FOR PARTIAL-ONSET SEIZURES

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

Meet Elijah*

Age: 11

Diagnosis: Epilepsy with partial-onset seizures

Current Treatment: Carbamazepine 200 mg QID

Challenges:

- Initially started on carbamazepine BID, but continued to experience periodic breakthrough partial-onset seizures
- Is a middle school student whose parents are concerned about the frequency with which Elijah must take his medication
- His parents are also worried about the impact of his treatment during the school day

Does Elijah sound similar to patients in your practice?

*Not actual patient. Used for illustrative purposes.

Abbreviations: BID, twice a day; QID, 4 times a day.

ONCE-DAILY

Oxtellar XR®

(oxcarbazepine) extended-release tablets

600 mg 300 mg 150 mg

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.

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

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IMPORTANT SAFETY INFORMATION

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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.

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

Patient	Presentation	Diagnosis	Treatment	Appointment Notes	Treatment Decision
Elijah, age 11; middle school student	Recurrent partial-onset seizures after a swimming accident	Temporal lobe epilepsy with partial-onset seizures	Currently taking carbamazepine 200 mg QID • Parents are having difficulty with timing administration of 4 pills throughout the day	Elijah would like control of his partial-onset seizures with a simplified treatment regimen that works for him and his parents	Elijah's physician decides to transition him to Oxtellar XR

Powerful evidence in pediatric patients in a variety of treatment scenarios[1-13]

10 POSITIVE OXC TRIALS INCLUDED PEDIATRIC PATIENTS

Monotherapy Trials	
Comparative/new-onset partial-onset seizures[1-4]	4
Low-dose vs. high-dose therapy (refractory partial-onset seizures)[5,6]	2
Placebo-controlled trial (recent partial-onset seizures)[7]	1
Placebo-controlled trial (presurgical)[8]	1
Adjunctive Therapy Trials	
Placebo-controlled trials (refractory partial-onset seizures)[9,10]	2
Positive clinical trials	**10**

A monotherapy with the power to improve partial-onset seizure control in pediatric patients[3]

60% PEDIATRIC — Partial-onset seizure freedom*

Of the 97 pediatric patients, 24 discontinued OXC treatment prematurely.[3]

Pediatric trial of 193 children, aged 5 to 17 years; 97 OXC and 96 PHT. A predominant proportion (75%) of the patients had partial-onset seizures as their main seizure type.[3]

Oxtellar XR is the only AED that provides 24-hour, controlled delivery of OXC.[11-13]

*A multicenter, randomized, double-blind, parallel group trial evaluated the efficacy and safety of OXC as monotherapy compared to phenytoin (PHT) in 193 patients ages 5 to 17 with partial-onset seizures or GTCS. Doses of OXC ranged from 450 to 2400 mg/day. The primary efficacy variable was proportion of seizure-free patients who had at least 1 seizure assessment during the maintenance period; the primary tolerability variable was a comparison of patients who prematurely discontinued due to AEs. Oxtellar XR is not indicated for treatment of GTCS.[3]

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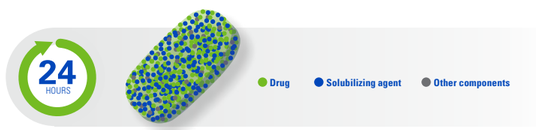
Patented delivery offers Elijah an even and controlled rate of absorption[11-13]

Solutrol® extended-release technology uses a unique matrix including drug and solubilizing agent to release oxcarbazepine evenly and in a controlled manner to provide delivery over 24 hours[11-13]



For illustration purposes only; does not represent Oxtellar XR or the actual time medicine is released.

Convenient titration and once-daily dosing help Elijah start and stay on Oxtellar XR[11]

Pediatric Patients (aged 6 to <17 years)[11]

- Initiate with 8 mg/kg to 10 mg/kg once per day. Titrate to target dose over 2 to 3 weeks. Increase in weekly increments of 8 mg/kg to 10 mg/kg once daily, not to exceed 600 mg, to achieve target daily dose

TARGET DAILY DOSE	WEIGHT
900 mg/day	20 to 29 kg
1200 mg/day	29.1 to 39 kg
1800 mg/day	Greater than 39 kg

Abbreviations: AEs, adverse events; AEDs, antiepileptic drugs; GTCS, generalized tonic-clonic seizures; ITT, intent to treat; OLE, open-label extension; OXC, oxcarbazepine.

References:

1. Christe W, Kramer G, Vigonius U, et al. A double-blind controlled clinical trial: oxcarbazepine versus sodium valproate in adults with newly diagnosed epilepsy. *Epilepsy Res.* 1997;26(3):451-460. **2.** Bill PA, Vigonius U, Pohlmann H, et al. A double-blind controlled clinical trial of oxcarbazepine versus phenytoin in adults with previously untreated epilepsy. *Epilepsy Res.* 1997;27(3):195-204. doi:10.1016/s0920-1211(97)00024-7 **3.** Guerreiro MM, Vigonius U, Pohlman H, et al. A double-blind controlled clinical trial of oxcarbazepine versus phenytoin in children and adolescents with epilepsy. *Epilepsy Res.* 1997;27(3):205-213. **4.** Dam M. Oxcarbazepine in monotherapy. *Behav Neurol.* 1990;3(1):31-34. **5.** 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. **6.** Sachdeo RC, Beydoun A, Schachter S, et al. Oxcarbazepine (Trileptal) as monotherapy in patients with partial seizures. *Neurology.* 2001;57(5):864-871. **7.** Sachdeo RC, Edwards K, Hasegawa H, et al. Safety and efficacy of oxcarbazepine 1200 mg/day in patients with recent-onset partial epilepsy. Abstract presented at: 51st Annual AAN Meeting; April 21, 1999. Los Angeles, CA. **8.** Schachter SC, Vazquez B, Fisher RS, et al. Oxcarbazepine—double-blind, randomized, placebo control, monotherapy trial for partial seizures. *Neurology.* 1999;52(4):732-737. **9.** Barcs G, Walker EB, Elger CE, et al. Oxcarbazepine placebo-controlled, dose ranging trial in refractory partial epilepsy. *Epilepsia.* 2000;41(12):1597-1607. **10.** Glauser TA, Nigro M, Sachdeo RC, et al. Adjunctive therapy with oxcarbazepine in children with partial seizures. *Neurology.* 2000;54(12):2237-2244. **11.** Oxtellar XR. Package insert. Supernus Pharmaceuticals Inc. **12.** Data on file. Supernus Pharmaceuticals Inc. **13.** 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. **14.** 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.* 2015;133(2):124-130.

Elijah 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[11-14]

	Phase 3 Trial*			OLE†
	Oxtellar XR 2400 mg/day (n=123)	**Oxtellar XR 1200 mg/day** (n=122)	Placebo (n=121)	**Oxtellar XR 600-2400 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 ≥2%, see full Prescribing Information.

In the phase 3 trial for Oxtellar XR, cognitive AEs were:

- **Similar to placebo[12]**
- **<1% for both 1200 and 2400 mg/day doses[12]**

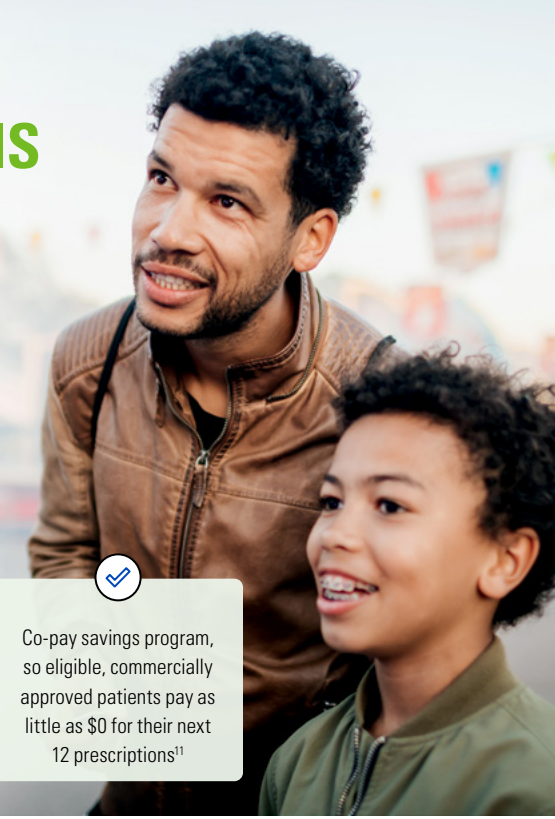
*Oxtellar XR was studied in a multinational, multicenter, double-blind, randomized, placebo-controlled, 3-arm, parallel-group, phase 3 trial of 366 adult patients with epilepsy and uncontrolled partial-onset seizures with or without secondary generalization, taking a stable regimen of 1 to 3 concomitant AEDs experiencing an average of 6 partial-onset seizures per 28 days.[11-13]

†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).[14]

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.[14]

HELP ELIJAH WITH HIS GOAL TO BE CLEAR AND IN CONTROL.



Not actual patients.
Used for illustrative purposes.

- Proven partial-onset seizure medication that provides controlled delivery over 24 hours[11-13]
- Once-daily dosing and a well-characterized safety profile[11-13] with cognitive AEs similar to placebo[12]
- Co-pay savings program, so eligible, commercially approved patients pay as little as $0 for their next 12 prescriptions[11]

Consider Oxtellar XR for your patients like Elijah.

Scan the QR code or see www.OxtellarXRhcp.com for samples and additional information

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Supernus® Pharmaceuticals