers: Closely monitor patients with known or suspected CYP2D6 deficiency. (8.6)

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling.

Revised: 10/2026

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FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

EVOXAC is indicated for the treatment of symptoms of dry mouth in adults with Sjögren's disease.

2 DOSAGE AND ADMINISTRATION

EVOXAC Capsules

The recommended dosage of EVOXAC capsules is 30 mg (1 capsule) orally three times a day with or without food.

EVOXAC Oral Solution

The recommended dosage of EVOXAC oral solution is 30 mg (5 mL) three times a day taken with a glass of water. Administer EVOXAC with or without food.

Missed Doses

If a dose is missed, administer it as soon as possible. If less than 4 hours remain before the next scheduled dose, wait until the next scheduled dose. Do not double the dose to make up for the missed dose.

3 DOSAGE FORMS AND STRENGTHS

- Capsules: 30 mg of cevimeline hydrochloride as a white, hard gelatin capsule with "EVOXAC" on the cap and "30 mg" with a black bar above "30 mg" on the body.
- Oral Solution: 30 mg of cevimeline hydrochloride per 5 mL as a clear, colorless to slightly yellow solution.

4 CONTRAINDICATIONS

EVOXAC is contraindicated in patients:

- when miosis is undesirable, e.g., acute iritis and narrow-angle (angle-closure) glaucoma [*see Warnings and Precautions (5.4)*].
- with known hypersensitivity to cevimeline.
- with uncontrolled asthma [*see Warnings and Precautions (5.2)*].

5 WARNINGS AND PRECAUTIONS

5.1 Cardiovascular Adverse Reactions

EVOXAC can alter cardiac conduction and/or heart rate. Monitor patients with a history of atrial fibrillation or cardiovascular disease during treatment with EVOXAC.

5.2 Pulmonary Adverse Reactions

EVOXAC can increase airway resistance, bronchial smooth muscle tone, and bronchial secretions. Monitor patients with controlled asthma, chronic bronchitis, or chronic obstructive pulmonary disease during treatment with EVOXAC.

5.3 Ophthalmic Adverse Reactions

EVOXAC may cause ophthalmic adverse reactions. Topical ophthalmic dosage forms of muscarinic agonists have been reported to cause visual blurring which may result in decreased visual acuity (especially at night and in patients with central lens changes) and impairment of depth perception. EVOXAC is not approved for topical ophthalmic use. Advise caution while driving or performing hazardous activities.

5.4 Cholinergic Adverse Reactions

EVOXAC is a cholinergic agonist and can cause adverse reactions related to its cholinergic effects. Monitor patients for adverse reactions related EVOXAC's cholinergic effects which may include headache, visual disturbance, lacrimation, sweating, respiratory distress, gastrointestinal spasm, nausea, vomiting, diarrhea, atrioventricular block, tachycardia, bradycardia, hypotension, hypertension, shock, mental confusion, cardiac arrhythmia, and tremors. Hyperhidrosis leading to dehydration may occur. If hyperhidrosis occurs, advise patients to keep hydrated and inform their healthcare provider.

Contractions of the gallbladder or biliary smooth muscle may occur which could precipitate complications such as cholecystitis, cholangitis and biliary obstruction. An increase in the ureteral smooth muscle tone may occur which could precipitate renal colic or ureteral reflux in patients with nephrolithiasis. Closely monitor patients with a history of nephrolithiasis or cholelithiasis during treatment with EVOXAC.

6 ADVERSE REACTIONS

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, 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 practice.

The safety of EVOXAC capsules was evaluated in placebo-controlled trials (Trials 1, 2, and 3) conducted in the U.S. that enrolled 320 adult subjects with Sjögren's disease who received EVOXAC capsules dosages ranging from 15 mg three times a day (0.5 times the approved recommended dosage) to 60 mg three times a day (2 times the approved recommended dosage) [*see Clinical Studies (14)*]. In these trials, 14.6% of subjects discontinued treatment with EVOXAC capsules due to adverse events. Although dosages ranging from 15 mg three times a day to 60 mg three times a day were evaluated in these trials, the recommended dosage of EVOXAC capsules is 30 mg three times a day [*see Dosage and Administration (2)*]. The safety of

EVOXAC oral solution was established from these trials of EVOXAC capsules [see *Clinical Pharmacology* (12.3)].

Table 1 shows the adverse reactions that were observed with EVOXAC capsules 30 mg three times a day compared to placebo in the clinical trials.

Table 1: Adverse Reactions Reported in $\geq 3\%$ of EVOXAC Capsules-Treated Subjects and More Frequently than Placebo-Treated Subjects

Adverse Reaction	EVOXAC Capsules 30 mg Three Times a Day n[*]=533	Placebo Three Times a Day n=164
Excessive Sweating	18.7%	2.4%
Nausea	13.8%	7.9%
Sinusitis	12.3%	10.9%
Upper Respiratory Tract Infection	11.4%	9.1%
Rhinitis	11.2%	5.4%
Abdominal Pain	7.6%	6.7%
Urinary Tract Infection	6.1%	3.0%
Coughing	6.1%	3.0%
Vomiting	4.6%	2.4%
Injury	4.5%	2.4%
Back Pain	4.5%	4.2%
Bronchitis	4.1%	1.2%
Arthralgia	3.7%	1.8%
Fatigue	3.3%	1.2%

*n is the total number of patients exposed to the dose at any time during the trial.

The following events were reported in Sjögren's patients at incidences of $<3\%$ and $\geq 1\%$: skeletal pain, insomnia, hot flushes, rigors, anxiety, constipation, tremor, abnormal vision, hypertonia, peripheral edema, chest pain, myalgia, fever, anorexia, eye pain, earache, dry mouth, vertigo, salivary gland pain, pruritus, influenza-like symptoms, eye infection, post operative pain, vaginitis, skin disorder, depression, hiccup, hyporeflexia, infection, fungal infection, sialadenitis, otitis media, erythematous rash, pneumonia, edema, salivary gland enlargement, allergy, gastroesophageal reflux, eye abnormality, migraine, tooth disorder, epistaxis, flatulence, toothache, ulcerative stomatitis, anemia, hypoesthesia, cystitis, leg cramps, abscess, eructation, moniliasis, palpitation, increased amylase, xerophthalmia, allergic reaction.

6.2 Postmarketing Experience

The following adverse reactions have been identified during post approval use of EVOXAC. Because these 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.

Gastrointestinal disorders: Diarrhea, excessive salivation, dyspepsia, pancreatitis

General disorders: Asthenia

Immune system disorders: Anaphylactic reaction

Musculoskeletal disorders: Pain in extremity

Nervous system disorders: Headache, dizziness

Respiratory disorders: Pharyngitis (nasopharyngitis)

Vascular disorders: Flushing

Skin and subcutaneous tissue disorders: Rash, Stevens-Johnson syndrome

7 DRUG INTERACTIONS

Beta-adrenergic Antagonists	
Prevention or Management	Closely monitor patients who concomitantly use EVOXAC with beta-adrenergic antagonists.
Mechanism and Clinical Effect(s)	Concomitant use of EVOXAC with beta-adrenergic antagonists may result in cardiac conduction disturbances.
Muscarinic Antagonists	
Prevention or Management	Closely monitor patients who concomitantly use EVOXAC with muscarinic antagonists.
Mechanism and Clinical Effect(s)	Concomitant use of EVOXAC with muscarinic antagonists may interfere with antimuscarinic drugs effects.
Cholinergic Agonists	
Prevention or Management	Closely monitor patients who concomitantly use EVOXAC with other cholinergic agonists.
Mechanism and Clinical Effect(s)	Concomitant use of EVOXAC with other cholinergic agonists can potentiate the cholinergic effects of EVOXAC and increase the risk of adverse reactions [see <i>Warnings and Precautions (5.4)</i>].
CYP2D6 and CYP3A3/4 Inhibitors	
Prevention or Management	Closely monitor patients who concomitantly use EVOXAC with CYP2D6 and/or CYP3A3/4 inhibitors for EVOXAC-associated adverse reactions.

Mechanism and Clinical Effect(s)	CYP2D6 and CYP3A3/4 inhibitors can inhibit the metabolism of cevimeline and may increase the risk of EVOXAC-associated adverse reactions.
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8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

There are no available data on EVOXAC use in pregnant women to evaluate for a drug-associated risk of major birth defects, miscarriage, or other adverse maternal or fetal outcomes. In animal reproduction studies, oral administration of cevimeline to pregnant rats and rabbits during the period of organogenesis did not cause significant embryofetal toxicity at doses up to 6 times the maximum recommended human dose (MRHD) in rats or 10 times the MRHD in rabbits, at which maternal toxicities were noted (*see Data*).

The background risk of major birth defects and miscarriage for the indicated population are unknown. All pregnancies have a background risk of birth defect, loss, or other adverse 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.

Data

Animal Data

In an embryofetal development study, cevimeline was administered to pregnant rats during the period of organogenesis at oral doses of 5, 30, and 60 mg/kg/day. Cholinergic stimulation (e.g., mydriasis, salivation, lacrimation, diarrhea) was noted at doses ≥ 30 mg/kg/day (≥ 3 times the MRHD based on mg/m² dose comparison). Maternal mortality was observed at 60 mg/kg/day (6 times the MRHD based on mg/m² dose comparison). No significant embryofetal toxicity was observed at doses up to 60 mg/kg/day. In another embryofetal development study, cevimeline was administered to pregnant rabbits during the period of organogenesis at oral doses of 0.2, 3, and 45 mg/kg/day. Increased salivation and tachypnea were noted at 45 mg/kg/day (10 times the MRHD based on mg/m² dose comparison). No significant embryofetal toxicity was noted at doses up to 45 mg/kg/day.

In a pre- and postnatal development study in rats, cevimeline was administered to pregnant rats during pregnancy and lactation periods at oral doses of 3, 12, and 45 mg/kg/day. Maternal toxicities (decreased body weight and mortality) were noted at 45 mg/kg/day (5 times the MRHD based on mg/m² dose comparison). No significant developmental toxicity was noted at doses up to 45 mg/kg/day.

8.2 Lactation

Risk Summary

There is no data on the presence of cevimeline or its metabolite in human or animal milk, the effects on the breastfed infant, or the effects on milk production. Because of the potential for serious adverse reactions in the breastfed infant, advise patients that breastfeeding is not recommended during treatment with EVOXAC and for one day after the last dose (approximately 5 elimination half-lives) [see *Clinical Pharmacology* (12.3)].

8.4 Pediatric Use

Safety and effectiveness of EVOXAC have not been established in pediatric patients.

8.5 Geriatric Use

Clinical trials of EVOXAC did not include sufficient numbers of subjects 65 years of age and older to determine whether they respond differently from younger adult subjects.

8.6 CYP2D6 Poor Metabolizers

Closely monitor patients with known or suspected CYP2D6 deficiency. Patients known or suspected to be deficient in CYP2D6 activity may be at a higher risk for EVOXAC-associated adverse reactions [see *Clinical Pharmacology* (12.3)].

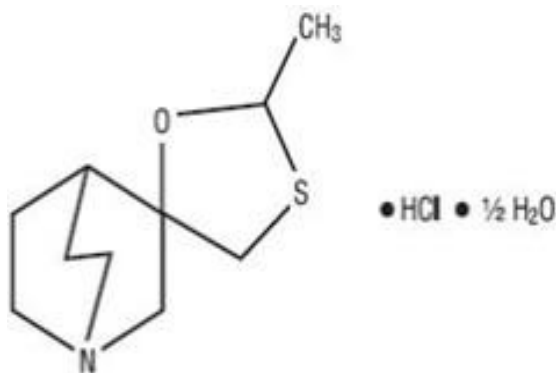
10 OVERDOSAGE

In the case of an overdose with EVOXAC, provide general supportive measures. If medically indicated, consider atropine, an anti-cholinergic drug, as an antidote for emergency use. If medically indicated, consider epinephrine in patients with severe cardiovascular depression or bronchoconstriction. It is not known if EVOXAC is dialyzable. Consider contacting the Poison Help line (1-800-222-1222) or a medical toxicologist for additional overdose management recommendations.

11 DESCRIPTION

EVOXAC capsules, for oral use, and oral solution contain cevimeline hydrochloride, a salt of cevimeline. Cevimeline is a cholinergic agonist and has a molecular weight of 244.79. It is a white to off white crystalline powder with a melting point range of 201 to 203°C. It is freely soluble in alcohol and chloroform, very soluble in water, and virtually insoluble in ether. The pH of a 1% solution ranges from 4.6 to 5.6. Cevimeline is cis -2'-methylspiro{1-azabicyclo [2.2.2] octane-3,

5'-[1,3] oxathiolane} hydrochloride, hydrate (2:1). Its empirical formula is $C_{10}H_{17}NOS \cdot HCl \cdot \frac{1}{2}H_2O$, and its structural formula is:



EVOXAC (cevimeline hydrochloride) capsules

Each capsule contains 30 mg of cevimeline hydrochloride (equivalent to 25.4 mg of cevimeline) and the following inactive ingredients: hydroxypropyl cellulose, lactose monohydrate, and magnesium stearate.

EVOXAC (cevimeline hydrochloride) oral solution

Each 5 mL contains 30 mg of cevimeline hydrochloride (equivalent to 25.4 mg of cevimeline) and the following inactive ingredients: anhydrous citric acid, carboxymethylcellulose sodium, edetate disodium, glycerin, masking agent flavor, methylparaben, propylparaben, propylene glycol, purified water, raspberry flavor, sodium citrate dihydrate, sodium thiosulfate, sorbitol solution 70%, sucralose. Each 5 mL of EVOXAC oral solution contains 10 mg of sodium.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Cevimeline is a cholinergic agonist which binds to muscarinic receptors in various exocrine glands.

12.2 Pharmacodynamics

Muscarinic agonists in sufficient dosage can increase secretion of exocrine glands, such as salivary and sweat glands and increase tone of the smooth muscle in the gastrointestinal and urinary tracts.

12.3 Pharmacokinetics

Absorption

Capsules

After administration of a single EVOXAC 30 mg capsule, cevimeline was rapidly absorbed with a mean time to peak concentration of 1.5 to 2 hours. No accumulation of active drug or its metabolites was observed following multiple dose administration. When administered with food, there is a decrease in the rate of absorption, with a fasting t_{MAX} of 1.53 hours and a t_{MAX} of

2.86 hours after a meal; the peak concentration is reduced by 17.3% [see *Dosage and Administration (2)*]. Single oral doses across the clinical dose range are dose proportional.

Oral Solution

In a bioavailability study performed in patients with Sjögren's disease, EVOXAC oral solution had a comparative bioavailability to EVOXAC capsules. After administration of EVOXAC 30 mg (5 mL) oral solution followed by a glass of water, cevimeline was absorbed with a mean time to peak concentration of 1.7 hour.

Distribution

Cevimeline has a volume of distribution of approximately 6 L/kg and is <20% bound to human plasma proteins. This suggests that cevimeline is extensively bound to tissues; however, the specific binding sites are unknown.

Elimination

Metabolism

Isozymes CYP2D6 and CYP3A3/4 are responsible for the metabolism of cevimeline. After 24 hours, 86.7% of the dose was recovered (16.0% unchanged, 44.5% as cis and trans-sulfoxide, 22.3% as glucuronic acid conjugate and 4% as N-oxide of cevimeline). Approximately 8% of the trans-sulfoxide metabolite is then converted into the corresponding glucuronic acid conjugate and eliminated.

Excretion

The mean half-life of cevimeline is 5 ± 1 hours. After 24 hours, 84% of a 30 mg dose of cevimeline was excreted in urine. After seven days, 97% of the dose was recovered in the urine and 0.5% was recovered in the feces.

Specific Populations

The effects of renal impairment, hepatic impairment, or ethnicity on the pharmacokinetics of cevimeline have not been investigated.

Drug Interaction Studies

In Vitro Studies

Cevimeline did not inhibit cytochrome P450 isozymes 1A2, 2A6, 2C9, 2C19, 2D6, 2E1, and 3A4.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenesis

Oral carcinogenicity studies were conducted in mice and rats. An increase in the incidence of adenocarcinomas of the uterus was observed in female rats that received cevimeline 100 mg/kg/day (8 times the MRHD based on AUC comparison). No drug-related tumors were observed in male rats at oral doses up to 100 mg/kg/day (5 times the MRHD based on AUC comparison) or in female rats at oral doses up to 50 mg/kg/day (4 times the MRHD based on AUC comparison). No drug-related tumors were observed in mice at oral doses up to 300 mg/kg/day (12 times the MRHD based on AUC comparison).

Mutagenesis

Cevimeline exhibited no evidence of mutagenicity or clastogenicity in a battery of assays that included the Ames assay, an *in vitro* chromosomal aberration assay in mammalian cells, a mouse lymphoma assay in L5178Y cells, or a micronucleus assay conducted in mice.

Impairment of Fertility

Cevimeline did not adversely affect the reproductive performance or fertility of male rats when administered for 63 days prior to mating and throughout the period of mating at oral doses up to 45 mg/kg/day (5 times the MRHD based on mg/m² dose comparison).

Female rats that were treated with cevimeline at an oral dose of 45 mg/kg/day (5 times the MRHD based on mg/m² dose comparison) from 14 days prior to mating through gestation day 7 exhibited decreased implantation. No adverse effects were noted at oral doses up to 3 mg/kg/day (0.3 times the MRHD based on mg/m² dose comparison).

14 CLINICAL STUDIES

The efficacy of EVOXAC capsules for the treatment of symptoms of dry mouth in adults with Sjögren's disease was studied in three trials (Trial 1, 2, and 3). Trial 1 was a 6-week, randomized, double blind, placebo-controlled trial conducted in 75 adult subjects (10 men, 65 women) with a mean age of 53.6 years (range 33-75). The racial distribution of enrolled subjects was 92% White, 1% Black, and 7% other. EVOXAC capsules 30 mg three times daily and EVOXAC capsules 60 mg three times daily (unapproved dosage), administered orally, were compared to placebo. Subjects were evaluated by a measure called global improvement, which is defined as a response of "better" to the question, "Please rate the overall condition of your dry mouth now compared with how you felt before starting treatment in this study." Subjects also had the option of selecting "worse" or "no change" as answers. Seventy-six percent of subjects in the EVOXAC capsules 30 mg three times daily group reported global improvement in their dry mouth symptoms compared to 35% of the subjects in the placebo group. This difference was statistically significant at $p=0.0043$. There was no evidence that subjects in the EVOXAC capsules 60 mg three times

daily group had better global evaluation scores than subjects in the EVOXAC capsules 30 mg three times daily group.

Trial 2 was a 12-week, randomized, double-blind, placebo-controlled trial conducted in 197 adult subjects (10 men, 187 women) with a mean age of 54.5 years (range 23-74). The racial distribution of enrolled subjects was 92% White, 3% Black, and 6% other. EVOXAC capsules 15 mg three times daily (unapproved dosage) and EVOXAC capsules 30 mg three times daily, administered orally, were compared placebo. Statistically significant global improvement in the symptoms of dry mouth ($p=0.0004$) was seen for the EVOXAC capsules 30 mg three times daily group compared to placebo, but not for the EVOXAC capsules 15 mg three times daily group when compared to placebo. EVOXAC capsules 30 mg three times daily demonstrated statistically significant increases in salivary flow compared to placebo.

Trial 3 was a 12-week, randomized, double-blind, placebo-controlled trial conducted in 212 adult subjects (11 men, 201 women) with a mean age of 55.3 years (range 24-75). The racial distribution of enrolled subjects was 89% White, 2% Black, and 9% other. EVOXAC capsules 15 mg three times daily (unapproved dosage) and EVOXAC capsules 30 mg three times daily were compared to placebo. No statistically significant differences were noted in the patient global evaluations. However, there was a higher placebo response rate in this trial compared to Trial 1 and 2. The EVOXAC capsules 30 mg three times daily group showed a statistically significant increase in salivary flow from pre-dose to post-dose compared to placebo ($p=0.0017$).

The efficacy of EVOXAC oral solution was established based on trials of EVOXAC capsules [see *Clinical Pharmacology (12.3)*].

16 HOW SUPPLIED/STORAGE AND HANDLING

How Supplied

- EVOXAC (cevimeline hydrochloride) capsules, 30 mg, are white, hard gelatin capsules with “EVOXAC” on the cap and “30 mg” with a black bar above “30 mg” on the body. It is supplied in child resistant bottles of 100 capsules (NDC 0713-0883-01).
- EVOXAC (cevimeline hydrochloride) oral solution, 30 mg/5 mL, is a clear, colorless to slightly yellow solution with a raspberry flavor. It is supplied in a tight, child-resistant container as defined in the USP/NF. Each bottle contains 473 mL of solution (NDC 0713-0915-75).

Storage and Handling

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

17 PATIENT COUNSELING INFORMATION

Advise patients to read the FDA-approved patient labeling (Patient Information).

Cardiovascular Adverse Reactions

Advise patients that EVOXAC can alter cardiac conduction and/or heart rate [*see Warnings and Precautions (5.1)*].

Pulmonary Adverse Reactions

Advise patients that EVOXAC can increase airway resistance, bronchial smooth muscle tone, and bronchial secretions [*see Warnings and Precautions (5.2)*].

Ophthalmic Adverse Reactions

Advise patients that EVOXAC may cause visual disturbances, especially at night, that could impair their ability to drive safely or perform hazardous activities [*see Warnings and Precautions (5.3)*].

Cholinergic Adverse Reactions

If hyperhidrosis occurs, advise patients to keep hydrated and inform their healthcare provider. Inform patients that EVOXAC may cause contractions of the gallbladder, biliary smooth muscle and ureteral smooth muscle, resulting in complications such as cholecystitis, cholangitis, biliary obstruction, renal colic and nephrolithiasis [*see Warnings and Precautions (5.4)*].

Lactation

Advise patients that breastfeeding is not recommended during treatment with EVOXAC and for one day after the last dose [*see Use in Specific Populations (8.2)*].

Distributed by:

Cosette Pharmaceuticals, Inc.

Bridgewater, NJ 08807

8-EVOCPLNC1

Rev. 10/2026

PATIENT INFORMATION	
EVOXAC (EE-voh-ZAK) (cevimeline hydrochloride) capsules, for oral use	EVOXAC (EE-voh-ZAK) (cevimeline hydrochloride) oral solution
What is EVOXAC? EVOXAC is a prescription medicine used to treat the symptoms of dry mouth in adults with Sjögren's disease. It is not known if EVOXAC is safe and effective in children.	
Do not take EVOXAC if you: • have certain eye conditions such as acute iritis and narrow-angle (angle-closure) glaucoma, in which small "pinpoint" pupil is not wanted. EVOXAC can cause tightening (constriction) of your eye pupils. • are allergic to cevimeline or any of the ingredients in EVOXAC. See the end of this Patient Information leaflet for a complete list of ingredients in EVOXAC. • have uncontrolled asthma.	
Before taking EVOXAC, tell your healthcare provider about all of your medical conditions, including if you: • have a history of a heart rhythm problem called atrial fibrillation or other heart or blood vessel problems. • have asthma, long-term (chronic) bronchitis, or chronic obstructive pulmonary disease • have a history of kidney stones or gallstones • have or think you have an inherited condition called CYP2D6 deficiency • are pregnant or plan to become pregnant. It is not known if EVOXAC will harm your unborn baby. • are breastfeeding or plan to breastfeed. It is not known if EVOXAC passes into your breast milk. Do not breastfeed during treatment with EVOXAC and for 1 day after your last dose. Talk to your healthcare provider about the best way to feed your baby during treatment with EVOXAC. Tell your healthcare provider about all the medicines you take , including prescription and over-the-counter medicines, vitamins, and herbal supplements. EVOXAC and other medicines may affect each other causing side effects. Know the medicines you take. Keep a list of them to show your healthcare provider and pharmacist when you get a new medicine.	
How should I take EVOXAC? • Take EVOXAC exactly as your healthcare provider tells you to. • Take EVOXAC with or without food. • If you are prescribed EVOXAC capsules: ○ Take 1 EVOXAC capsule by mouth three times a day. • If you are prescribed EVOXAC oral solution: ○ Take 5 mL of EVOXAC oral solution by mouth three times a day with a glass of water. • If you miss a dose of EVOXAC, take it as soon as you remember. If it is less than 4 hours before your next scheduled dose, skip the dose. Take the next dose at your regular scheduled time. Do not take 2 doses at the same time to make up for the missed dose. If you take too much EVOXAC, call your healthcare provider or the Poison Help line at 1-800-222-1222 or go to the nearest hospital emergency room right away.	
What should I avoid while taking EVOXAC? • EVOXAC may cause changes in vision, especially at night. Do not drive or do other hazardous activities until you know how EVOXAC affects you.	
What are the possible side effects of EVOXAC? EVOXAC can cause serious side effects, including: • Heart rhythm and heart rate problems. Your healthcare provider will check you for heart rhythm and heart rate problems. Tell your healthcare provider if you get any of these symptoms: ○ Dizziness ○ feeling faint or lightheaded ○ tiredness or weakness ○ feeling that your heart is pounding or racing ○ chest discomfort ○ shortness of breath • Lung problems. EVOXAC can make it harder for air to move through your airways, cause the muscles in your lungs to tighten, and increase the amount of mucus in your lungs. Tell your healthcare provider if you develop: ○ trouble breathing or shortness of breath ○ wheezing ○ increased mucus • Changes in vision. See "What should I avoid while taking EVOXAC?"	

- **Cholinergic reactions (nervous system problems).** Your healthcare provider will check you for nervous system problems during treatment with EVOXAC. Tell your healthcare provider if you get any of the following symptoms:
 - headache
 - change in vision
 - watery eyes
 - sweating
 - breathing problems
 - stomach (abdominal) cramping or pain
 - nausea
 - vomiting
 - diarrhea
 - fast heartbeat
 - change in blood pressure
 - dizziness
 - shock
 - confusion
 - tremors

Especially tell your healthcare provider if you develop heavy sweating or sweat more than normal and drink fluids to keep hydrated.

The most common side effects of EVOXAC include:

- heavy sweating or sweating more than normal
- nausea
- swelling of the inside of your nose, throat or sinuses (sinusitis)
- upper respiratory tract infection
- runny nose
- stomach area (abdominal) pain
- urinary tract infection
- coughing
- vomiting
- injury
- back pain
- bronchitis
- joint pain (arthralgia)
- tired or lack of energy (fatigue)

These are not all of the possible side effects of EVOXAC.

Call your doctor for medical advice about side effects.

You may also report side effects to FDA at 1-800-FDA-1088.

How should I store EVOXAC?

- Store EVOXAC at room temperature between 68°F to 77°F (20°C to 25°C).
- EVOXAC capsules bottle and EVOXAC oral solution container have a child resistant closure.

Keep EVOXAC and all medicines out of the reach of children.

General information about the safe and effective use of EVOXAC.

Medicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet. Do not use EVOXAC for a condition for which it was not prescribed. Do not give EVOXAC to other people, even if they have the same symptoms that you have. It may harm them. You can ask your pharmacist or healthcare provider for information about EVOXAC that is written for health professionals.

What are the ingredients in EVOXAC?

Active ingredient: cevimeline hydrochloride

Inactive ingredients in the capsules: hydroxypropyl cellulose, lactose monohydrate, and magnesium stearate.

Inactive ingredients in the oral solution: anhydrous citric acid, carboxymethylcellulose sodium, edetate disodium, glycerin, masking agent flavor, methylparaben, propylparaben, propylene glycol, purified water, raspberry flavor, sodium citrate dihydrate, sodium thiosulfate, sorbitol solution 70%, sucralose. Each 5 mL of EVOXAC oral solution contains 10 mg of sodium.

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For more information, call 1-800-922-1038.

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This Patient Information has been approved by the U.S. Food and Drug Administration

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