Levetiracetam [6]

PHARMACOLOGIC CATEGORY:

Anticonvulsant

DOSAGE FORMS AND STRENGTHS:

250 mg, 500 mg, 750 mg and 1000 mg film-coated, scored tablets

INDICATIONS AND USAGE:

Partial-Onset Seizures:
Eleppra is indicated for the treatment of partial-onset seizures in patients 1 month of age and older.
Myoclonic Seizures in Patients with Juvenile Myoclonic Epilepsy:
Eleppra is indicated as adjunctive therapy for the treatment of myoclonic seizures in patients 12 years of age and older with juvenile myoclonic epilepsy.
Primary Generalized Tonic-Clonic Seizures: Eleppra is indicated as adjunctive therapy for the treatment of primary generalized tonic-clonic seizures in patients 6 years of age and older with idiopathic generalized epilepsy.

METHOD OF ADMINISTRATION:

Adults 16 Years of Age and Older:
initiate with 500 mg twice daily; increase dosage every 2 weeks by 500 mg twice daily based on response and tolerability to the maximum recommended dose of 1500 mg twice daily.
Eleppra tablet dosing in pediatric patients:
Weight 20 to 40 kg: initiate treatment with dose of 250 mg twice daily. Increase the daily dose every 2 weeks by increments of 500 mg/day to a maximum recommended dose of 750 mg twice daily.
Weight more than 40 kg: initiate treatment with a dose of 500 mg twice daily. Increase the daily dose every 2 weeks by increments of 1000 mg/day to a maximum recommended dose of 1500 mg twice daily.

CONTRAINDICATIONS:

Hypersensitivity to the active substance or other pyrrolidone derivatives or to any of the excipients

SPECIAL WARNINGS AND PRECAUTIONS FOR USE:

Renal impairment:
May require dose adjustment. In patients with severely impaired hepatic function, assessment of renal function is recommended before dose selection.
Acute kidney injury:
The use of levetiracetam has been very rarely associated with acute kidney injury with a time to onset ranging from a few days to several months.
Blood cell counts:
Rare cases of decreased blood cell counts have been described in association with Levetiracetam administration, generally at the beginning of the treatment. Complete blood cell counts are advised in patients experiencing important weakness, pyrexia, recurrent infections or coagulation disorders.
Suicide:
suicide attempt, suicidal ideation and behavior have been reported in patients treated with anti-epileptic agents (including levetiracetam).

Abnormal and aggressive behaviour:
Levetiracetam may cause psychotic symptoms and behavioral abnormalities including irritability and aggressiveness. Patients treated with levetiracetam should be monitored for developing psychiatric signs suggesting important mood and/or personality changes.

Pediatric population:
Tablet formulation is not adapted for use in infants and children under the age of 6 years.

ADVERSE REACTIONS:

Most common adverse reactions include:
Adult patients: somnolence, asthenia, infection and dizziness, behavioral problems, weakness
Pediatric patients: fatigue, aggression, nasal congestion, decreased appetite, and irritability, increased blood pressure, behavioral problems, vomiting.

INTERACTIONS:

Methotrexate:
Concomitant administration of levetiracetam and methotrexate has been reported to decrease methotrexate clearance, resulting in increased/prolonged blood methotrexate concentration to potentially toxic levels.

Laxatives:
There have been isolated reports of decreased levetiracetam efficacy when the osmotic laxative has been concomitantly administered with oral levetiracetam.

Food:
The extent of absorption of levetiracetam was not altered by food, but the rate of absorption was slightly reduced.

PREGNANCY AND LACTATION:

Plasma levels of levetiracetam may be decreased and therefore need to be monitored closely during pregnancy. Based on animal data, may cause fetal harm. Levetiracetam can be used during pregnancy, if after careful assessment it is considered clinically needed. In such case, the lowest effective dose is recommended. Levetiracetam is excreted in human breast milk. Therefore, breast-feeding is not recommended. However, if levetiracetam treatment is needed during breastfeeding, the benefit/risk of the treatment should be weighed considering the importance of breast-feeding.

Ref:
1. Lyseng-Williamson KA. Levetiracetam. Drugs. 2011 Mar 1;71(4):489-514.
2. UCB Group of companies, KEPPRA (levetiracetam) [package insert]. U.S. Food and Drug Administration. https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/021035s102,021505s042lbl.pdf, Revised: 10/2019
3. Werhahn KJ, Klimpe S, Balkaya S, Trinka E, Krämer G. The safety and efficacy of add-on levetiracetam in elderly patients with focal epilepsy: a one-year observational study. Seizure. 2011 May 1;20(4):305-11.
4. Mäkinen J, Peltola J, Raitanen J, Alapirtti T, Rainesalo S. Comparative effectiveness of eight antiepileptic drugs in adults with focal refractory epilepsy: the influence of age, gender, and the sequence in which drugs were introduced onto the market. Journal of neurology. 2017 Jul 1;264(7):1345-53.
5. Helmstaedter C, Witt JA. Cognitive outcome of antiepileptic treatment with levetiracetam versus carbamazepine monotherapy: a non-interventional surveillance trial. Epilepsy & Behavior. 2010 May 1;18(1-2):74-80.
6. Levetiracetam: Drug information. In: UpToDate, Post TW (Ed), UpToDate, Waltham, MA. (Accessed on 2020.).

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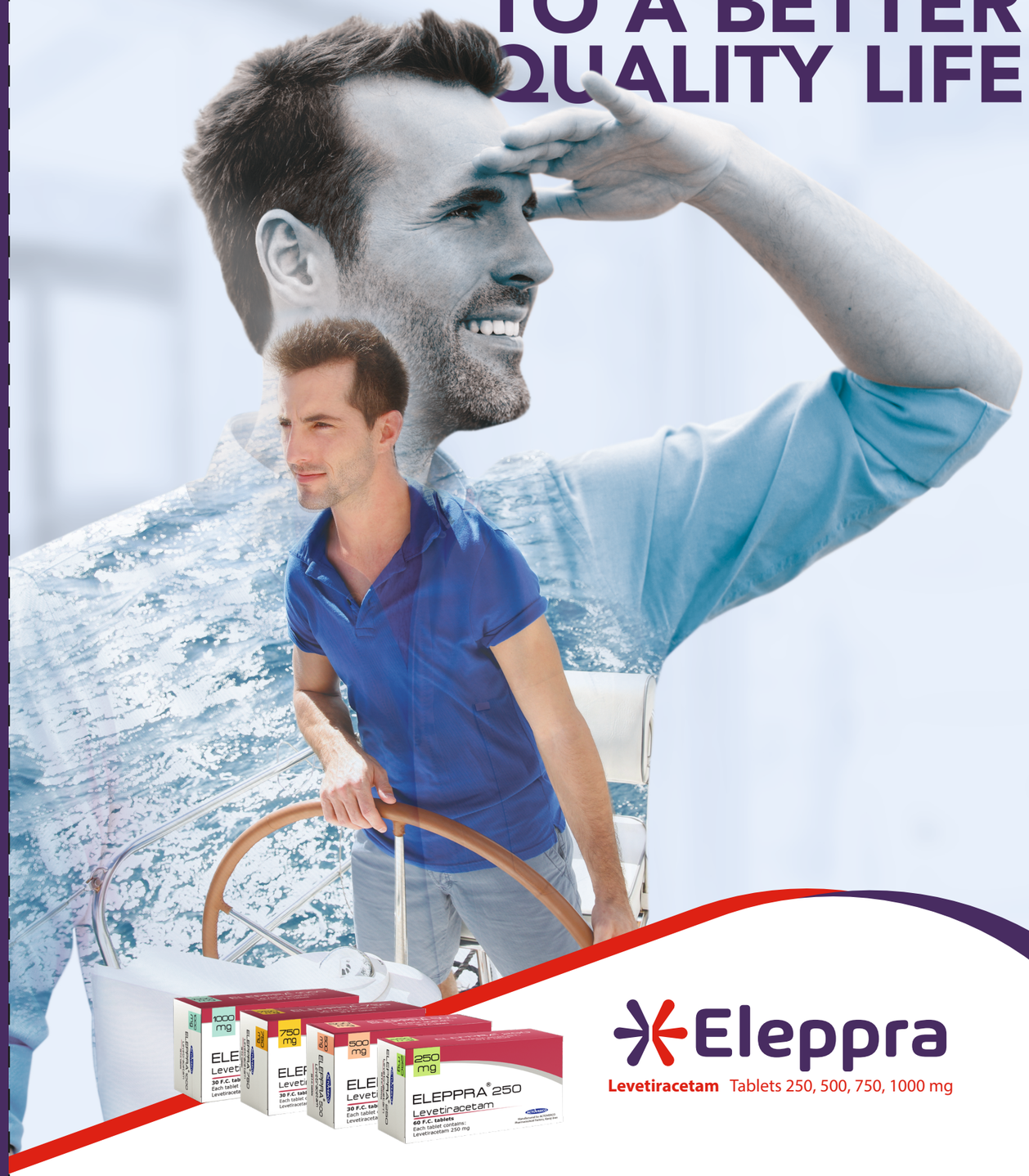

Eleppra

Levetiracetam Tablets 250, 500, 750, 1000 mg

Levetiracetam is an Antiepileptic Drug [1]

Unique mechanism of action:
Binding to a unique protein known as synaptic vesicle protein 2A (SV2A).

The pharmacokinetics of Levetiracetam are similar when used as monotherapy or as adjunctive therapy:

- Rapid and complete absorption
- High oral bioavailability (100%)
- Minimal metabolism
- Primarily renal elimination

Levetiracetam is not associated with clinically significant pharmacokinetic interactions with other drugs, including other AEDs.

- Very little hepatic metabolism by the cytochrome P450

Levetiracetam is a Broad-spectrum Antiepileptic [2]

Levetiracetam is indicated for the treatment of partial-onset seizures in patients 1 month of age and older

Levetiracetam is indicated for adjunctive therapy for the treatment of:

- Myoclonic seizures in patients 12 years of age and older with juvenile myoclonic epilepsy
- Primary generalized tonic-clonic seizures in patients 6 years of age and older with idiopathic generalized epilepsy

Eleppra
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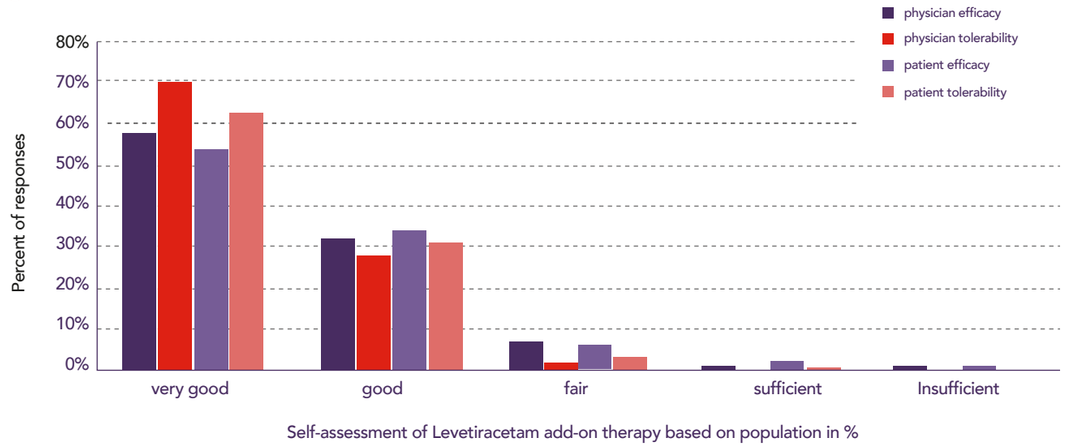
Levetiracetam is Proving to be Safe and Well-tolerated. [3, 4]

- Generally well tolerated
- Favorable adverse event profile
- Adverse events are not dose dependent
- Low discontinuation rate due to adverse events
- Patients more frequently rated their cognition and quality of life has improved with Levetiracetam than with Carbamazepine.[5]

At the 12 month follow-up visit, efficacy was rated as "good" or "very good" by 90.1% of physicians and 89.6% of patients



Self-assessment of Levetiracetam add-on therapy based on population in %

Retention rates for clobazam, gabapentin, lacosamide, lamotrigine, levetiracetam, pregabalin, topiramate, and zonisamide in patients with focal epilepsy by Kaplan-Meier analysis