FOR PARTIAL-ONSET SEIZURES

ALLIE'S GOAL IS TO BE CLEAR AND IN CONTROL.

Not actual patient.

Meet Allie

Age: 17

Occupation: High school senior

Diagnosis: Epilepsy with partial-onset seizures

Current Treatment: Oxtellar XR® (oxcarbazepine) 1200 mg/day

Challenges:

- Has had reliable partial-onset seizure control on Oxtellar XR since age 9
- Is going off to college across the country and will have a busy schedule as a pre-med student
- Her parents are hoping a once-daily formula will make it easy for her to remember her medication out of the home*

*Oxtellar XR has not been shown to improve adherence.

Does Allie sound similar to patients in your practice?

INDICATION

Oxtellar XR® is indicated for the treatment of partial-onset seizures in patients 6 years of age and older.

CONTRAINDICATIONS

Oxtellar XR is contraindicated in patients with a known hypersensitivity to oxcarbazepine, or to any of the components of Oxtellar XR, or to eslicarbazepine acetate. Reactions have included anaphylaxis and angioedema.

ONCE-DAILY
Oxtellar XR®
(oxcarbazepine) extended-release tablets
600 mg 300 mg 150 mg

Please refer to the Important Safety Information (page 2) and the full Prescribing Information for complete information on Oxtellar XR, or visit www.OxtellarXRhcp.com.

Oxtellar XR (oxcarbazepine) extended-release tablets for oral use

INDICATION

Oxtellar XR® is indicated for the treatment of partial-onset seizures in patients 6 years of age and older.

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

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WARNINGS & PRECAUTIONS

- Clinically significant hyponatremia (sodium <125 mmol/L) may develop during treatment. Measurement and laboratory tests of serum sodium concentrations should be considered for patients during maintenance treatment with Oxtellar XR, particularly if the patient is receiving other medications known to decrease serum sodium levels. Discontinuation of oxcarbazepine treatment may be clinically required.
- 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. Angioedema associated with laryngeal edema can be fatal. If a patient develops any of these reactions after treatment with Oxtellar XR, the drug should be discontinued and an alternative treatment started. Do not rechallenge these patients with Oxtellar XR.
- Approximately 25% to 30% of patients who have had hypersensitivity reactions to carbamazepine will experience hypersensitivity reactions with Oxtellar XR. Patients with a history of hypersensitivity reactions to carbamazepine should ordinarily be treated with Oxtellar XR only if the potential benefit justifies the potential risk. Discontinue Oxtellar XR immediately if signs or symptoms of hypersensitivity develop.
- Serious dermatological reactions, including Stevens-Johnson syndrome and toxic epidermal necrolysis, have been reported in association with oxcarbazepine use. Should a patient develop a skin reaction while using Oxtellar XR, consideration should be given to discontinuing its use. (Please see WARNINGS section of complete prescribing information.)
- Anyone considering prescribing Oxtellar XR must balance the risk of suicidal thoughts or behavior with the risk of untreated illness. Epilepsy and many other illnesses for which antiepileptic drugs 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 Oxtellar XR treatment, the prescriber needs to consider whether the emergence of these symptoms in any given patient may be related to the illness being treated.
- Withdrawal of Oxtellar XR should be done gradually to minimize the potential of increased seizure frequency and status epilepticus.
- Multi-organ hypersensitivity reactions have occurred in patients on oxcarbazepine therapy. Some of these cases resulted in hospitalization and some were life-threatening. Signs and symptoms of this disorder were diverse; however, patients typically, although not exclusively, presented with fever and rash associated with other organ system involvement disorders. If an alternative etiology cannot be established, discontinue Oxtellar XR.
- Rare reports of hematologic events such as pancytopenia, agranulocytosis, and leukopenia have been seen in patients treated with oxcarbazepine and discontinuation of therapy should be considered if any evidence of these hematologic events develop.
- Due to physiological changes during pregnancy, plasma concentrations of the active metabolite of oxcarbazepine may gradually decrease throughout pregnancy. An increase in seizure frequency may occur. Monitor patients carefully during pregnancy and through the postpartum period.
- Exacerbation of or new onset primary generalized seizures has been reported with immediate-release oxcarbazepine. The risk is seen especially in children, but may also occur in adults. Discontinue Oxtellar XR if it occurs.
- Data on a limited number of pregnancies from pregnancy registries suggest that oral clefts and ventricular septal defects are associated with oxcarbazepine monotherapy use.

DOSING CONSIDERATIONS

- Enzyme inducing antiepileptic drugs such as carbamazepine, phenobarbital, and phenytoin decrease the exposure to MHD, the active metabolite of Oxtellar XR. Dosage increases or discontinuation of enzyme inducers may be necessary.
- In adult patients with severe renal impairment, initiate Oxtellar XR at a lower starting dose and increase, if necessary, at a slower than usual rate until the desired clinical response is achieved.
- Use of Oxtellar XR with certain hormonal contraceptives may decrease hormone plasma levels and render these contraceptives less effective. Additional or alternative non-hormonal forms of contraception are recommended.

ADVERSE REACTIONS

The most commonly observed adverse reactions (≥ 5% and more frequent than placebo) seen in adults were (1200 mg, 2400 mg, v placebo): dizziness (20%, 41%, v 15%), somnolence (12%, 14%, v 9%), headache (8%, 15%, v 7%), balance disorder (5%, 7%, v 5%), tremor (5%, 1%, v 2%), vomiting (6%, 15%, v 9%), diplopia (10%, 13%, v 4%), asthenia (3%, 7%, v 1%), and fatigue (6%, 3%, v 1%). Adverse reactions in pediatric patients are similar to those seen in adults.

Please refer to the full Prescribing Information for complete information on Oxtellar XR, or visit www.OxtellarXRhcp.com.

Consider making Oxtellar XR® (oxcarbazepine) your sodium channel blocker of choice for patients like Allie.

Patient	Presentation	Diagnosis	Treatment	Appointment Notes	Treatment Decision
Allie, age 17; high school senior	Recurrent partial-onset seizures, currently managed with medication	Cryptogenic frontal lobe epilepsy with partial-onset seizures	Oxtellar XR started at initial presentation of partial-onset seizures at age 9; currently taking 1200 mg/day	Allie would like to continue to control her partial-onset seizures with a convenient treatment that works for her as she goes off to college	Allie's physician decides to continue Oxtellar XR as her treatment regimen

A monotherapy with the power to improve partial-onset seizure control in adolescent patients[1]

Improved partial-onset seizure control in patients previously taking 1 to 2 AED(s)[1]

Study Design

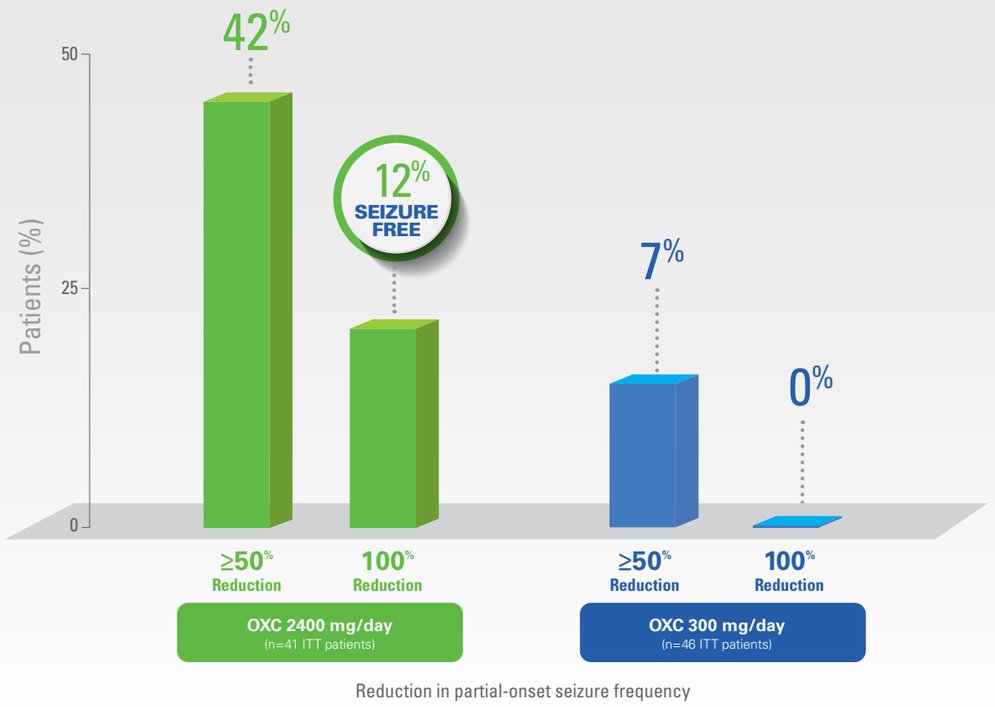
Multicenter, randomized, double-blind, dose-controlled, monotherapy substitution study evaluating the safety and efficacy of monotherapy with OXC 2400 mg/day vs. OXC 300 mg/day in 87 patients aged 11 to 66 years with medically refractory partial-onset epilepsy (41 ITT patients receiving OXC 2400 mg/day and 46 ITT patients receiving OXC 300 mg/day). The study included a 56-day baseline phase, followed by an 18-week double-blind treatment phase, which comprised a 14-day titration period and a 112-day maintenance period. Median numbers of partial-onset seizures per 28 days at baseline were 10.5 for the OXC 2400 mg/day group and 6.5 for the OXC 300 mg/day group.[1]

Study Results—Primary Endpoint

The percentage of patients meeting 1 of the exit criteria was significantly lower ($P<0.0001$) for the OXC 2400 mg/day treatment group 14/34 (41%) relative to the OXC 300 mg/day treatment group 42/45 (93%).[1]

Study Results—Responder Rate

Percentage of patients transitioned to OXC monotherapy who were previously taking 1 to 2 AED(s) and achieved ≥50% reduction in partial-onset seizures.[1]



Abbreviations: AED, antiepileptic drug; ITT, intent to treat; OXC, oxcarbazepine.

IMPORTANT SAFETY INFORMATION (CONT'D)

WARNINGS & PRECAUTIONS

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Allie wants a proven therapy with demonstrated tolerability

AEs occurring in ≥5% of patients receiving Oxtellar XR with concomitant AEDs and more frequent than with placebo[2-5]

	PHASE 3 TRIAL*			OLE†
	Oxtellar XR 2400 mg/day (n=123)	**Oxtellar XR 1200 mg/day** (n=122)	Placebo (n=121)	**Oxtellar XR 600 to 2400 mg/day** (n=214)
Dizziness	41%	**20%**	15%	**15%**
Somnolence	14%	**12%**	9%	**6%**
Nausea	12%	**12%**	12%	**8%**
Diplopia	13%	**10%**	4%	**9%**
Headache	15%	**8%**	7%	**11%**
Fatigue	3%	**6%**	1%	**0%**
Vomiting	15%	**6%**	9%	**6%**
Tremor	1%	**5%**	2%	**0%**
Balance disorder	7%	**5%**	5%	**5%**
Asthenia	7%	**3%**	1%	**0%**
Upper respiratory tract infection	0%	**0%**	0%	**5%**

For a complete listing of AEs greater than or equal to 2%, see full Prescribing Information.

Cognitive-related AEs in the Phase 3 study were similar to placebo[4]

COGNITIVE-RELATED AEs IN THE RANDOMIZED, CONTROLLED STUDY[4]

	Oxtellar XR 2400 mg/day (n=123)	**Oxtellar XR 1200 mg/day** (n=122)	Placebo (n=121)
Memory impairment	0.8%	**0%**	1.7%
Disturbance in attention	0.8%	**0%**	0.8%
Altered state of consciousness	0%	**0.8%**	0%
Dysphasia	0%	**0.8%**	0%
Amnesia	0%	**0%**	0.8%
Confusional state	0.8%	**0%**	0.8%
Disorientation	0.8%	**0%**	0.8%

For a complete listing of AEs ≥2%, see full Prescribing Information.

OLE Study Limitations

AED additions/withdrawals may influence partial-onset seizure control. Many patients entering OLEs have already demonstrated tolerability of study medication during double-blind treatment and, therefore, may be less likely to withdraw due to AEs. Patient retention may also be influenced by the intensive follow-up that occurs in a clinical study.[5]

Abbreviations: AEs, adverse events; AEDs, antiepileptic drugs; OLE, open-label extension.

*In a multinational, multicenter, double-blind, randomized, placebo-controlled, 3-arm, parallel-group, Phase 3 trial of 366 adult patients with epilepsy and uncontrolled partial-onset seizures with or without secondary generalization, taking a stable regimen of 1 to 3 concomitant AEDs experiencing an average of 6 partial-onset seizures per 28 days.[2-4]

†Oxtellar XR was studied in a blinded, open-label extension study with patients converted over 3 weeks to 12 months to once-daily Oxtellar XR 1200 mg/day. Subsequent dose adjustments were made as clinically indicated (increments/decrements, 300 mg/day to 600 mg/day; maximum dosage, 2400 mg/day).[5]

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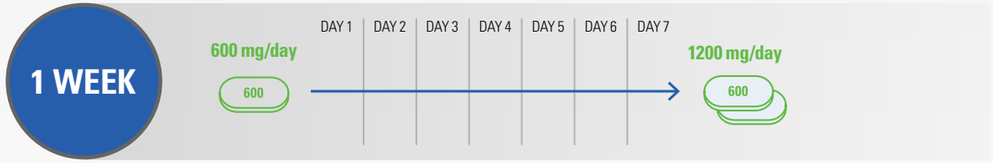
Oxtellar XR has a once-daily dosing regimen with a convenient titration schedule

1 WEEK to 1200 mg/day

once-daily maintenance dose in adults[2]

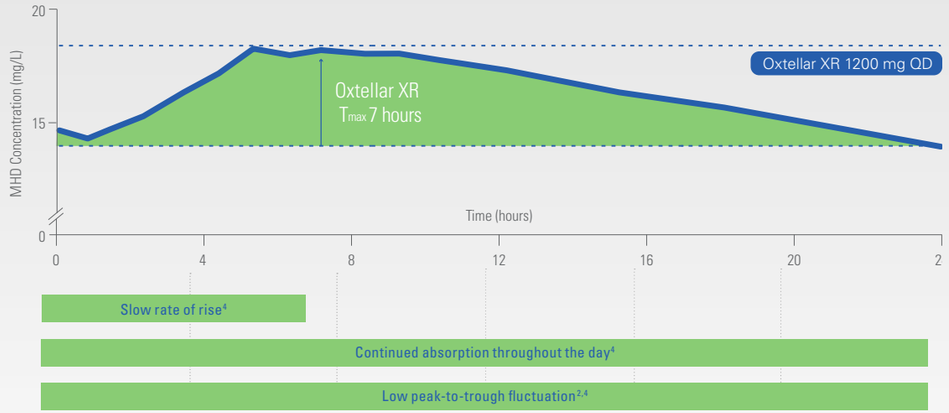


- Initiate treatment at a dosage of 600 mg/day given orally once daily for 1 week. Subsequent dosage increases can be made at weekly intervals in 600 mg/day increments[2]
- Maintain at 1200 mg/day to 2400 mg/day once daily[2]

Allie benefits from a steady 24-hour absorption with low fluctuation[2,4]

MHD plasma concentrations in healthy adults at steady state[2-4]

SINGLE-CENTER, MULTIPLE-DOSE, OPEN-LABEL, RANDOMIZED, 2-TREATMENT CROSSOVER STUDY[4]



Adapted from data on file, Supernus Pharmaceuticals, Inc.

Visit www.OxtellarXRhcp.com to learn more about the pharmacokinetic profile of Oxtellar XR.

Abbreviations: MHD, 10-monohydroxy derivative; QD, once-daily.

FOR PARTIAL-ONSET SEIZURES

HELP ALLIE **WITH HER GOAL** TO BE CLEAR AND **IN CONTROL.**

Consider Oxtellar XR for your patients like Allie.

Visit www.OxtellarXR.com/Allie to order samples and for additional information.

Not actual patient.

- Proven partial-onset seizure medication that provides controlled delivery over 24 hours[2-4]
- Once-daily dosing and a well-characterized safety profile with cognitive AEs similar to placebo[2-4]
- Co-pay savings program so eligible, commercially approved patients pay as little as $0 for their next 2 prescriptions[‡]

[‡]For full terms and conditions, please see the Oxtellar XR co-pay savings card, or visit www.OxtellarXR.com.

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References:

1. Beydoun A, Sachdeo RC, Rosenfeld WE, et al. Oxcarbazepine monotherapy for partial-onset seizures: a multicenter, double-blind, clinical trial. *Neurology.* 2000;54(12):2245-2251. **2.** Oxtellar XR. Package insert. Supernus Pharmaceuticals Inc. **3.** French JA, Baroldi P, Brittain ST, Johnson JK; PROSPER Investigators Study Group. Efficacy and safety of extended-release oxcarbazepine (Oxtellar XR™) as adjunctive therapy in patients with refractory partial-onset seizures: a randomized controlled trial. *Acta Neurol Scand.* 2014;129(3):143-153. **4.** Data on file. Supernus Pharmaceuticals Inc. **5.** Chung SS, Johnson JK, Brittain ST, Baroldi P. Long-term efficacy and safety of adjunctive extended-release oxcarbazepine (Oxtellar XR®) in adults with partial-onset seizures. *Acta Neurol Scand.* 2016;133(2):124-130.

Supernus® Pharmaceuticals