



EUROPEAN MEDICINES AGENCY  
SCIENCE MEDICINES HEALTH

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Pharmacovigilance Risk Assessment Committee (PRAC)

## New product information wording – Extracts from PRAC recommendations on signals

Adopted at the 26-29 September 2016 PRAC

The product information wording in this document is extracted from the document entitled 'PRAC recommendations on signals' which contains the whole text of the PRAC recommendations for product information update, as well as some general guidance on the handling of signals. It can be found [here](#) (in English only).

New text to be added to the product information is underlined. Current text to be deleted is ~~struck through~~.

### 1. Levetiracetam(oral solution) – Medication errors associated with accidental overdose (EPITT no 10519)

#### Package leaflet

#### 3 – How to take Keppra

Always take this medicine exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure. Keppra must be taken twice a day, once in the morning and once in the evening, at about the same time each day. Take the oral solution following your doctor's instructions.

#### *Monotherapy*

#### **Dose in adults and adolescents from <del>16 years of age</del>:**

Measure the appropriate dosage using the 10 ml syringe included in the package for patients 4 years and above.

~~General dose: between 10 ml (1000 mg) and 30 ml (3,000 mg) each day, divided in 2 intakes per day. Keppra is taken twice daily, in two equally divided doses, each individual dose being measured between 5 ml (500mg) and 15 ml (1500mg).~~

When you will first start taking Keppra, your doctor will prescribe you a **lower dose** during 2 weeks before giving you the lowest general dose.

#### *Add-on therapy*

#### **Dose in adults and adolescents (12 to 17 years) weighing 50 kg or more:**

Measure the appropriate dosage using the 10 ml syringe included in the package for patients of 4 years and above.



General dose: between 10 ml (1,000 mg) and 30 ml (3,000 mg) each day, divided in 2 intakes per day.

Keppra is taken twice daily, in two equally divided doses, each individual dose being measured between 5 ml (500mg) and 15 ml (1500mg).

**Dose in children 6 months and older ~~weighing less than 50 Kg~~ Dose in infants (6 to 23 months), children (2 to 11 years) and adolescents (12 to 17 years) weighing less than 50 kg:**

Your doctor will prescribe the most appropriate pharmaceutical form of Keppra according to the age, weight and dose.

**For children 6 months to 4 years**, measure the appropriate dosage using the 3 ml syringe included in the package.

**For children above 4 years**, measure the appropriate dosage using the 10 ml syringe included in the package.

General dose: Keppra is taken twice daily, in two equally divided doses, each individual dose being measured between 0.1 ml (10mg) and 0.3 ml (30mg), per kg bodyweight of the child. (see table below for dose examples).

Your doctor will prescribe the most appropriate pharmaceutical form of Keppra according to the age, weight and dose.

General dose: between 0.2 ml (20 mg) and 0.6 ml (60 mg) per kg bodyweight each day, divided in 2 intakes per day.

The exact quantity of oral solution formulation should be delivered using the syringe provided in the cardboard box.

**Dose in children 6 months and older ~~weighing less than 50 kg~~:**

Weight	Starting dose: 0.1 ml/kg twice daily	Maximum dose: 0.3 ml/kg twice daily
6 kg	0.6 ml twice daily	1.8 ml twice daily
8 kg	0.8 ml twice daily	2.4 ml twice daily
10 kg	1 ml twice daily	3 ml twice daily
15 kg	1.5 ml twice daily	4.5 ml twice daily
20 kg	2 ml twice daily	6 ml twice daily
25 kg	2.5 ml twice daily	7.5 ml twice daily
From 50 kg	5 ml twice daily	15 ml twice daily

**Dose in infants (1 month to less than 6 months):**

**For infants 1 month to less than 6 months**, measure the appropriate dosage using the **1 ml** syringe included in the package.

General dose: Keppra is taken twice daily, in two equally divided doses, each individual dose being measured between 0.07 ml (7mg) and 0.21 ml (21mg), per kg bodyweight of the infant. (see table below for dose examples).

General dose: between 0.14 ml (14 mg) and 0.42 ml (42 mg) per kg bodyweight each day, divided in 2 intakes per day. The exact quantity of oral solution formulation should be delivered using the syringe provided in the cardboard box.

**Dose in infants (1 month to less than 6 months):**

Weight	Starting dose: 0.07 ml/kg twice daily	Maximum dose: 0.21 ml/kg twice daily
4 kg	0.3 ml twice daily	0.85 ml twice daily
5 kg	0.35 ml twice daily	1.05 ml twice daily
6 kg	0.45 ml twice daily	1.25 ml twice daily
7 kg	0.5 ml twice daily	1.5 ml twice daily

**Method of administration:**

After measuring the correct dose with an appropriate syringe, Keppra oral solution may be diluted in a glass of water or baby's bottle.

## 2. Metronidazole – Severe hepatic and neurologic toxicity in patients with Cockayne syndrome (EPITT no 18663)

### Summary of product characteristics (except for products for external use on the skin)

#### 4.4. Special warnings and precautions for use

Cases of severe hepatotoxicity/acute hepatic failure, including cases with a fatal outcome with very rapid onset after treatment initiation in patients with Cockayne syndrome have been reported with products containing metronidazole for systemic use. In this population, metronidazole should therefore be used after careful benefit-risk assessment and only if no alternative treatment is available. Liver function tests must be performed just prior to the start of therapy, throughout and after end of treatment until liver function is within normal ranges, or until the baseline values are reached. If the liver function tests become markedly elevated during treatment, the drug should be discontinued.

Patients with Cockayne syndrome should be advised to immediately report any symptoms of potential liver injury to their physician and stop taking metronidazole.

### Package leaflet (except for products for external use on the skin)

#### 2 – What you need to know before you use metronidazole

##### Warnings and precautions

Cases of severe liver toxicity/acute liver failure, including cases with a fatal outcome, in patients with Cockayne syndrome have been reported with product containing metronidazole.

If you are affected by Cockayne syndrome, your doctor should also monitor your liver function frequently while you are being treated with metronidazole and afterwards.

Tell your doctor immediately and stop taking metronidazole if you develop:

- Stomach pain, anorexia, nausea, vomiting, fever, malaise, fatigue, jaundice, dark urine, putty or mastic coloured stools or itching.