270.00 mm

28.00 mm

29.00 mm

OXCARBAZEPINE TABLETS

11254

206368

750.00 mm

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use OXCARBAZEPINE TABLETS safely and effectively. See full prescribing information for OXCARBAZEPINE TABLETS.

OXCARBAZEPINE tablets, for oral use

Initial U.S. Approval: 2000

------------------------------------ RECENT MAJOR CHANGES ------------------------------------

Dosage and Administration (2.8) 9/2025

------------------------------------ INDICATIONS AND USAGE ------------------------------------

Oxcarbazepine tablets is indicated for:
- Adults: Monotherapy or adjunctive therapy in the treatment of partial-onset seizures
- Pediatrics:
  - Monotherapy in the treatment of partial-onset seizures in children 4-16 years
  - Adjunctive therapy in the treatment of partial-onset seizures in children 2-16 years (1)

------------------------------------ DOSAGE AND ADMINISTRATION ------------------------------------

Adults: Initiate with a dose of 600 mg/day, given twice a day
- Adjunctive Therapy: Maximum increment of 600 mg/day at approximately weekly intervals. The recommended daily dose is 1200 mg/day (2.1)
- Conversion to Monotherapy: Withdrawal concomitant over 3 to 6 weeks; reach maximum dose of oxcarbazepine tablets in 2 to 4 weeks with increments of 600 mg/day at weekly intervals to a recommended daily dose of 2400 mg/day (2.2)
- Initiation of Monotherapy: Increments of 300 mg/day every third day to a dose of 1200 mg/day (2.3)
- Initiate at one-half the usual starting dose and increase slowly in patients with a creatinine clearance < 30 mL/min (2.7)

Pediatrics: Initiation with 8 to 10 mg/kg/day, given twice a day. For patients aged 2 to < 4 years and under 20 kg, a starting dose of 16 to 20 mg/kg/day may be considered. Recommended daily dose is dependent upon patient weight.
- Adjunctive Patients (Aged 2-16 Years): For patients aged 4 to 16 years, target maintenance dose should be achieved over 2 weeks (2.4). For patients aged 2 to < 4 years, maximum maintenance dose should be achieved over 2 to 4 weeks and should not exceed 60 mg/kg/day (2.4)
- Conversion to Monotherapy for Patients (Aged 4-16 Years): Maximum increment of 10 mg/kg/day at weekly intervals, concomitant antiepileptic drugs (AEDs) can be completely withdrawn over 3 to 6 weeks (2.5)
- Initiation of Monotherapy for Patients (Aged 4-16 Years): Increments of 5 mg/kg/day every third day (2.6)

------------------------------------ DOSAGE FORMS AND STRENGTHS ------------------------------------

- Film-coated tablets: 150 mg, 300 mg and 600 mg (3)

------------------------------------ CONTRAINDICATIONS ------------------------------------

Known hypersensitivity to oxcarbazepine or to any of its components, or to eslicarbazepine acetate (4, 5.2)

------------------------------------ WARNINGS AND PRECAUTIONS ------------------------------------

- Hyponatremia: Monitor serum sodium levels (5.1)
- Cross Hypersensitivity Reaction to Carbamazepine: Discontinue immediately if hypersensitivity occurs (5.3)
- Serious Dermatological Reactions: If occurs, consider discontinuation (5.4)
- Suicidal Behavior and Ideation: Monitor for suicidal thoughts/behavior (5.5)
- Withdrawal of AEDs: Withdraw oxcarbazepine tablets gradually (5.6)
- Cognitive/Neuropsychiatric Adverse Reactions: May cause cognitive dysfunction, somnolence, and coordination abnormalities. Use caution when operating machinery (5.7)
- Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS)/Multi-Organ Hypersensitivity: Monitor and discontinue if another cause cannot be established (5.8)
- Hematologic Events: Consider discontinuing (5.9)
- Seizure Control During Pregnancy: Active metabolite may decrease (5.10)
- Risk of Seizure Aggravation: Discontinue if occurs (5.11)

------------------------------------ ADVERSE REACTIONS ------------------------------------

The most common (≥ 10% more than placebo for adjunctive or low dose for monotherapy) adverse reactions in adults and pediatrics were: dizziness, somnolence, diplopia, fatigue, nausea, vomiting, ataxia, abnormal vision, headache, nystagmus, tremor, and abnormal gait (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Umedica Laboratories USA Inc. at 1-855-288-5777 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch

------------------------------------ DRUG INTERACTIONS ------------------------------------

- Phenytoin: Increased phenytoin levels. Reduced dose of phenytoin may be required (7.1)
- Carbamazepine, Phenytoin, and Phenobarbital: Decreased plasma levels of MHD (the active metabolite). Dose adjustments may be necessary (7.1)
- Oral Contraceptive: Oxcarbazepine tablets may decrease the effectiveness of hormonal contraceptives (7.3)

------------------------------------ USE IN SPECIFIC POPULATIONS ------------------------------------

- Pregnancy: May cause fetal harm (8.1)

See 17 for PATIENT COUNSELING INFORMATION and Medication Guide.

Revised: 04/2026

FULL PRESCRIBING INFORMATION: CONTENTS*

1 INDICATIONS AND USAGE
2 DOSAGE AND ADMINISTRATION
2.1 Adjunctive Therapy for Adults
2.2 Conversion to Monotherapy for Adults
2.3 Initiation of Monotherapy for Adults
2.4 Adjunctive Therapy for Pediatric Patients (Aged 2-16 Years)
2.5 Conversion to Monotherapy for Pediatric Patients (Aged 4-16 Years)
2.6 Initiation of Monotherapy for Pediatric Patients (Aged 4-16 Years)
2.7 Dosage Modification for Patients With Renal Impairment
2.8 Administration Information
3 DOSAGE FORMS AND STRENGTHS
4 CONTRAINDICATIONS
5 WARNINGS AND PRECAUTIONS
5.1 Hyponatremia
5.2 Anaphylactic Reactions and Angioedema
5.3 Cross Hypersensitivity Reaction to Carbamazepine
5.4 Serious Dermatological Reactions
5.5 Suicidal Behavior and Ideation
5.6 Withdrawal of Antiepileptic Drugs
5.7 Cognitive/Neuropsychiatric Adverse Reactions
5.8 Drug Reaction With Eosinophilia and Systemic Symptoms/Multi-Organ Hypersensitivity
5.9 Hematologic Events
5.10 Seizure Control During Pregnancy
5.11 Risk of Seizure Aggravation
6 ADVERSE REACTIONS
6.1 Clinical Trial Experience
6.2 Postmarketing Experience
7 DRUG INTERACTIONS
7.1 Effect of oxcarbazepine tablets on Other Drugs
7.2 Effect of Other Drugs on oxcarbazepine tablets
7.3 Hormonal Contraceptives
8 USE IN SPECIFIC POPULATIONS
8.1 Pregnancy
8.2 Lactation
8.3 Females and Males of Reproductive Potential
8.4 Pediatric Use
8.5 Geriatric Use
8.6 Renal Impairment
9 DRUG ABUSE AND DEPENDENCE
9.2 Abuse
9.3 Dependence
10 OVERDOSAGE
10.1 Human Overdose Experience
10.2 Teatment and Management
11 DESCRIPTION
12 CLINICAL PHARMACOLOGY
12.1 Mechanism of Action
12.2 Pharmacodynamics
12.3 Pharmacokinetics
13 NONCLINICAL TOXICOLOGY
13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility
14 CLINICAL STUDIES
14.1 Oxcarbazepine tablets Monotherapy Trials
14.2 Oxcarbazepine tablets Adjunctive Therapy Trials
16 HOW SUPPLIED/STORAGE AND HANDLING
17 PATIENT COUNSELING INFORMATION

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

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

Oxcarbazepine tablets is indicated for use as monotherapy or adjunctive therapy in the treatment of partial-onset seizures in adults and as monotherapy in the treatment of partial-onset seizures in pediatric patients aged 4 years and above, and as adjunctive therapy in pediatric patients aged 2 years and above with partial-onset seizures.

2 DOSAGE AND ADMINISTRATION

2.1 Adjunctive Therapy for Adults

Initiate oxcarbazepine tablets with a dose of 600 mg/day, given twice a day. If clinically indicated, the dose may be increased by a maximum of 600 mg/day at approximately weekly intervals; the maximum recommended daily dose is 1200 mg/day. Daily doses above 1200 mg/day show somewhat greater effectiveness in controlled trials, but most patients were not able to tolerate the 2400 mg/day dose, primarily because of central nervous (CNS) effects.

Dosage adjustment is recommended with concomitant use of strong CYP3A4 enzyme inducers or UDP-glucuronosyltransferases (UGT) inducers, which include certain antiepileptic drugs (AEDs) *[see Drug Interactions (7.1, 7.2)]*.

2.2 Conversion to Monotherapy for Adults

Patients receiving concomitant AEDs may be converted to monotherapy by initiating treatment with oxcarbazepine tablets at 600 mg/day (given in a twice a day regimen) while simultaneously initiating the reduction of the dose of the concomitant AEDs. The concomitant AEDs should be completely withdrawn over 3 to 6 weeks, while the maximum dose of oxcarbazepine tablets should be reached in about 2 to 4 weeks. Oxcarbazepine tablets may be increased as clinically indicated by a maximum increment of 600 mg/day at approximately weekly intervals to achieve the maximum recommended daily dose of 2400 mg/day. A daily dose of 1200 mg/day has been shown in one study to be effective in patients in whom monotherapy has been initiated with oxcarbazepine tablets. Patients should be observed closely during this transition phase.

2.3 Initiation of Monotherapy for Adults

Patients not currently being treated with AEDs may have monotherapy initiated with oxcarbazepine tablets. In these patients, initiate oxcarbazepine tablets at a dose of 600 mg/day (given twice a day); the dose should be increased by 300 mg/day every third day to a dose of 1200 mg/day. Controlled trials in these patients examined the effectiveness of a 1200 mg/day dose; a dose of 2400 mg/day has been shown to be effective in patients converted from other AEDs to oxcarbazepine tablets monotherapy (see above).

2.4 Adjunctive Therapy for Pediatric Patients (Aged 2-16 Years)

In pediatric patients aged 4-16 years, initiate oxcarbazepine tablets at a daily dose of 8 to 10 mg/kg generally not to exceed 600 mg/day, given twice a day. The target maintenance dose of oxcarbazepine tablets should be achieved over 2 weeks, and is dependent upon patient weight, according to the following chart:

- 20 to 29 kg-900 mg/day
- 29.1 to 39 kg-1200 mg/day
- 39 kg-1800 mg/day

In the clinical trial, in which the intention was to reach these target doses, the median daily dose was 31 mg/kg with a range of 6 to 51 mg/kg.

In pediatric patients aged 2 to < 4 years, initiate oxcarbazepine tablets at a daily dose of 8 to 10 mg/kg generally not to exceed 600 mg/day, given twice a day. For patients less than 20 kg, a starting dose of 16 to 20 mg/kg may be considered *[see Clinical Pharmacology (12.3)]*. The maximum maintenance dose of oxcarbazepine tablets should be achieved over 2 to 4 weeks and should not exceed 60 mg/kg/day in a twice a day regimen.

In the clinical trial in pediatric patients (2 to 4 years of age), in which the intention was to reach the target dose of 60 mg/kg/day, 50% of patients reached a final dose of at least 55 mg/kg/day.

Under adjunctive therapy (with and without enzyme-inducing AEDs), when normalized by body weight, apparent clearance (L/hr/kg) decreased when age increased such that children 2 to < 4 years of age may require up to twice the oxcarbazepine dose per body weight compared to adults; and children 4 to ≤ 12 years of age may require a 50% higher oxcarbazepine dose per body weight compared to adults.

Dosage adjustment is recommended with concomitant use of strong CYP3A4 enzyme inducers or UGT inducers, which include certain AEDs *[see Drug Interactions (7.1, 7.2)]*

2.5 Conversion to Monotherapy for Pediatric Patients (Aged 4-16 Years)

Patients receiving concomitant AEDs may be converted to monotherapy by initiating treatment with oxcarbazepine tablets at approximately 8 to 10 mg/kg/day given twice a day, while simultaneously initiating the reduction of the dose of the concomitant AEDs. The concomitant AEDs can be completely withdrawn over 3 to 6 weeks, while oxcarbazepine tablets may be increased as clinically indicated by a maximum increment of 10 mg/kg/day at approximately weekly intervals to achieve the recommended daily dose. Patients should be observed closely during this transition phase.

The recommended total daily dose of oxcarbazepine tablets is shown in Table 1.

2.6 Initiation of Monotherapy for Pediatric Patients (Aged 4-16 Years)

Patients not currently being treated with AEDs may have monotherapy initiated with oxcarbazepine tablets. In these patients, initiate oxcarbazepine tablets at a dose of 8 to 10 mg/kg/day given twice a day. The dose should be increased by 5 mg/kg/day every third day to the recommended daily dose shown in the table below.

Table 1: Range of Maintenance Doses of Oxcarbazepine tablets for Pediatrics by Weight During Monotherapy

	From	To
Weight in kg	**Dose (mg/day)**	**Dose (mg/day)**
20	600	900
25	900	1200
30	900	1200
35	900	1500
40	900	1500
45	1200	1500
50	1200	1800
55	1200	1800
60	1200	2100
65	1200	2100
70	1500	2100

2.7 Dosage Modification for Patients With Renal Impairment

In patients with impaired renal function (creatinine clearance < 30 mL/min), initiate oxcarbazepine tablets at one-half the usual starting dose (300 mg/day, given twice a day), and increase slowly to achieve the desired clinical response *[see Clinical Pharmacology (12.3)]*.

2.8 Administration Information

Oxcarbazepine tablets can be taken with or without food *[see Clinical Pharmacology (12.3)]*.

TRILEPTAL oral suspension and oxcarbazepine film-coated tablets may be substituted at equal doses.

3 DOSAGE FORMS AND STRENGTHS

Film-coated Tablets:
- 150 mg: pale yellow to brownish light green, oval shaped, film coated tablets, scored (functionally scored) on both sides and debossed with "OX 150" on one side.
- 300 mg: light yellow to yellow, oval shaped, film coated tablets, scored (functionally scored) on both sides and debossed with "OX 300" on one side.
- 600 mg: light Pink to Pink, oval shaped, film coated tablets, scored (functionally scored) on both sides and debossed with "OX 600" on one side.

4 CONTRAINDICATIONS

Oxcarbazepine tablets is contraindicated in patients with a known hypersensitivity to oxcarbazepine or to any of its components, or to eslicarbazepine acetate *[see Warnings and Precautions (5.2, 5.3)]*.

5 WARNINGS AND PRECAUTIONS

5.1 Hyponatremia

Clinically significant hyponatremia (sodium < 125 mmol/L) can develop during oxcarbazepine tablets use. In the 14 controlled epilepsy studies, 2.5% of oxcarbazepine tablets-treated patients (38/1524) had a sodium of less than 125 mmol/L at some point during treatment, compared to no such patients assigned placebo or active control (carbamazepine and phenobarbital for adjunctive and monotherapy substitution studies, and phenytoin and valproate for the monotherapy initiation studies). Clinically significant hyponatremia generally occurred during the first 3 months of treatment with oxcarbazepine tablets, although there were patients who first developed a serum sodium < 125 mmol/L more than 1 year after initiation of therapy. Most patients who developed hyponatremia were asymptomatic, but patients in the clinical trials were frequently monitored and some had their oxcarbazepine tablets dose reduced, discontinued, or had their fluid intake restricted for hyponatremia. Whether or not these maneuvers prevented the occurrence of more severe events is unknown.Cases of symptomatic hyponatremia and syndrome of inappropriate antidiuretic hormone secretion (SIADH) have been reported during postmarketing use. In clinical trials, patients whose treatment with oxcarbazepine tablets was discontinued due to hyponatremia generally experienced normalization of serum sodium within a few days without additional treatment.

Measurement of serum sodium levels should be considered for patients during maintenance treatment with oxcarbazepine tablets, particularly if the patient is receiving other medications known to decrease serum sodium levels (e.g., drugs associated with inappropriate ADH secretion), or if symptoms possibly indicating hyponatremia develop (e.g., nausea, malaise, headache, lethargy, confusion, obtundation, or increase in seizure frequency or severity).

5.2 Anaphylactic Reactions and Angioedema

Rare cases of anaphylaxis and angioedema involving the larynx, glottis, lips and eyelids have been reported in patients after taking the first or subsequent doses of oxcarbazepine tablets. Angioedema associated with laryngeal edema can be fatal. If a patient develops any of these reactions after treatment with oxcarbazepine tablets, the drug should be discontinued and an alternative treatment started. These patients should not be rechallenged with the drug *[see Warnings and Precautions (5.3)]*.

5.3 Cross Hypersensitivity Reaction to Carbamazepine

Approximately 25% to 30% of patients who have had hypersensitivity reactions to carbamazepine will experience hypersensitivity reactions with oxcarbazepine tablets. For this reason, patients should be specifically questioned about any prior experience with carbamazepine, and patients with a history of hypersensitivity reactions to carbamazepine should ordinarily be treated with oxcarbazepine tablets only if the potential benefit justifies the potential risk. If signs or symptoms of hypersensitivity develop, oxcarbazepine tablets should be discontinued immediately *[see Warnings and Precautions (5.2, 5.8)]*.

5.4 Serious Dermatological Reactions

Serious dermatological reactions, including Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN), have been reported in both children and adults in association with oxcarbazepine tablets use. Such serious skin reactions may be life threatening, and some patients have required hospitalization with very rare reports of fatal outcome. The median time of onset for reported cases was 19 days after treatment initiation.Recurrence of the serious skin reactions following rechallenge with oxcarbazepine tablets has also been reported.

The reporting rate of TEN and SJS associated with oxcarbazepine tablets use, which is generally accepted to be an underestimate due to underreporting, exceeds the background incidence rate estimates by a factor of 3- to 10-fold. Estimates of the background incidence rate for these serious skin reactions in the general population range between 0.5 to 6 cases per million-person years. Therefore, if a patient develops a skin reaction while taking oxcarbazepine tablets, consideration should be given to discontinuing oxcarbazepine tablets use and prescribing another antiepileptic medication.

Association With HLA-B*1502

Patients carrying the HLA-B*1502 allele may be at increased risk for SJS/TEN with oxcarbazepine tablets treatment. Human Leukocyte Antigen (HLA) allele B*1502 increases the risk for developing SJS/TEN in patients treated with carbamazepine. The chemical structure of oxcarbazepine tablets is similar to that of carbamazepine. Available clinical evidence, and data from nonclinical studies showing a direct interaction between oxcarbazepine tablets and HLA- B*1502 protein, suggest that the HLA-B*1502 allele may also increase the risk for SJS/TEN with oxcarbazepine tablets.

The frequency of HLA-B*1502 allele ranges from 2% to 12% in Han Chinese populations, is about 8% in Thai populations, and above 15% in the Philippines, and in some Malaysian populations. Allele frequencies up to about 2% and 6% have been reported in Korea and India, respectively. The frequency of the HLA-B*1502 allele is negligible in people from European descent, several African populations, indigenous peoples of the Americas, Hispanic populations, and in Japanese (< 1%).

Testing for the presence of the HLA-B*1502 allele should be considered in patients with ancestry in genetically at-risk populations, prior to initiating treatment with oxcarbazepine tablets. The use of oxcarbazepine tablets should be avoided in patients positive for HLA-B*1502 unless the benefits clearly outweigh the risks. Consideration should also be given to avoid the use of other drugs associated with SJS/TEN in HLA-B*1502 positive patients, when alternative therapies are otherwise equally acceptable. Screening is not generally recommended in patients from populations in which the prevalence of HLA-B*1502 is low, or in current oxcarbazepine tablets users, as the risk of SJS/TEN is largely confined to the first few months of therapy, regardless of HLA-B*1502 status.

The use of HLA-B*1502 genotyping has important limitations, and must never substitute for appropriate clinical vigilance and patient management. The role of other possible factors in the development of, and morbidity from, SJS/TEN, such as AED dose, compliance, concomitant medications, comorbidities, and the level of dermatologic monitoring have not been well characterized.

5.5 Suicidal Behavior and Ideation

Antiepileptic drugs, including oxcarbazepine tablets, increase the risk of suicidal thoughts or behavior in patients taking these drugs for any indication. Patients treated with any AED for any indication should be monitored for the emergence or worsening of depression, suicidal thoughts or behavior, and/or any unusual changes in mood or behavior.

Pooled analyses of 199 placebo-controlled clinical trials (mono- and adjunctive therapy) of 11 different AEDs showed that patients randomized to one of the AEDs had approximately twice the risk (adjusted Relative Risk 1.8, 95% CI:1.2, 2.7) of suicidal thinking or behavior compared to patients randomized to placebo. In these trials, which had a median treatment duration of 12 weeks, the estimated incidence rate of suicidal behavior or ideation among 27,863 AED-treated patients was 0.43%, compared to 0.24% among 16,029 placebo-treated patients, representing an increase of approximately one case of suicidal thinking or behavior for every 530 patients treated. There were 4 suicides in drug-treated patients in the trials and none in placebo-treated patients, but the number is too small to allow any conclusion about drug effect on suicide.

The increased risk of suicidal thoughts or behavior with AEDs was observed as early as one week after starting drug treatment with AEDs, and persisted for the duration of treatment assessed. Because most trials included in the analysis did not extend beyond 24 weeks, the risk of suicidal thoughts or behavior beyond 24 weeks could not be assessed.

The risk of suicidal thoughts or behavior was generally consistent among drugs in the data analyzed. The finding of increased risk with AEDs of varying mechanisms of action and across a range of indications suggests that the risk applies to all AEDs used for any indication. The risk did not vary substantially by age (5 to 100 years) in the clinical trials analyzed. Table 2 shows absolute and relative risk by indication for all evaluated AEDs.

Table 2: Risk by Indication for Antiepileptic Drugs in the Pooled Analysis

Indication	Placebo patients with events per 1000 patients	Drug patients with events per 1000 patients	Relative risk: incidence of events in drug patients/incidence in placebo patients	Risk difference: additional drug patients with events per 1000 patients
Epilepsy	1.0	3.4	3.5	2.4
Psychiatric	5.7	8.5	1.5	2.9
Other	1.0	1.8	1.9	0.9
Total	2.4	4.3	1.8	1.9

The relative risk for suicidal thoughts or behavior was higher in clinical trials for epilepsy than in clinical trials for psychiatric or other conditions, but the absolute risk differences were similar for the epilepsy and psychiatric indications.

Anyone considering prescribing oxcarbazepine tablets or any other AED must balance the risk of suicidal thoughts or behavior with the risk of untreated illness. Epilepsy and many other illnesses for which AEDs are prescribed are themselves associated with morbidity and mortality and an increased risk of suicidal thoughts and behavior. Should suicidal thoughts and behavior emerge during treatment, the prescriber needs to consider whether the emergence of these symptoms in any given patient may be related to the illness being treated.

Patients, their caregivers, and families should be informed that AEDs increase the risk of suicidal thoughts and behavior and should be advised of the need to be alert for the emergence or worsening of the signs and symptoms of depression, any unusual changes in mood or behavior, or the emergence of suicidal thoughts, behavior, or thoughts about self-harm. Behaviors of concern should be reported immediately to healthcare providers.

5.6 Withdrawal of Antiepileptic Drugs

As with most AEDs, oxcarbazepine tablets should generally be withdrawn gradually because of the risk of increased seizure frequency and status epilepticus *[see Dosage and Administration (2.4) and Clinical Studies (14)]*. But if withdrawal is needed because of a serious adverse event, rapid discontinuation can be considered.

5.7 Cognitive/Neuropsychiatric Adverse Reactions

Use of oxcarbazepine tablets has been associated with CNS-related adverse reactions. The most significant of these can be classified into three general categories: 1) cognitive symptoms, including psychomotor slowing, difficulty with concentration, and speech or language problems; 2) somnolence or fatigue; and 3) coordination abnormalities, including ataxia and gait disturbances.

Patients should be monitored for these signs and symptoms and advised not to drive or operate machinery until they have gained sufficient experience on oxcarbazepine tablets to gauge whether it adversely affects their ability to drive or operate machinery.

Adult Patients

In one large, fixed-dose study, oxcarbazepine tablets was added to existing AED therapy (up to three concomitant AEDs). By protocol, the dosage of the concomitant AEDs could not be reduced as oxcarbazepine tablets was added, reduction in oxcarbazepine tablets dosage was not allowed if intolerance developed, and patients were discontinued if unable to tolerate their highest target maintenance doses. In this trial, 65% of patients were discontinued because they could not tolerate the 2400 mg/day dose of oxcarbazepine tablets on top of existing AEDs. The adverse events seen in this study were primarily CNS related and the risk for discontinuation was dose related.

In this trial, 7.1% of oxcarbazepine-treated patients and 4% of placebo-treated patients experienced a cognitive adverse reaction. The risk of discontinuation for these events was about 6.5 times greater on oxcarbazepine than on placebo. In addition, 26% of oxcarbazepine-treated patients and 12% of placebo-treated patients experienced somnolence. The risk of discontinuation for somnolence was about 10 times greater on oxcarbazepine than on placebo. Finally, 28.7% of oxcarbazepine-treated patients and 6.4% of placebo-treated patients experienced ataxia or gait disturbances. The risk for discontinuation for these events was about 7 times greater on oxcarbazepine than on placebo.

In a single placebo-controlled monotherapy trial evaluating 2400 mg/day of oxcarbazepine tablets, no patients in either treatment group discontinued double-blind treatment because of cognitive adverse events, somnolence, ataxia, or gait disturbance.

In the 2 dose-controlled conversion to monotherapy trials comparing 2400 mg/day and 300 mg/day oxcarbazepine tablets, 1.1% of patients in the 2400 mg/day group discontinued double-blind treatment because of somnolence or cognitive adverse reactions compared to 0% in the 300 mg/day group. In these trials, no patients discontinued because of ataxia or gait disturbances in either treatment group.

Pediatric Patients

A study was conducted in pediatric patients (3 to 17 years old) with inadequately controlled partial-onset seizures in which oxcarbazepine tablets was added to existing AED therapy (up to 2 concomitant AEDs). By protocol, the dosage of concomitant AEDs could not be reduced as oxcarbazepine tablets was added. Oxcarbazepine tablets was titrated to reach a target dose ranging from 30 mg/kg to 46 mg/kg (based on a patient's body weight with fixed doses for predefined weight ranges).

Cognitive adverse events occurred in 5.8% of oxcarbazepine-treated patients (the single most common event being concentration impairment, 4 of 138 patients) and in 3.1% of patients treated with placebo. In addition, 34.8% of oxcarbazepine-treated patients and 14.0% of placebo-treated patients experienced somnolence (no patient discontinued due to a cognitive adverse reaction or somnolence). Finally, 23.2% of oxcarbazepine-treated patients and 7.0% of placebo-treated patients experienced ataxia or gait disturbances. Two (1.4%) oxcarbazepine-treated patients and 1 (0.8%) placebo-treated patient discontinued due to ataxia or gait disturbances.

5.8 Drug Reaction With Eosinophilia and Systemic Symptoms/Multi-Organ Hypersensitivity

Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS), also known as multi- organ hypersensitivity, has occurred with oxcarbazepine tablets. Some of these events have been fatal or life-threatening. DRESS typically, although not exclusively, presents with fever, rash, lymphadenopathy and/or facial swelling, in association with other organ system involvement, such as hepatitis, nephritis, hematologic abnormalities, myocarditis, or myositis sometimes resembling an acute viral infection. Eosinophilia is often present. This disorder is variable in its expression, and other organ systems not noted here may be involved. It is important to note that early manifestations of hypersensitivity (e.g., fever, lymphadenopathy) may be present even though rash is not evident. If such signs or symptoms are present, the patient should be evaluated immediately. Oxcarbazepine tablets should be discontinued if an alternative etiology for the signs or symptoms cannot be established.

5.9 Hematologic Events

Rare reports of pancytopenia, agranulocytosis, and leukopenia have been seen in patients treated with oxcarbazepine tablets during postmarketing experience. Discontinuation of the drug should be considered if any evidence of these hematologic events develops.

5.10 Seizure Control During Pregnancy

Due to physiological changes during pregnancy, plasma levels of the active metabolite of oxcarbazepine, the 10-monohydroxy derivative (MHD), may gradually decrease throughout pregnancy. It is recommended that patients be monitored carefully during pregnancy. Close monitoring should continue through the postpartum period because MHD levels may return after delivery.

5.11 Risk of Seizure Aggravation

Exacerbation of or new onset primary generalized seizures has been reported with oxcarbazepine tablets. The risk of aggravation of primary generalized seizures is seen especially in children but may also occur in adults. In case of seizure aggravation, oxcarbazepine tablets should be discontinued.

6 ADVERSE REACTIONS

The following serious adverse reactions are described below and elsewhere in the labeling:
- Hyponatremia *[see Warnings and Precautions (5.1)]*
- Anaphylactic Reactions and Angioedema *[see Warnings and Precautions (5.2)]*
- Cross Hypersensitivity Reaction to Carbamazepine *[see Warnings and Precautions (5.3)]*
- Serious Dermatological Reactions *[see Warnings and Precautions (5.4)]*
- Suicidal Behavior and Ideation *[see Warnings and Precautions (5.5)]*
- Cognitive/Neuropsychiatric Adverse Reactions *[see Warnings and Precautions (5.7)]*
- Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS)/Multi-Organ Hypersensitivity *[see Warnings and Precautions (5.8)]*
- Hematologic Events *[see Warnings and Precautions (5.9)]*

6.1 Clinical Trial 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.

Most Common Adverse Reactions in All Clinical Studies

Adjunctive Therapy/Monotherapy in Adults Previously Treated With Other AEDs

The most common (≥ 10% more than placebo for adjunctive or low dose for monotherapy) adverse reactions with oxcarbazepine tablets: dizziness, somnolence, diplopia, fatigue, nausea, vomiting, ataxia, abnormal vision, headache, nystagmus tremor, and abnormal gait.

Approximately 23% of these 1537 adult patients discontinued treatment because of an adverse reaction. The adverse reactions most commonly associated with discontinuation were: dizziness (6.4%), diplopia (5.9%), ataxia (5.2%), vomiting (5.1%), nausea (4.9%), somnolence (3.8%), headache (2.9%), fatigue (2.1%), abnormal vision (2.1%), tremor (1.8%), abnormal gait (1.7%), rash (1.4%), and hyponatremia (1.0%).

Monotherapy in Adults Not Previously Treated With Other AEDs

The most common (≥ 5%) adverse reactions with oxcarbazepine tablets in these patients were similar to those in previously treated patients.

Approximately 9% of these 295 adult patients discontinued treatment because of an adverse reaction. The adverse reactions most commonly associated with discontinuation were: dizziness (1.7%), nausea (1.7%), rash (1.7%), and headache (1.4%).

Adjunctive Therapy/Monotherapy in Pediatric Patients 4 Years Old and Above Previously Treated With Other AEDs

The most common (≥ 5%) adverse reactions with oxcarbazepine tablets in these patients were similar to those seen in adults.

Approximately 11% of these 456 pediatric patients discontinued treatment because of an adverse reaction. The adverse reactions most commonly associated with discontinuation were: somnolence (2.4%), vomiting (2.0%), ataxia (1.8%), diplopia (1.3%), dizziness (1.3%), fatigue (1.1%), and nystagmus (1.1%).

Monotherapy in Pediatric Patients 4 Years Old and Above Not Previously Treated With Other AEDs

The most common (≥ 5%) adverse reactions with oxcarbazepine tablets in these patients were similar to those in adults.

Approximately 9.2% of 152 pediatric patients discontinued treatment because of an adverse reaction. The adverse reactions most commonly associated (≥ 1%) with discontinuation were rash (5.3%) and maculopapular rash (1.3%).

Adjunctive Therapy/Monotherapy in Pediatric Patients 1 Month to < 4 Years Old Previously Treated or Not Previously Treated with Other AEDs:

The most common (≥ 5%) adverse reactions with oxcarbazepine tablets in these patients were similar to those seen in older children and adults, except for infections and infestations which were more frequently seen in these younger children.

Approximately 11% of these 241 pediatric patients discontinued treatment because of an adverse reaction. The adverse reactions most commonly associated with discontinuation were: convulsions (3.7%), status epilepticus (1.2%), and ataxia (1.2%).

Controlled Clinical Studies of Adjunctive Therapy/Monotherapy in Adults Previously Treated With Other AEDs

Table 3 lists adverse reactions that occurred in at least 2% of adult patients with epilepsy, treated with oxcarbazepine tablets or placebo as adjunctive treatment and were numerically more common in the patients treated with any dose of oxcarbazepine tablets.

Table 4 lists adverse reactions in patients converted from other AEDs to either high-dose oxcarbazepine tablets (2400 mg/day) or low-dose (300 mg/day) oxcarbazepine tablets. Note that in some of these monotherapy studies patients who dropped out during a preliminary tolerability phase are not included in the tables.

Table 3: Adverse Reactions in a Controlled Clinical Study of Adjunctive Therapy With Oxcarbazepine tablets in Adults

	Oxcarbazepine tablets dosage (mg/day)			
Body system/ Adverse reaction	**Oxcarbazepine 600 N = 163 %**	**Oxcarbazepine 1200 N = 171 %**	**Oxcarbazepine 2400 N = 126 %**	**Placebo N = 166 %**
Body as a whole				
Fatigue	15	12	15	7
Asthenia	6	3	6	5
Leg edema	2	1	2	1
Increased weight	1	2	2	1
Feeling abnormal	0	1	2	0
Cardiovascular system				
Hypotension	0	1	2	0
Digestive system				
Nausea	15	25	29	10
Vomiting	13	25	36	5
Abdominal pain	10	13	11	5
Diarrhea	5	6	7	6
Dyspepsia	5	5	6	2
Constipation	2	2	6	4
Gastritis	2	1	2	1
Metabolic and nutritional disorders				
Hyponatremia	3	1	2	1
Musculoskeletal system				
Muscle weakness	1	2	2	0
Sprains and strains	0	2	2	1
Nervous system				
Headache	32	28	26	23
Dizziness	26	32	49	13
Somnolence	20	28	36	12
Ataxia	9	17	31	5
Nystagmus	7	20	26	5
Abnormal gait	5	10	17	1
Insomnia	4	2	3	1
Tremor	3	8	16	5
Nervousness	2	4	2	1
Agitation	1	1	2	1
Abnormal coordination	1	3	2	1
Abnormal EEG	0	0	2	0
Speech disorder	1	1	3	0
Confusion	1	1	2	1
Cranial injury NOS	1	0	2	1
Dysmetria	1	2	3	0
Abnormal thinking	0	2	4	0
Respiratory system				
Rhinitis	2	4	5	4
Skin and appendages				
Acne	1	2	2	0
Special senses				
Diplopia	14	30	40	5
Vertigo	6	12	15	2
Abnormal vision	6	14	13	4
Abnormal accommodation	0	0	2	0

Abbreviations: EEG, electroencephalogram; NOS, not otherwise specified.

Table 4: Adverse Reactions in Controlled Clinical Studies of Monotherapy With Oxcarbazepine tablets in Adults Previously Treated With Other Antiepileptic Drugs

	Oxcarbazepine tablets dosage (mg/day)	
Body system/ Adverse reaction	**Oxcarbazepine 2400 mg/day N = 86 %**	**Oxcarbazepine 300 mg/day N = 86 %**
Body as a whole		
Fatigue	21	5
Fever	3	0
Allergy	2	0
Generalized edema	2	1
Chest pain	2	0
Digestive system		
Nausea	22	7
Vomiting	15	5
Diarrhea	7	5
Dyspepsia	6	1
Anorexia	5	3
Abdominal pain	5	3
Dry mouth	3	0
Hemorrhage rectum	2	0
Toothache	2	1
Hemic and lymphatic system		
Lymphadenopathy	2	0
Infections and infestations		
Viral infection	7	5
Infection	2	0
Metabolic and nutritional disorders		
Hyponatremia	5	0
Thirst	2	0
Nervous system		
Headache	31	15
Dizziness	28	8
Somnolence	19	5
Anxiety	7	5
Ataxia	7	1
Confusion	7	0
Nervousness	7	0
Insomnia	6	3
Tremor	6	3
Amnesia	5	1
Aggravated convulsions	5	2
Emotional lability	3	2
Hypoesthesia	3	1
Abnormal coordination	2	1
Nystagmus	2	0
Speech disorder	2	0
Respiratory system		
Upper respiratory tract infection	10	5
Coughing	5	0
Bronchitis	3	0
Pharyngitis	3	0
Skin and appendages		
Hot flushes	2	1
Purpura	2	0
Special senses		
Abnormal vision	14	2
Diplopia	12	1
Taste perversion	5	0
Vertigo	3	0
Earache	2	1
Ear infection NOS	2	0
Urogenital and reproductive system		
Urinary tract infection	5	1
Micturition frequency	2	1
Vaginitis	2	0

Abbreviation: NOS, not otherwise specified.

Controlled Clinical Study of Monotherapy in Adults Not Previously Treated With Other AEDs

Table 5 lists adverse reactions in a controlled clinical study of monotherapy in adults not previously treated with other AEDs that occurred in at least 2% of adult patients with epilepsy treated with oxcarbazepine tablets or placebo and were numerically more common in the patients treated with oxcarbazepine tablets.

Table 5: Adverse Reactions in a Controlled Clinical Study of Monotherapy With Oxcarbazepine tablets in Adults Not Previously Treated With Other Antiepileptic Drugs

Body system/Adverse reaction	Oxcarbazepine N = 55 %	Placebo N = 49 %
Body as a whole		
Falling down NOS	4	0
Digestive system		
Nausea	16	12
Diarrhea	7	2
Vomiting	7	6
Constipation	5	0
Dyspepsia	5	4
Musculoskeletal system		
Back pain	4	2
Nervous system		
Dizziness	22	6
Headache	13	10
Ataxia	5	0
Nervousness	5	2
Amnesia	4	2
Abnormal coordination	4	2
Tremor	4	0
Respiratory system		
Upper respiratory tract infection	7	0
Epistaxis	4	0
Infection chest	4	0
Sinusitis	4	2
Skin and appendages		
Rash	4	2
Special senses		
Vision abnormal	4	0

Abbreviation: NOS, not otherwise specified.

Controlled Clinical Studies of Adjunctive Therapy/Monotherapy in Pediatric Patients Previously Treated With Other AEDs

Table 6 lists adverse reactions that occurred in at least 2% of pediatric patients with epilepsy treated with oxcarbazepine tablets or placebo as adjunctive treatment and were numerically more common in the patients treated with oxcarbazepine tablets.

Table 6: Adverse Reactions in Controlled Clinical Studies of Adjunctive Therapy/Monotherapy With Oxcarbazepine tablets in Pediatric Patients Previously Treated With Other Antiepileptic Drugs

Body system/ Adverse reaction	Oxcarbazepine N = 171 %	Placebo N = 139 %
Body as a whole		
Fatigue	13	9
Allergy	2	0
Asthenia	2	1
Digestive system		
Vomiting	33	14
Nausea	19	5
Constipation	4	1
Dyspepsia	2	0
Nervous system		
Headache	31	19
Somnolence	31	13
Dizziness	28	8
Ataxia	13	4
Nystagmus	9	1
Emotional lability	8	4
Abnormal gait	8	3
Tremor	6	4
Speech disorder	3	1
Impaired concentration	2	1
Convulsions	2	1
Involuntary muscle contractions	2	1
Respiratory system		
Rhinitis	10	9
Pneumonia	2	1
Skin and appendages		
Bruising	4	2
Increased sweating	3	0
Special senses		
Diplopia	17	1
Abnormal vision	13	1
Vertigo	2	0

Other Events Observed in Association With the Administration of oxcarbazepine tablets

In the paragraphs that follow, the adverse reactions, other than those in the preceding tables or text, that occurred in a total of 565 children and 1574 adults exposed to oxcarbazepine tablets and that are reasonably likely to be related to drug use are presented. Events common in the population, events reflecting chronic illness and events likely to reflect concomitant illness are omitted particularly if minor. They are listed in order of decreasing frequency. Because the reports cite events observed in open label and uncontrolled trials, the role of oxcarbazepine tablets in their causation cannot be reliably determined.

Body as a Whole: fever, malaise, pain chest precordial, rigors, weight decrease

Cardiovascular System: bradycardia, cardiac failure, cerebral hemorrhage, hypertension, hypotension postural, palpitation, syncope, tachycardia

Digestive System: appetite increased, blood in stool, cholelithiasis, colitis, duodenal ulcer, dysphagia, enteritis, eructation, esophagitis, flatulence, gastric ulcer, gingival bleeding, gum hyperplasia, hematemesis, hemorrhage rectum, hemorrhoids, hiccup, mouth dry, pain biliary, pain right hypochondrium, retching, sialoadenitis, stomatitis, stomatitis ulcerative

Hematologic and Lymphatic System: thrombocytopenia

Laboratory Abnormality: gamma-GT increased, hyperglycemia, hypocalcemia, hypoglycemia, hypokalemia, liver enzymes elevated, serum transaminase increased

Musculoskeletal System: hypertonia muscle

Nervous System: aggressive reaction, amnesia, anguish, anxiety, apathy, aphasia, aura, convulsions aggravated, delirium, delusion, depressed level of consciousness, dysphonia, dystonia, emotional lability, euphoria, extrapyramidal disorder, feeling drunk, hemiplegia, hyperkinesia, hyperreflexia, hypoesthesia, hypokinesia, hyporeflexia, hypotonia, hysteria, libido decreased, libido increased, manic reaction, migraine, muscle contractions involuntary, nervousness, neuralgia, oculogyric crisis, panic disorder, paralysis, paroníria, personality disorder, psychosis, ptosis, stupor, tetany

Respiratory System: asthma, dyspnea, epistaxis, laryngismus, pleurisy

Skin and Appendages: acne, alopecia, angioedema, bruising, dermatitis contact, eczema, facial rash, flushing, folliculitis, heat rash, hot flushes, photosensitivity reaction, pruritus genital, psoriasis, purpura, rash erythematous, rash maculopapular, vitiligo, urticaria

Special Senses: accommodation abnormal, cataract, conjunctival hemorrhage, edema eye, hemianopia, mydriasis, otitis externa, photophobia, scotoma, taste perversion, tinnitus, xerophthalmia

Surgical and Medical Procedures: procedure dental oral, procedure female reproductive, procedure musculoskeletal, procedure skin

Urogenital and Reproductive System: dysuria, hematuria, intermenstrual bleeding, leukorrhea, menorrhagia, micturition frequency, pain renal, pain urinary tract, polyuria, priapism, renal calculus

Other: Systemic lupus erythematosus

Laboratory Tests

Serum sodium levels below 125 mmol/L have been observed in patients treated with oxcarbazepine tablets *[see Warnings and Precautions (5.1)]*. Experience from clinical trials indicates that serum sodium levels return toward normal when the oxcarbazepine tablets dosage is reduced or discontinued, or when the patient was treated conservatively (e.g., fluid restriction).

Laboratory data from clinical trials suggest that oxcarbazepine tablets use was associated with decreases in T_4, without changes in T_3 or TSH.

6.2 Postmarketing Experience

The following adverse reactions have been identified during postapproval use of oxcarbazepine tablets. 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.

Body as a Whole: multi-organ hypersensitivity disorders characterized by features such as rash, fever, lymphadenopathy, abnormal liver function tests, eosinophilia and arthralgia *[see Warnings and Precautions (5.8)]*

Cardiovascular System: atrioventricular block

Immune System Disorders: anaphylaxis *[see Warnings and Precautions (5.2)]*

Digestive System: pancreatitis and/or lipase and/or amylase increase

Hematologic and Lymphatic Systems: aplastic anemia *[see Warnings and Precautions (5.9)]*

Metabolism and Nutrition Disorders: hypothyroidism and syndrome of inappropriate antidiuretic hormone secretion (SIADH)

Skin and Subcutaneous Tissue Disorders: erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis *[see Warnings and Precautions (5.4)]*, Acute Generalized Exanthematous Pustulosis (AGEP)

Musculoskeletal, Connective Tissue and Bone Disorders: There have been reports of decreased bone mineral density, osteoporosis, and fractures in patients on long-term therapy with oxcarbazepine tablets.

Injury, Poisoning, and Procedural Complications: fall

Nervous System Disorders: dysarthria

7 DRUG INTERACTIONS

7.1 Effect of oxcarbazepine tablets on Other Drugs

Phenytoin levels have been shown to increase with concomitant use of oxcarbazepine tablets at doses greater than 1200 mg/day *[see Clinical Pharmacology (12.3)]*. Therefore, it is recommended that the plasma levels of phenytoin be monitored during the period of oxcarbazepine tablets titration and dosage modification. A decrease in the dose of phenytoin may be required.

7.2 Effect of Other Drugs on oxcarbazepine tablets

Strong inducers of cytochrome P450 enzymes and/or inducers of UGT (e.g., rifampin, carbamazepine, phenytoin and phenobarbital) have been shown to decrease the plasma/serum levels of MHD, the active metabolite of oxcarbazepine tablets (25% to 49%) *[see Clinical Pharmacology (12.3)]*. If oxcarbazepine tablets and strong CYP3A4 inducers, or UGT inducers are administered concurrently, it is recommended that the plasma levels of MHD be monitored during the period of oxcarbazepine tablets titration. Dose adjustment of oxcarbazepine tablets may be required after initiation, dosage modification, or discontinuation of such inducers.

7.3 Hormonal Contraceptives

Concurrent use of oxcarbazepine tablets with hormonal contraceptives may render these contraceptives less effective *[see Use in Specific Populations (8.3) and Clinical Pharmacology (12.3)]*. Studies with other oral or implant contraceptives have not been conducted.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

Although oxcarbazepine tablets is closely related structurally to carbamazepine, which is considered to be teratogenic in humans, available human data from published literature and ongoing pregnancy registry studies on use of oxcarbazepine during pregnancy have not demonstrated an increased prevalence of major congenital malformations with first trimester exposure. However, all published studies reviewed have important methodological limitations, including unmeasured confounding and a small number of exposed cases (see Data). There are risks to the mother and fetus associated with partial onset seizures (see Clinical Considerations). There are no data on the risks associated with the use of oxcarbazepine tablets and miscarriage or other adverse maternal outcomes.

Increased incidences of fetal structural abnormalities and other manifestations of developmental toxicity (embryolethality, growth retardation) were observed in the offspring of animals treated with either oxcarbazepine or its active 10-hydroxy metabolite (MHD) during pregnancy at doses similar to the maximum recommended human dose (MRHD).

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. All pregnancies have a background risk of birth defect, loss, or other adverse outcomes.

Clinical Considerations

Disease-associated Maternal and/or Embryofetal Risk

Epilepsy, with or without exposure to antiepileptic drugs, has been associated with several adverse outcomes during pregnancy, including preeclampsia, preterm labor, antepartum and postpartum hemorrhage, placental abruption, poor fetal growth, prematurity, fetal death, and maternal mortality. The risk of maternal or fetal injury may be greatest for patients with untreated or poorly controlled convulsive seizures. Women with epilepsy who become pregnant should not abruptly discontinue antiepileptic drugs, including oxcarbazepine tablets, due to the risk of status epilepticus or severe seizures, which may be life-threatening [see Warnings and Precautions (5.6)].

Maternal Adverse Reactions

An increase in seizure frequency may occur during pregnancy because of altered levels of the active metabolite of oxcarbazepine. Monitor patients carefully during pregnancy and through the postpartum period [see Warnings and Precautions (5.10)].

Data

Human Data

Data from a published retrospective cohort study and ongoing pregnancy registry studies on the use of oxcarbazepine during pregnancy have not demonstrated an increased prevalence of major congenital malformations with first trimester exposure. A retrospective cohort study conducted in Nordic countries (Denmark, Finland, Iceland, Norway, and Sweden) from 1996-2020 found that there was no increased prevalence of major congenital malformations when pregnancies exposed to oxcarbazepine during the first trimester were compared to pregnancies exposed to lamotrigine (adjusted risk ratio =1.09; 95% CI 0.83 to 1.44; n pregnancies exposed to oxcarbazepine= 1,313, n exposed cases = 58). In an ongoing pregnancy registry that included data from over 40 countries from 1999 to 2022 and 443 pregnancies exposed to oxcarbazepine, oxcarbazepine exposure during the first trimester was not associated with major congenital malformations (adjusted odds ratio =1.09; 95% CI 0.56 to 2.13, n exposed cases = 10). However, there are important methodological limitations of these studies including unmeasured confounding factors and a small number of exposed cases in the registry.

Animal Data

When pregnant rats were given oxcarbazepine (0, 30, 300, or 1000 mg/kg/day) orally throughout the period of organogenesis, increased incidences of fetal malformations (craniofacial, cardiovascular, and skeletal) and variations were observed at the intermediate and high doses (approximately 1.2 and 4 times, respectively, the MRHD on a mg/m^2 basis). Increased embryofetal death and decreased fetal body weights were seen at the high dose. Doses ≥300 mg/kg/day were also maternally toxic (decreased body weight gain, clinical signs), but there is no evidence to suggest that teratogenicity was secondary to the maternal effects.

In a study in which pregnant rabbits were orally administered MHD (0, 20, 100, or 200 mg/kg/day) during organogenesis, embryofetal mortality was increased at the highest dose (1.5 times the MRHD on a mg/m^2 basis). This dose produced only minimal maternal toxicity.

In a study in which female rats were dosed orally with oxcarbazepine (0, 25, 50, or 150 mg/kg/day) during the latter part of gestation and throughout the lactation period, a persistent reduction in body weights and altered behavior (decreased activity) were observed in offspring exposed to the highest dose (less than the MRHD on a mg/m^2 basis). Oral administration of MHD (0, 25, 75, or 250 mg/kg/day) to rats during gestation and lactation resulted in a persistent reduction in offspring weights at the highest dose (equivalent to the MRHD on a mg/m^2 basis).

8.2 Lactation

Risk Summary

Oxcarbazepine and its active metabolite (MHD) are present in human milk after oxcarbazepine tablets administration. The effects of oxcarbazepine and its active metabolite (MHD) on the breastfed infant or on milk production are unknown. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for oxcarbazepine tablets and any potential adverse effects on the breastfed infant from oxcarbazepine tablets or from the underlying maternal condition.

8.3 Females and Males of Reproductive Potential

Contraception

Use of oxcarbazepine tablets with hormonal contraceptives containing ethinylestradiol or levonorgestrel is associated with decreased plasma concentrations of these hormones and may result in a failure of the therapeutic effect of the oral contraceptive drug. Advise women of reproductive potential taking oxcarbazepine tablets who are using a contraceptive containing ethinylestradiol or levonorgestrel to use additional or alternative non- hormonal birth control *[see Drug Interactions (7.3) and Clinical Pharmacology (12.3)]*.

8.4 Pediatric Use

Oxcarbazepine tablets is indicated for use as adjunctive therapy for partial-onset seizures in patients aged 2 to 16 years.

The safety and effectiveness for use as adjunctive therapy for partial-onset seizures in pediatric patients below the age of 2 have not been established.

Oxcarbazepine tablets is also indicated as monotherapy for partial-onset seizures in patients aged 4 to 16 years.

The safety and effectiveness for use as monotherapy for partial-onset seizures in pediatric patients below the age of 4 have not been established.

Oxcarbazepine tablets has been given to 898 patients between the ages of 1 month to 17 years in controlled clinical trials (332 treated as monotherapy) and about 677 patients between the ages of 1 month to 17 years in other trials *[see Warnings and Precautions (5.11), Adverse Reactions (6.1), Clinical Pharmacology (12.3), and Clinical Studies (14)]*.

8.5 Geriatric Use

There were 52 patients over age 65 in controlled clinical trials and 565 patients over the age of 65 in other trials. Following administration of single (300 mg) and multiple (600 mg/day) doses of oxcarbazepine tablets in elderly volunteers (60 to 82 years of age), the maximum plasma concentrations and area under the curve (AUC) values of MHD were 30% to 60% higher than in younger volunteers (18 to 32 years of age). Comparisons of creatinine clearance in young and elderly volunteers indicate that the difference was due to age-related reductions in creatinine clearance. Close monitoring of sodium levels is required in elderly patients at risk for hyponatremia *[see Warnings and Precautions (5.1)]*.

8.6 Renal Impairment

Dose adjustment is recommended for renally impaired patients (creatinine clearance < 30 mL/min) *[see Dosage and Administration (2.7) and Clinical Pharmacology (12.3)]*.

9 DRUG ABUSE AND DEPENDENCE

9.2 Abuse

The abuse potential of oxcarbazepine tablets has not been evaluated in human studies.

9.3 Dependence

Intragastric injections of oxcarbazepine to 4 cynomolgus monkeys demonstrated no signs of physical dependence as measured by the desire to self-administer oxcarbazepine by lever pressing activity.

10 OVERDOSAGE

10.1 Human Overdose Experience

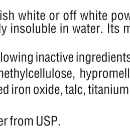
Isolated cases of overdose with oxcarbazepine tablets have been reported. The maximum dose taken was approximately 48,000 mg. All patients recovered with symptomatic treatment. Nausea, vomiting, somnolence, aggression, agitation, hypotension, and tremor each occurred in more than one patient. Coma, confusional state, convulsion, dyscoordination, depressed level of consciousness, diplopia, dizziness, dyskinesia, dyspnea, QT prolongation, headache, miosis, nystagmus, overdose, decreased urine output, and blurred vision also occurred.

10.2 Treatment and Management

There is no specific antidote. Symptomatic and supportive treatment should be administered as appropriate. Removal of the drug by gastric lavage and/or inactivation by administering activated charcoal should be considered.

11 DESCRIPTION

Oxcarbazepine tablets, USP is an AED available as 150 mg, 300 mg, and 600 mg film-coated tablets for oral administration. Oxcarbazepine, USP is 10,11-Dihydro-10-oxo-5*H*-dibenz[*b,f*]azepine-5- carboxamide, and its structural formula is:



Oxcarbazepine, USP is a light orange to creamish white or off white powder. It is soluble in acetic acid, sparingly soluble in chloroform, practically insoluble in water. Its molecular weight is 252.27 g/mol.

Oxcarbazepine film-coated tablets contain the following inactive ingredients: black iron oxide, colloidal silicon dioxide, crospovidone, hydroxypropyl methylcellulose, hypromellose, magnesium stearate, microcrystalline cellulose, polyethylene glycol, red iron oxide, talc, titanium dioxide, yellow iron oxide.

Organic Impurities Procedure 2 used.

FDA approved dissolution test specifications differ from USP.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

The pharmacological activity of oxcarbazepine tablets is primarily exerted through the 10-monohydroxy metabolite (MHD) of oxcarbazepine *[see Clinical Pharmacology (12.3)]*. The precise mechanism by which oxcarbazepine and MHD exert their anti-seizure effect is unknown; however, in vitro electrophysiological studies indicate that they produce blockade of voltage-sensitive sodium channels, resulting in stabilization of hyperexcited neural membranes, inhibition of repetitive neuronal firing, and diminution of propagation of synaptic impulses. These actions are thought to be important in the prevention of seizure spread in the intact brain. In addition, increased potassium conductance and modulation of high-voltage activated calcium channels may contribute to the anticonvulsant effects of the drug. No significant interactions of oxcarbazepine or MHD with brain neurotransmitter or modulator receptor sites have been demonstrated.

12.2 Pharmacodynamics

Oxcarbazepine and its active metabolite (MHD) exhibit anticonvulsant properties in animal seizure models. They protected rodents against electrically induced tonic extension seizures and, to a lesser degree, chemically induced clonic seizures, and abolished or reduced the frequency of chronically recurring focal seizures in Rhesus monkeys with aluminum implants. No development of tolerance (i.e., attenuation of anticonvulsive activity) was observed in the maximal electroshock test when mice and rats were treated daily for 5 days and 4 weeks, respectively, with oxcarba-zepine or MHD.

12.3 Pharmacokinetics

Following oral administration of oxcarbazepine tablets, oxcarbazepine is completely absorbed and extensively metabolized to its pharmacologically active 10-monohydroxy metabolite (MHD). In a mass balance study in people, only 2% of total radioactivity in plasma was due to unchanged oxcarbazepine, with approximately 70% present as MHD, and the remainder attributable to minor metabolites.

The half-life of the parent is about 2 hours, while the half-life of MHD is about 9 hours, so that MHD is responsible for most antiepileptic activity.

Absorption

Based on MHD concentrations, oxcarbazepine tablets and suspension were shown to have similar bioavailability.

After single-dose administration of oxcarbazepine tablets to healthy male volunteers under fasted conditions, the median t_{max} was 4.5 (range, 3 to 13) hours. After single-dose administration of TRILEPTAL oral suspension to healthy male volunteers under fasted conditions, the median t_{max} was 6 hours.

Steady-state plasma concentrations of MHD are reached within 2 to 3 days in patients when oxcarbazepine tablets is given twice a day. At steady state the pharmacokinetics of MHD are linear and show dose proportionality over the dose range of 300 to 2400 mg/day.

Food has no effect on the rate and extent of absorption of oxcarbazepine from oxcarbazepine tablets. Although not directly studied, the oral bioavailability of the TRILEPTAL suspension is unlikely to be affected under fed conditions Therefore, oxcarbazepine tablets and suspension can be taken with or without food.

Distribution

The apparent volume of distribution of MHD is 49 L.

Approximately 40% of MHD is bound to serum proteins, predominantly to albumin. Binding is independent of the serum concentration within the therapeutically relevant range. Oxcarbazepine and MHD do not bind to alpha-1-acid glycoprotein.

Metabolism and Excretion

Oxcarbazepine is rapidly reduced by cytosolic enzymes in the liver to its 10-monohydroxy metabolite, MHD, which is primarily responsible for the pharmacological effect of oxcarbazepine tablets. MHD is metabolized further by conjugation with glucuronic acid. Minor amounts (4% of the dose) are oxidized to the pharmacologically inactive 10,11-dihydroxy metabolite (DHD).

Oxcarbazepine is cleared from the body mostly in the form of metabolites which are predominantly excreted by the kidneys. More than 95% of the dose appears in the urine, with less than 1% as unchanged oxcarbazepine. Fecal excretion accounts for less than 4% of the administered dose. Approximately 80% of the dose is excreted in the urine either as glucuronides of MHD (49%) or as unchanged MHD (27%); the inactive DHD accounts for approximately 3% and conjugates of MHD and oxcarbazepine account for 13% of the dose.

The half-life of the parent is about 2 hours, while the half-life of MHD is about 9 hours.

Specific Populations

Geriatrics

Following administration of single (300 mg) and multiple (600 mg/day) doses of oxcarbazepine tablets to elderly volunteers (60 to 82 years of age), the maximum plasma concentrations and AUC values of MHD were 30% to 60% higher than in younger volunteers (18 to 32 years of age). Comparisons of creatinine clearance in young and elderly volunteers indicate that the difference was due to age-related reductions in creatinine clearance.

Pediatrics

Weight-adjusted MHD clearance decreases as age and weight increases, approaching that of adults. The mean weight-adjusted clearance in children 2 years to < 4 years of age is approximately 80% higher on average than that of adults. Therefore, MHD exposure in these children is expected to be about one-half that of adults when treated with a similar weight-adjusted dose. The mean weight-adjusted clearance in children 4 to 12 years of age is approximately 40% higher on average than that of adults. Therefore, MHD exposure in these children is expected to be about three-quarters that of adults when treated with a similar weight-adjusted dose. As weight increases, for patients 13 years of age and above, the weight-adjusted MHD clearance is expected to reach that of adults.

Pediatric Patients With Obesity

A population PK analysis of oxcarbazepine was conducted that included n = 92 obese and non-obese pediatric patients < 18 years of age to evaluate the potential impact of obesity on plasma oxcarbazepine exposures. Obesity was defined as BMI ≥ 95th percentile for age and sex based on CDC 2000 growth chart recommendations. Simulated results from this analysis suggested that the target maintenance doses for oxcarbazepine, applied in pediatric patients ≥ 2 years of age, produced equivalent steady-state exposure of MHD between pediatric patients with and without obesity. This finding is consistent when using total body weight, or when using fat-free mass in patients ≥ 3 years and total body weight in patients < 3 years in the simulations. Dosage adjustment according to obesity status is not necessary.

Gender

No gender-related pharmacokinetic differences have been observed in children, adults, or the elderly.

Race

No specific studies have been conducted to assess what effect, if any, race may have on the disposition of oxcarbazepine.

Renal Impairment

There is a linear correlation between creatinine clearance and the renal clearance of MHD. When oxcarbazepine tablets is administered as a single 300 mg dose in renally-impaired patients (creatinine clearance < 30 mL/min), the elimination half-life of MHD is prolonged to 19 hours, with a 2-fold increase in AUC *[see Dosage and Administration (2.7) and Use in Specific Populations (8.6)]*.

Hepatic Impairment

The pharmacokinetics and metabolism of oxcarbazepine and MHD were evaluated in healthy volunteers and hepatically-impaired subjects after a single 900-mg oral dose. Mild-to-moderate hepatic impairment did not affect the pharmacokinetics of oxcarbazepine and MHD *[see Dosage and Administration (2.8)]*.

Pregnancy

Due to physiological changes during pregnancy, MHD plasma levels may gradually decrease throughout pregnancy *[see Use in Specific Populations (8.1)]*.

Drug Interactions:

• *In Vitro*

Oxcarbazepine can inhibit CYP2C19 and induce CYP3A4/5 with potentially important effects on plasma concentrations of other drugs. In addition, several AEDs that are cytochrome P450 inducers can decrease plasma concentrations of oxcarbazepine and MHD. No autoinduction has been observed with oxcarbazepine tablets.

Oxcarbazepine was evaluated in human liver microsomes to determine its capacity to inhibit the major cytochrome P450 enzymes responsible for the metabolism of other drugs. Results demonstrate that oxcarbazepine and its pharmacologically active 10- monohydroxy metabolite (MHD) have little or no capacity to function as inhibitors for most of the human cytochrome P450 enzymes evaluated (CYP1A2, CYP2A6, CYP2C9, CYP2D6, CYP2E1, CYP4A9, and CYP4A11) with the exception of CYP2C19 and CYP3A4/5. Although inhibition of CYP3A4/5 by oxcarbazepine and MHD did occur at high concentrations, it is not likely to be of clinical significance. The inhibition of CYP2C19 by oxcarbazepine and MHD can cause increased plasma concentrations of drugs that are substrates of CYP2C19, which is clinically relevant.

In vitro, the UDP-glucuronyl transferase level was increased, indicating induction of this enzyme. Increases of 22% with MHD and 47% with oxcarbazepine were observed. As MHD, the predominant plasma substrate, is only a weak inducer of UDP-glucuronyl transferase, it is unlikely to have an effect on drugs that are mainly eliminated by conjugation through UDP-glucuronyl transferase (e.g., valproic acid, lamotrigine).

In addition, oxcarbazepine and MHD induce a subgroup of the cytochrome P450 3A family (CYP3A4 and CYP3A5) responsible for the metabolism of dihydropyridine calcium antagonists, oral contraceptives and cyclosporine resulting in a lower plasma concentration of these drugs.

As binding of MHD to plasma proteins is low (40%), clinically significant interactions with other drugs through competition for protein binding sites are unlikely.

• *In Vivo*

Other Antiepileptic Drugs

Potential interactions between oxcarbazepine tablets and other AEDs were assessed in clinical studies. The effect of these interactions on mean AUCs and C_{min} are summarized in Table 7 *[see Drug Interactions (7.1, 7.2)]*.

Table 7: Summary of Antiepileptic Drug Interactions With Oxcarbazepine tablets

AED coadministered	Dose of AED (mg/day)	Oxcarbazepine tablets dose (mg/day)	Influence of oxcarbazepine on AED concentration (mean change, 90% confidence interval)	Influence of AED on MHD concentration (mean change, 90% confidence interval)
Carbamazepine	400-2000	900	nc[1]	40% decrease [CI: 17% decrease, 57% decrease]
Phenobarbital	100-150	600-1800	14% increase [CI: 2% increase, 24% increase]	25% decrease [CI: 12% decrease, 51% decrease]
Phenytoin	250-500	600-1800 > 1200-2400	nc[1,2] up to 40% increase[3] [CI: 12%increase, 60% increase]	30% decrease [CI: 3% decrease, 48% decrease]
Valproic acid	400-2800	600-1800	nc[1]	18% decrease [CI: 13%decrease, 40% decrease]
Lamotrigine	200	1200	nc[1]	nc[1]

Abbreviations: AED, antiepileptic drugs; CI, confidence interval; MHD, 10-monohydroxy derivative.

[1]nc denotes a mean change of less than 10%.

[2]Pediatrics.

[3]Mean increase in adults at high oxcarbazepine tablets doses.

Hormonal Contraceptives

Coadministration of oxcarbazepine tablets with an oral contraceptive has been shown to influence the plasma concentrations of the two hormonal components: ethinylestradiol (EE) and levonorgestrel (LNG) *[see Drug Interactions (7.3)]*. The mean AUC values of EE were decreased by 48% [90% CI: 22 to 65] in one study and 52% [90% CI: 38 to 52] in another study. The mean AUC values of LNG were decreased by 32% [90% CI: 20 to 45] in one study and 52% [90% CI: 42 to 52] in another study.

Other Drug Interactions

Calcium Antagonists: After repeated coadministration of oxcarbazepine tablets, the AUC of felodipine was lowered by 28% [90% CI: 20 to 33]. Verapamil produced a decrease of 20% [90% CI: 18 to 27] of the plasma levels of MHD.

Cimetidine, erythromycin and dextropropoxyphene had no effect on the pharmacokinetics of MHD. Results with warfarin show no evidence of interaction with either single or repeated doses of oxcarbazepine tablets.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenesis

In 2-year carcinogenicity studies, oxcarbazepine was administered in the diet at doses of up to 100 mg/kg/day to mice and by gavage at doses of up to 250 mg/kg/day to rats, and the pharmacologically active 10-hydroxy metabolite (MHD) was administered orally at doses of up to 600 mg/kg/day to rats. In mice, a dose-related increase in the incidence of hepatocellular adenomas was observed at oxcarbazepine doses ≥ 70 mg/kg/day, which is less than the maximum recommended human dose (MRHD) on a mg/m^2 basis. In rats, the incidence of hepatocellular carcinomas was increased in females treated with oxcarbazepine at doses ≥ 25 mg/kg/day (less than the MRHD on a mg/m^2 basis), and incidences of hepatocellular adenomas and/or carcinomas were increased in males and females treated with MHD at doses of 600 mg/kg/day (2.4 times the MRHD on a mg/m^2 basis) and ≥ 250 mg/kg/day (equivalent to the MRHD on a mg/m^2 basis), respectively. There was an increase in the incidence of benign testicular interstitial cell tumors in rats at 250 mg oxcarbazepine/kg/day and at ≥ 250 mg MHD/kg/day, and an increase in the incidence of granular cell tumors in the cervix and vagina in rats at 600 mg MHD/kg/day.

Mutagenesis

Oxcarbazepine increased mutation frequencies in the *in vitro* Ames test in the absence of metabolic activation. Both oxcarbazepine and MHD produced increases in chromosomal aberrations and polyploidy in the Chinese hamster ovary assay *in vitro* in the absence of metabolic activation. MHD was negative in the Ames test, and no mutagenic or clastogenic activity was found with either oxcarbazepine or MHD in V79 Chinese hamster cells *in vitro*. Oxcarbazepine and MHD were both negative for clastogenic or aneugenic effects (micronucleus formation) in an in vivo rat bone marrow assay.

Impairment of Fertility

In a study in which male and female rats were administered oxcarbazepine (0, 25, 75, and 150 mg/kg/day) orally prior to and during mating and continuing in females during gestation, no adverse effects on fertility or reproductive performance were observed. The highest dose tested is less than the MRHD on a mg/m^2 basis. In a fertility study in which rats were administered MHD (0, 50, 150, or 450 mg/kg/day) orally prior to and during mating and early gestation, estrous cyclicity was disrupted and numbers of corpora lutea, implantations, and live embryos were reduced in females receiving the highest dose (approximately 2 times the MRHD on a mg/m^2 basis).

14 CLINICAL STUDIES

The effectiveness of oxcarbazepine tablets as adjunctive and monotherapy for partial-onset seizures in adults, and as adjunctive therapy in children aged 2 to 16 years was established in seven multicenter, randomized, controlled trials.

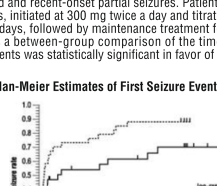
The effectiveness of oxcarbazepine tablets as monotherapy for partial-onset seizures in children aged 4 to 16 years was determined from data obtained in the studies described, as well as by pharmacokinetic/pharmacodynamic considerations.

14.1 Oxcarbazepine tablets Monotherapy Trials

Four randomized, controlled, double-blind, multicenter trials, conducted in a predominately adult population, demonstrated the efficacy of oxcarbazepine tablets as monotherapy. Two trials compared oxcarbazepine tablets to placebo and 2 trials used a randomized withdrawal design to compare a high dose (2400 mg) with a low dose (300 mg) of oxcarbazepine tablets, after substituting oxcarbazepine tablets 2400 mg/day for 1 or more AEDs. All doses were administered on a twice a day schedule. A fifth randomized, controlled, rater-blind, multicenter study, conducted in a pediatric population, failed to demonstrate a statistically significant difference between low- and high-dose oxcarbazepine tablets-treatment groups.

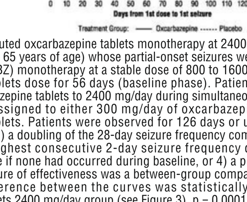
One placebo-controlled trial was conducted in 102 patients (11 to 62 years of age) with refractory partial-onset seizures who had completed an inpatient evaluation for epilepsy surgery. Patients had been withdrawn from all AEDs and were required to have 2 to 10 partial-onset seizures within 48 hours prior to randomization. Patients were randomized to receive either placebo or oxcarbazepine tablets given as 1500 mg/day on Day 1 and 2400 mg/day thereafter for an additional 9 days, or until 1 of the following 3 exit criteria occurred: 1) the occurrence of a fourth partial-onset seizure, excluding Day 1, 2) 2 new- onset secondarily generalized seizures, where such seizures were not seen in the 1-year period prior to randomization, or 3) occurrence of serial seizures or status epilepticus. The primary measure of effectiveness was a between-group comparison of the time to meet exit criteria. There was a statistically significant difference in favor of oxcarbazepine tablets (see Figure 1), p = 0.0001.

Figure 1: Kaplan-Meier Estimates of Exit Rate by Treatment Group



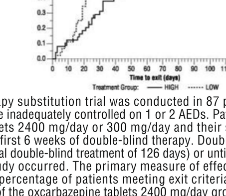
The second placebo-controlled trial was conducted in 67 untreated patients (8 to 69 years of age) with newly-diagnosed and recent-onset partial seizures. Patients were randomized to placebo or oxcarbazepine tablets, initiated at 300 mg twice a day and titrated to 1200 mg/day (given as 600 mg twice a day) in 6 days, followed by maintenance treatment for 84 days. The primary measure of effectiveness was a between-group comparison of the time to first seizure. The difference between the 2 treatments was statistically significant in favor of oxcarbazepine tablets (see Figure 2), p = 0.046.

Figure 2: Kaplan-Meier Estimates of First Seizure Event Rate by Treatment Group



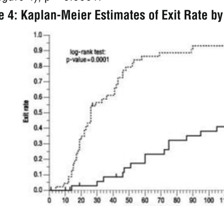
A third trial substituted oxcarbazepine tablets monotherapy at 2400 mg/day for carbamazepine in 143 patients (12 to 65 years of age) whose partial-onset seizures were inadequately controlled on carbamazepine (CBZ) monotherapy at a stable dose of 800 to 1600 mg/day, and maintained this oxcarbazepine tablets dose for 56 days (baseline phase). Patients who were able to tolerate titration of oxcarbazepine tablets to 2400 mg/day during simultaneous carbamazepine withdrawal were randomly assigned to either 300 mg/day of oxcarbazepine tablets or 2400 mg/day oxcarbazepine tablets. Patients were observed for 126 days or until 1 of the following 4 exit criteria occurred: 1) a doubling of the 28-day seizure frequency compared to baseline, 2) a 2-fold increase in the highest consecutive 2-day seizure frequency during baseline, 3) a single generalized seizure if none had occurred during baseline, or 4) a prolonged generalized seizure. The primary measure of effectiveness was a between-group comparison of the time to meet exit criteria. The difference between the curves was statistically significant in favor of the oxcarbazepine tablets 2400 mg/day group (see Figure 3), p = 0.0001.

Figure 3: Kaplan-Meier Estimates of Exit Rate by Treatment Group



Another monotherapy substitution trial was conducted in 87 patients (11 to 66 years of age) whose seizures were inadequately controlled on 1 or 2 AEDs. Patients were randomized to either oxcarbazepine tablets 2400 mg/day or 300 mg/day and their standard AED regimen(s) were eliminated over the first 6 weeks of double-blind therapy. Double-blind treatment continued for another 84 days (total double-blind treatment of 126 days) or until 1 of the 4 exit criteria described for the previous study occurred. The primary measure of effectiveness was a between-group comparison of the percentage of patients meeting exit criteria. The results were statistically significant in favor of the oxcarbazepine tablets 2400 mg/day group (14/34; 41.2%) compared to the oxcarbazepine tablets 300 mg/day group (42/45; 93.3%) (p< 0.0001). The time to meeting one of the exit criteria was also statistically significant in favor of the oxcarbazepine tablets 2400 mg/day group (see Figure 4), p = 0.0001.

Figure 4: Kaplan-Meier Estimates of Exit Rate by Treatment Group



A monotherapy trial was conducted in 92 pediatric patients (1 month to 16 years of age) with inadequately-controlled or new-onset partial seizures. Patients were hospitalized and randomized to either oxcarbazepine tablets 10 mg/kg/day or were titrated up to 40 to 60 mg/kg/day within 3 days while withdrawing the previous AED on the second day of oxcarbazepine tablets. Seizures were recorded through continuous video-EEG monitoring from Day 3 to Day 5. Patients either completed the 5-day treatment or met 1 of the 2 exit criteria: 1) three study-specific seizures (i.e., electrographic partial-onset seizures with a behavioral correlate), 2) a prolonged study-specific seizure. The primary measure of effectiveness was a between-group comparison of the time to meet exit criteria in which the difference between the curves was not statistically significant (p = 0.904). The majority of patients from both dose groups completed the 5-day study without exiting.

Although this study failed to demonstrate an effect of oxcarbazepine as monotherapy in pediatric patients, several design elements, including the short treatment and assessment period, the absence of a true placebo, and the likely persistence of plasma levels of previously administered AEDs during the treatment period, make the results uninterpretable. For this reason, the results do not undermine the conclusion, based on pharmacokinetic/pharmacodynamic considerations, that oxcarbazepine is effective as monotherapy in pediatric patients 4 years old and older.

14.2 Oxcarbazepine tablets Adjunctive Therapy Trials

The effectiveness of oxcarbazepine tablets as an adjunctive therapy for partial-onset seizures was established in 2 multicenter, randomized, double-blind, placebo-controlled trials, one in 692 patients (15 to 66 years of age) and one in 264 pediatric patients (3 to 17 years of age), and in one multicenter, rater-blind, randomized, age-stratified, parallel-group study comparing 2 doses of oxcarbazepine in 128 pediatric patients (1 month to < 4 years of age).

Patients in the 2 placebo-controlled trials were on 1 to 3 concomitant AEDs. In both of the trials, patients were stabilized on optimum dosages of their concomitant AEDs during an 8-week baseline phase. Patients who experienced at least 8 (minimum of 1 to 4 per month) partial-onset seizures during the baseline phase were randomly assigned to placebo or to a specific dose of oxcarbazepine tablets in addition to their other AEDs.

In these studies, the dose was increased over a 2-week period until either the assigned dose was reached, or intolerance prevented increases. Patients then entered a 14- (pediatrics) or 24-week (adults) maintenance period.

In the adult trial, patients received fixed doses of 600, 1200 or 2400 mg/day. In the pediatric trial, patients received maintenance doses in the range of 30 to 46 mg/kg/day, depending on baseline weight. The primary measure of effectiveness in both trials was a between-group comparison of the percentage change in partial-onset seizure frequency in the double-blind treatment phase relative to baseline phase. This comparison was statistically significant in favor of oxcarbazepine tablets at all doses tested in both trials (p = 0.0001 for all doses for both trials). The number of patients randomized to each dose, the median baseline seizure rate, and the median percentage seizure rate reduction for each trial are shown in Table 8. It is important to note that in the high-dose group in the study in adults, over 65% of patients discontinued treatment because of adverse events; only 46 (27%) of the patients in this group completed the 28-week study *[see Adverse Reactions (6)]*, an outcome not seen in the monotherapy studies.

Table 8: Summary of Percentage Change in Partial-Onset Seizure Frequency From Baseline for Placebo-Controlled Adjunctive Therapy Trials

Trial	Treatment group	N	Baseline median seizure rate*	Median % reduction
1(pediatrics)	Oxcarbazepine	136	12.5	34.8[†]
	Placebo	128	13.1	9.4
2 (adults)	Oxcarbazepine 2400 mg/day	174	10.0	49.9[†]
	Oxcarbazepine 1200 mg/day	177	9.8	40.2[†]
	Oxcarbazepine 600 mg/day	168	9.6	26.4[†]
	Placebo	173	8.6	7.6

[†]p = 0.0001.

* = number of seizures per 28 days.

Subset analyses of the antiepileptic efficacy of oxcarbazepine tablets with regard to gender in these trials revealed no important differences in response between men and women. Because there were very few patients over the age of 65 years in controlled trials, the effect of the drug in the elderly has not been adequately assessed.

The third adjunctive therapy trial enrolled 128 pediatric patients (1 month to < 4 years of age) with inadequately-controlled partial-onset seizures on 1 to 2 concomitant AEDs. Patients who experienced at least 2 study-specific seizures (i.e., electrographic partial- onset seizures with a behavioral correlate) during the 72-hour baseline period were randomly assigned to either oxcarbazepine tablets 10 mg/kg/day or were titrated up to 60 mg/kg/day within 26 days. Patients were maintained on their randomized target dose for 9 days and seizures were recorded through continuous video-EEG monitoring during the last 72 hours of the maintenance period. The primary measure of effectiveness in this trial was a between-group comparison of the change in seizure frequency per 24 hours compared to the seizure frequency at baseline. For the entire group of patients enrolled, this comparison was statistically significant in favor of oxcarbazepine tablets 60 mg/kg/day. In this study, there was no evidence that oxcarbazepine tablets was effective in patients below the age of 2 years (N = 75).

16 HOW SUPPLIED/STORAGE AND HANDLING

Tablets

150 mg Film-Coated Tablets: Pale yellow to brownish light green, oval shaped, film coated tablets, scored (functionally scored) on both sides and debossed with "OX 150" on one side.

Bottle of 100 . . . . NDC-60290-067-01
Bottle of 500 . . . . NDC-60290-067-02

300 mg Film-Coated Tablets: Light yellow to yellow, oval shaped, film coated tablets, scored (functionally scored) on both sides and debossed with "OX 300" on one side.

Bottle of 100 . . . . NDC-60290-068-01
Bottle of 500 . . . . NDC-60290-068-02

600 mg Film-Coated Tablets: Light Pink to Pink, oval shaped, film coated tablets, scored (functionally scored) on both sides and debossed with "OX 600" on one side.

Bottle of 100 . . . . NDC-60290-069-01
Bottle of 500 . . . . NDC-60290-069-02

Store at 20°C to 25°C (68°F to 77°F), excursions permitted between 15°C and 30°C (59°F and 86°F) [see USP Controlled Room Temperature]. Dispense in tight container (USP).

17 PATIENT COUNSELING INFORMATION

Advise the patient to read the FDA-approved patient labeling (Medication Guide).

Administration Information

Counsel patients that oxcarbazepine tablets may be taken with or without food.

Hyponatremia

Advise patients that oxcarbazepine tablets may reduce the serum sodium concentrations especially if they are taking other medications that can lower sodium. Instruct patients to report symptoms of low sodium like nausea, tiredness, lack of energy, confusion, and more frequent or more severe seizures *[see Warnings and Precautions (5.1)]*.

Anaphylactic Reactions and Angioedema

Anaphylactic reactions and angioedema may occur during treatment with oxcarbazepine tablets. Advise patients to report immediately signs and symptoms suggesting angioedema (swelling of the face, eyes, lips, tongue, or difficulty in swallowing or breathing) and to stop taking the drug until they have consulted with their physician *[see Warnings and Precautions (5.2)]*.

Cross Hypersensitivity Reaction to Carbamazepine

Inform patients who have exhibited hypersensitivity reactions to carbamazepine that approximately 25% to 30% of these patients may experience hypersensitivity reactions with oxcarbazepine tablets. Patients should be advised that if they experience a hypersensitivity reaction while taking oxcarbazepine tablets they should consult with their physician immediately *[see Warnings and Precautions (5.3)]*.

Serious Dermatological Reactions

Advise patients that serious skin reactions have been reported in association with oxcarbazepine tablets. In the event a skin reaction should occur while taking oxcarbazepine tablets, patients should consult with their physician immediately *[see Warnings and Precautions (5.4)]*.

Suicidal Behavior and Ideation

Patients, their caregivers, and families should be counseled that AEDs, including oxcarbazepine tablets, may increase the risk of suicidal thoughts and behavior and should be advised of the need to be alert for the emergence or worsening of symptoms of depression, any unusual changes in mood or behavior, or the emergence of suicidal thoughts, behavior, or thoughts about self-harm. Behaviors of concern should be reported immediately to healthcare providers *[see Warnings and Precautions (5.5)]*.

Driving and Operating Machinery

Advise patients that oxcarbazepine tablets may cause adverse reactions, such as dizziness, somnolence, ataxia, visual disturbances, and depressed level of consciousness. Accordingly, advise patients not to drive or operate machinery until they have gained sufficient experience on oxcarbazepine tablets to gauge whether it adversely affects their ability to drive or operate machinery *[see Warnings and Precautions (5.7) and Adverse Reactions (6)]*.

Multi-Organ Hypersensitivity

Instruct patients that a fever associated with other organ system involvement (e.g., rash, lymphadenopathy, hepatic dysfunction) may be drug-related and should be reported to their healthcare provider immediately *[see Warnings and Precautions (5.8)]*.

Hematologic Events

Advise patients that there have been rare reports of blood disorders reported in patients treated with oxcarbazepine tablets. Instruct patients to immediately consult with their physician if they experience symptoms suggestive of blood disorders *[see Warnings and Precautions (5.9)]*.

Drug Interactions

Caution female patients of reproductive potential that the concurrent use of oxcarbazepine tablets with hormonal contraceptives may render this method of contraception less effective *[see Drug Interactions (7.2) and Use in Specific Populations (8.1)]*. Additional non- hormonal forms of contraception are recommended when using oxcarbazepine tablets.

Caution should be exercised if alcohol is taken in combination with oxcarbazepine tablets, due to a possible additive sedative effect.

Trademarks are property of their respective owners.

Manufactured by:
Umedica Laboratories Pvt. Ltd.
Vapi, Gujarat 396195, INDIA.

Distributed by:
Umedica Laboratories USA Inc.
Parsippany, NJ, 07054.

Product of India

Revised: 04/2026, V-00

MEDICATION GUIDE
Oxcarbazepine (ox" kar baz' e peen)
Tablets USP, for oral use

What is the most important information I should know about oxcarbazepine tablets?

Do not stop taking oxcarbazepine tablets without first talking to your healthcare provider. Stopping oxcarbazepine tablets suddenly can cause serious problems.

Oxcarbazepine tablets can cause serious side effects, including:

1. **Oxcarbazepine tablets may cause the level of sodium in your blood to be low** Symptoms of low blood sodium include:
   - nausea
   - tiredness (lack of energy)
   - headache
   - confusion
   - more frequent or more severe seizures

Similar symptoms that are not related to low sodium may occur from taking oxcarbazepine tablets. You should tell your healthcare provider if you have any of these side effects and if they bother you or they do not go away.

Some other medicines can also cause low sodium in your blood. Be sure to tell your healthcare provider about all the other medicines that you are taking.

Your healthcare provider may do blood tests to check your sodium levels during your treatment with oxcarbazepine tablets.

2. **Oxcarbazepine tablets may also cause allergic reactions or serious problems which may affect organs and other parts of your body like the liver or blood cells.** You may or may not have a rash with these types of reactions.

Call your healthcare provider right away if you have any of the following:
- swelling of your face, eyes, lips, or tongue
- trouble swallowing or breathing
- a skin rash
- hives
- fever, swollen glands, or sore throat that do not go away or come and go
- painful sores in the mouth or around your eyes
- yellowing of your skin or eyes
- unusual bruising or bleeding
- severe fatigue or weakness
- severe muscle pain
- frequent infections or infections that do not go away

Many people who are allergic to carbamazepine are also allergic to oxcarbazepine tablets. Tell your healthcare provider if you are allergic to carbamazepine.

3. **Like other antiepileptic drugs (AEDs), oxcarbazepine tablets may cause suicidal thoughts or actions in a very small number of people, about 1 in 500.**

Call a healthcare provider right away if you have any of these symptoms, especially if they are new, worse, or worry you:
- thoughts about suicide or dying
- attempts to commit suicide
- new or worse depression
- new or worse anxiety
- feeling agitated or restless
- panic attacks
- trouble sleeping (insomnia)
- new or worse irritability
- acting aggressive, being angry, or violent
- acting on dangerous impulses
- an extreme increase in activity and talking (mania)
- other unusual changes in behavior or mood

How can I watch for early symptoms of suicidal thoughts and actions?
- Pay attention to any changes, especially sudden changes, in mood, behaviors, thoughts, or feelings.
- Keep all follow-up visits with your healthcare provider as scheduled.

Call your healthcare provider between visits as needed, especially if you are worried about symptoms.

Do not stop taking oxcarbazepine tablets without first talking to a healthcare provider
- Stopping oxcarbazepine tablets suddenly can cause serious problems.
- Stopping a seizure medicine suddenly in a patient who has epilepsy may cause seizures that will not stop (status epilepticus).

Suicidal thoughts or actions may be caused by things other than medicines. If you have suicidal thoughts or actions, your healthcare provider may check for other causes.

What is oxcarbazepine tablets?

Oxcarbazepine tablets is a prescription medicine used:
- alone or with other medicines to treat partial-onset seizures in adults
- alone to treat partial-onset seizures in children 4 years of age and older
- with other medicines to treat partial-onset seizures in children 2 years of age and older

It is not known if oxcarbazepine tablets is safe and effective for use alone to treat partial-onset seizures in children less than 4 years of age **or** for use with other medicines to treat partial-onset seizures in children less than 2 years of age.

Do not take oxcarbazepine tablets if you are allergic to oxcarbazepine tablets or any of the other ingredients in oxcarbazepine tablets, or to eslicarbazepine acetate. See the end of this Medication Guide for a complete list of ingredients in oxcarbazepine tablets.

Many people who are allergic to carbamazepine are also allergic to oxcarbazepine tablets. Tell your healthcare provider if you are allergic to carbamazepine.

Before taking oxcarbazepine tablets, tell your healthcare provider about all your medical conditions, including if you:
- have or have had suicidal thoughts or actions, depression or mood problems
- have liver problems
- have kidney problems
- are allergic to carbamazepine. Many people who are allergic to carbamazepine are also allergic to oxcarbazepine tablets.
- use birth control medicine. Oxcarbazepine tablets may cause your birth control medicine to be less effective. Talk to your healthcare provider about the best birth control method to use.
- are pregnant or plan to become pregnant. It is not known if oxcarbazepine tablets may harm your unborn baby. Tell your healthcare provider right away if you become pregnant while taking oxcarbazepine tablets. You and your healthcare provider will decide if you should take oxcarbazepine tablets while you are pregnant.
- are breastfeeding or plan to breastfeed. Oxcarbazepine passes into breast milk. Talk with your healthcare provider about the best way to feed your baby if you take oxcarbazepine tablets.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements. Taking oxcarbazepine tablets with certain other medicines may cause side effects or affect how well they work. Do not start or stop other medicines without talking to your healthcare provider.

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 oxcarbazepine tablets?
- Do not stop taking oxcarbazepine tablets without talking to your healthcare provider. Stopping oxcarbazepine tablets suddenly can cause serious problems, including seizures that will not stop (status epilepticus).
- Take oxcarbazepine tablets exactly as prescribed. Your healthcare provider may change your dose. Your healthcare provider will tell you how much oxcarbazepine tablets to take.
- Take oxcarbazepine tablets 2 times a day.
- Take oxcarbazepine tablets with or without food.
- If you take too much oxcarbazepine tablets, call your healthcare provider right away.

What should I avoid while taking oxcarbazepine tablets?
- Do not drive or operate machinery until you know how oxcarbazepine tablets affects you. Oxcarbazepine tablets may slow your thinking and motor skills.
- Do not drink alcohol or take other drugs that make you sleepy or dizzy while taking oxcarbazepine tablets until you talk to your healthcare provider. Oxcarbazepine tablets taken with alcohol or drugs that cause sleepiness or dizziness may make your sleepiness or dizziness worse.

What are the possible side effects of oxcarbazepine tablets?

See "**What is the most important information I should know about oxcarbazepine tablets**?"

Oxcarbazepine tablets may cause other serious side effects, including:
- trouble concentrating
- problems with your speech and language
- feeling confused
- feeling sleepy and tired
- trouble with walking and coordination
- seizures that can happen more often or become worse, especially in children

Get medical help right away if you have any of the symptoms listed above or listed in "What is the most important information I should know about oxcarbazepine tablets?"

The most common side effects of oxcarbazepine tablets include:
- dizziness
- sleepiness
- double vision
- tiredness
- nausea
- vomiting
- problems with vision
- trembling
- problems with walking and coordination (unsteadiness)
- rash
- headache

These are not all the possible side effects of oxcarbazepine tablets. Tell your healthcare provider if you have any side effect that bothers you or that does not go away.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

How should I store oxcarbazepine tablets?
- Store oxcarbazepine film-coated tablets at room temperature 20°C to 25°C (68°F to 77°F), excursions permitted between 15°C and 30°C (59°F and 86°F). Keep oxcarbazepine film-coated tablets dry.

Keep oxcarbazepine tablets and all medicines out of the reach of children.

General Information about the safe and effective use of oxcarbazepine tablets.

Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. Do not use oxcarbazepine tablets for a condition for which it was not prescribed. Do not give oxcarbazepine tablets 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 oxcarbazepine tablets that is written for health professionals.

What are the ingredients in oxcarbazepine tablets?

Active ingredient: oxcarbazepine

Inactive ingredients: black iron oxide, colloidal silicon dioxide, crospovidone, hydroxypropyl methylcellulose, hypromellose, magnesium stearate, microcrystalline cellulose, polyethylene glycol, red iron oxide, talc, titanium dioxide, yellow iron oxide.

Manufactured by:
Umedica Laboratories Pvt. Ltd.
Vapi, Gujarat 396195, INDIA.

Distributed by:
Umedica Laboratories USA Inc.
Parsippany, NJ, 07054.

Product of India

For more information, go to https://www.umedicalabsusa.com/Oxcarbazepine.html

This Medication Guide has been approved by the U.S. Food and Drug Administration Revised:04/2026, V-00