ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Kigabeq 100 mg soluble tablets
Kigabeq 500 mg soluble tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Kigabeq 100 mg soluble tablets

Each soluble tablet contains 100 mg vigabatrin.

Kigabeq 500 mg soluble tablets

Each soluble tablet contains 500 mg vigabatrin.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Soluble tablet

White oval tablets. The tablets are scored on one side and can be divided into equal doses.
- 500 mg tablet size: 16.0 mm x 9.0 mm
- 100 mg tablet size: 9.4 mm x 5.3 mm

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Kigabeq is indicated in infants and children from 1 month to less than 7 years of age for:
- Treatment in monotherapy of infantile spasms (West's syndrome).
- Treatment in combination with other antiepileptic medicinal products for patients with resistant partial epilepsy (focal onset seizures) with or without secondary generalisation, that is where all other appropriate medicinal product combinations have proved inadequate or have not been tolerated.

4.2 Posology and method of administration

Vigabatrin treatment may only be initiated by a specialist in epileptology, neurology or paediatric neurology. Follow-up should be arranged under supervision of a specialist in epileptology, neurology or paediatric neurology.

Posology

Monotherapy for infantile spasms (West's Syndrome)

The recommended starting dose is 50 mg/kg/day. Subsequent dosing can be titrated by 25 mg/kg/day increments every 3 days up to the maximum recommended dose of 150 mg/kg/day. Doses of vigabatrin should be given twice daily according to the table below.

Table 1: Number of soluble tablets according to body weight, starting dose and dose increment in infantile spasms

Body weight (kg)	Starting dose of 50 mg/kg/day	Proposed doses for first titration step (75 mg/kg/day) (Day 3)	Proposed doses for second titration step (100 mg/kg/day) (Day 6)
3	0.5 x 100 mg tablet morning 1 x 100 mg tablet evening	1 x 100 mg tablet morning 1.5 x 100 mg tablet evening	1.5 x 100 mg tablet morning 1.5 x 100 mg tablet evening
4	1 x 100 mg tablet morning 1 x 100 mg tablet evening	1.5 x 100 mg tablet morning 1.5 x 100 mg tablet evening	2 x 100 mg tablet morning 2 x 100 mg tablet evening
5	1 x 100 mg tablet morning 1.5 x 100 mg tablet evening	1.5 x 100 mg tablet morning 2 x 100 mg tablet evening	2.5 x 100 mg tablet morning 2.5 x 100 mg tablet evening
6	1.5 x 100 mg tablet morning 1.5 x 100 mg tablet evening	2 x 100 mg tablet morning 2.5 x 100 mg tablet evening	3 x 100 mg tablet morning 3 x 100 mg tablet evening
7	1.5 x 100 mg tablet morning 2 x100 mg tablet evening	2.5 x 100 mg tablet morning 2.5 x 100 mg tablet evening	3.5 x 100 mg tablet morning 3.5 x 100 mg tablet evening
8	2 x 100 mg tablet morning 2 x 100 mg tablet evening	3 x 100 mg tablet morning 3 x 100 mg tablet evening	4 x 100 mg tablet morning 4 x 100 mg tablet evening
9	2 x 100 mg tablet morning 2.5 x 100 mg tablet evening	3.5 x 100 mg tablet morning 3.5 x 100 mg tablet evening	4.5 x 100 mg tablet morning 4.5 x 100 mg tablet evening
10	0.5 x 500 mg tablet morning 0.5 x 500 mg tablet evening	0.5 x 500 mg tablet morning 1 x 500 mg tablet evening	1 x 500 mg tablet morning 1 x 500 mg tablet evening
11	2.5 x 100 mg tablet morning 3 x 100 mg tablet evening	4 x 100 mg tablet morning 4 x 100 mg tablet evening	1 x 500 mg tablet morning 1 x 500 mg and 1 x 100 mg tablet evening
12	3 x 100 mg tablet morning 3 x 100 mg tablet evening	4.5 x 100 mg tablet morning 4.5 x 100 mg tablet evening	1 x 500 mg and 1 x 100 mg tablet morning 1 x 500 mg and 1 x 100 mg tablet evening
13	3 x 100 mg tablet morning 3.5 x 100 mg tablet evening	4.5 x 100 mg tablet morning 1 x 500 mg tablet evening	1 x 500 mg and 1 x 100 mg tablet morning 1 x 500 mg and 2 x 100 mg tablet evening
14	3.5 x 100 mg tablet morning 3.5 x 100 mg tablet evening	1 x 500 mg tablet morning 1 x 500 mg tablet evening	1 x 500 mg and 2 x 100 mg tablet morning 1 x 500 mg and 2 x 100 mg tablet evening
15	0.5 x 500 mg tablet morning 1 x 500 mg tablet evening	1 x 500 mg tablet morning 1 x 500 mg and 1 x 100 mg tablet evening	1.5 x 500 mg tablet morning 1.5 x 500 mg tablet evening
16	4 x 100 mg tablet morning 4 x 100 mg tablet evening	1 x 500 mg and 1 x 100 mg tablet morning 1 x 500 mg and 1 x 100 mg tablet evening	1 x 500 mg and 3 x 100 mg tablet morning 1 x 500 mg and 3 x 100 mg tablet evening

Resistant partial epilepsy (focal onset seizures)

The recommended starting dose is 40 mg/kg/day.

Maintenance recommendations in relation to bodyweight are:
Bodyweight: 10 to 15 kg: 0.5 to 1 g/day
15 to 30 kg: 1 to 1.5 g/day

Doses of vigabatrin should be given twice daily according to the table below.

Table 2: Number of soluble tablets according to body weight and starting dose in resistant partial epilepsy

Body weight (kg)	Starting dose of 40 mg/kg/day
3	0.5 x 100 mg tablet morning 0.5 x 100 mg tablet evening
4	0.5 x 100 mg tablet morning 1 x 100 mg tablet evening
5	1 x 100 mg tablet morning 1 x 100 mg tablet evening
6	1 x 100 mg tablet morning 1.5 x 100 mg tablet evening
7	1.5 x 100 mg tablet morning 1.5 x 100 mg tablet evening
8	1.5 x 100 mg tablet morning 2 x 100 mg tablet evening
10	2 x 100 mg tablet morning 2 x 100 mg tablet evening
13	2.5 x 100 mg tablet morning 2.5 x 100 mg tablet evening
15	3 x 100 mg tablet morning 3 x 100 mg tablet evening
17	3.5 x 100 mg tablet morning 3.5 x 100 mg tablet evening
19	3.5 x 100 mg tablet morning 4 x 100 mg tablet evening
22	4.5 x 100 mg tablet morning 4.5 x 100 mg tablet evening
25	1 x 500 mg tablet morning 1 x 500 mg tablet evening
28	1 x 500 mg tablet morning 1 x 500 mg and 1 x 100 mg tablet evening
30	1 x 500 mg and 1 x 100 mg tablet morning 1 x 500 mg and 1 x 100 mg tablet evening

Kigabeq is for oral or gastric administration twice daily and may be taken before or after meals.

The maximum recommended dose should not be exceeded**.**

If control of epilepsy is not clinically significantly improved after an adequate treatment course, vigabatrin treatment should be discontinued. Vigabatrin should be gradually withdrawn under close medical supervision.

Special populations

Renal impairment
Since vigabatrin is eliminated via the kidneys, caution should be exercised when administering the medicinal product to patients with creatinine clearance less than 60 ml/min. Adjustment of dose should be considered. Such patients may respond to a lower maintenance dose. Patients should be monitored for adverse reactions such as sedation or confusion (see sections 4.4 and 4.8).

Hepatic impairment

Vigabatrin is not metabolised by hepatic enzymes, hence there is no need of adjustment of dose or frequency of administration. Interference of vigabatrin administration with serological testing of some hepatic enzymes including ALT has been evidenced (see section 4.4).

Paediatric population
There is no relevant use of Kigabeq in neonates (below 27 days of age) in the indication "infantile spasms" and in children and adolescents above 7 years of age in the indication "resistant partial epilepsy" (focal onset seizures). Other appropriate vigabatrin-containing medicinal products are already available for administration to this latter population.

Method of administration

Kigabeq is for oral or gastric use and may be taken before or after meals.
Gastric administration should be used for children who cannot swallow, but can be fed by enteral route.
The method of administration will be determined by a physician specialised in epileptology, neurology or paediatric neurology.

For instructions on dissolution and handling of the medicinal product before administration, see section 6.6.

Oral administration

Since no stability studies have been performed with other solvents than water, for preparing oral solution only water should be used. When the tablets are fully disintegrated, the whole content of solution should be administered straight away to the child directly from the drinking glass. If there is a risk of regurgitation or if the child is not old enough to drink from a glass, the whole content of solution should be withdrawn with a syringe for oral use, the end of the syringe should be put in the mouth of the child and gently pushed on the plunger.

Once the child has entirely drunk the medicine solution, the drinking glass should be rinsed with one or two teaspoons of water (approximately 5 or 10 ml) and dispensed to the child by the same way.

Gastric administration

For patients who cannot swallow, administration of Kigabeq using a gastric tube is possible.
Tablets are disintegrated in approximately 5 or 10 ml of water and the resulting solution is introduced into the tube using an adapted syringe. The gastric tube should be rinsed with 10 ml of water.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

Visual field defects (VFD) have been reported in patients receiving vigabatrin with a high prevalence (about 1/3 of patients). Frequencies found in an open clinical study are presented in section 4.8. The onset is usually after months to years of vigabatrin therapy. The degree of visual field constriction may be severe and this may have practical consequences for the patient. Vigabatrin can cause permanent vision loss.

Most of the patients with perimetry-confirmed defects have been asymptomatic. Hence, this undesirable effect can only be reliably detected by systematic perimetry which is usually possible only in patients with a developmental age of more than 9 years. For younger patients electroretinography should be used (see visual field defects).
Available data suggests that visual field defects are irreversible even after discontinuation of vigabatrin. A deterioration of VFD after the treatment is discontinued cannot be excluded.

Therefore, vigabatrin should only be used after careful benefit/ risk assessment compared with alternatives.

Vigabatrin is not recommended for use in patients with any pre-existing clinically significant visual field defect.

Patients should undergo systematic screening examination when starting vigabatrin and at regular intervals for detection of visual field defects. Visual field testing should continue at 6-month intervals for the whole duration of treatment. The assessment must be continued 6 to 12 months after the discontinuation of therapy (see visual field defects).

Visual field defects (VFD)

Based on available data, the usual pattern is a concentric constriction of the visual field of both eyes, which is generally more marked nasally than temporally. In the central visual field (within 30 degree of eccentricity), frequently an annular nasal defect is seen. However, the VFDs reported in patients receiving vigabatrin have ranged from mild to severe. Severe cases are potentially disabling and may be characterized by tunnel vision. Blindness was also reported in severe cases.

Most patients with perimetry-confirmed defects had not previously spontaneously noticed any symptoms, even in cases where a severe defect was observed in perimetry. Available evidence suggests that the VFD is irreversible even after discontinuation of vigabatrin. A deterioration of VFD after the treatment is discontinued cannot be excluded.
Pooled data from prevalence surveys suggest that as many as 1/3 of patients receiving vigabatrin therapy have VFDs. Males may be at greater risk than females. Frequencies found in an open clinical study are presented in section 4.8. A possible association between the risk of visual field defects and the extent of vigabatrin exposure, both in terms of daily dose (from 1 gram to more than 3 grams) and in terms of duration of treatment (maximum during the first three years) has been shown in this study.

All patients should have ophthalmological consultation before or shortly after the initiation of vigabatrin treatment.

Perimetry is seldom possible in children less than 9 years of developmental age. The risks of treatment must be very carefully weighed against possible benefit in children. Currently, there is no established method to diagnose or exclude visual field defects in children in whom a standardised perimetry cannot be performed. Frequency and severity have only been indirectly characterised in this population on the presence of electroretinogram or visual evoked potential anomalies.

Electroretinography is recommended in infants and children who are unable to cooperate with perimetry. Based on the available data the first oscillatory potential and 30 Hz flicker responses of the electroretinogram appear to be correlated with a vigabatrin associated VFD. These responses are delayed and reduced beyond the normal limits. Such changes have not been seen in vigabatrin treated patients without a VFD.

The parents and/or caregivers must be given a thorough description of the frequency and Implications of the development of VFD during vigabatrin treatment.
VFD may not be detected until it is severe and undetected moderate defects may affect child integrity. Therefore, vision assessment is required at baseline (no later than 4 weeks after starting treatment) and at least every 6 months while on therapy. The assessment must be continued 6 to 12 months after the discontinuation of therapy.

Available data suggests that visual field defects are irreversible.

If a visual field constriction is observed during follow-up, consideration should be given to gradual discontinuation of vigabatrin. If the decision to continue treatment is made, consideration should be

given to more frequent follow-up (perimetry) in order to detect progression or sight threatening defects.

Vigabatrin should not be used concomitantly with other retinotoxic medicinal products.

Neurologic and psychiatric conditions

In view of the results of the animal safety studies (see section 5.3) it is recommended that patients treated with vigabatrin are closely observed for adverse reactions on neurological function.

Rare reports of encephalopathic symptoms such as marked sedation, stupor and confusion in association with non-specific slow wave activity on electroencephalogram have been described soon after the initiation of vigabatrin treatment. Risk factors for the development of these reactions include higher than recommended starting dose, faster dose escalation at higher steps than recommended and renal failure. These events have been reversible following dose reduction or discontinuation of vigabatrin (see section 4.8).

Abnormal magnetic resonance imaging signals

Abnormal magnetic resonance imaging (MRI) signal changes characterised by increased T2 signal and restricted diffusion in a symmetric pattern involving the thalamus, basal ganglia, brain stem, and cerebellum have been observed in some infants treated with vigabatrin for infantile spasms. In a retrospective epidemiologic study in infants with infantile spasms (N = 205), the prevalence of these changes was 22 % in vigabatrin treated patients versus 4 % in patients treated with other therapies.

In the study above, in post-marketing experience, and in published literature reports, these changes generally resolved with discontinuation of treatment. In a few patients, the lesion resolved despite continued use.

Additionally, cases of intramyelinic oedema (IME) have been reported, particularly in infants treated for infantile spasms (see section 4.8 and 5.3). IME has been reported to be reversible following vigabatrin discontinuation, and it is therefore recommended to progressively discontinue vigabatrin when IME is observed.

Movement disorders including dystonia, dyskinesia and hypertonia, have been reported in patients treated with vigabatrin for infantile spasms. The benefit/risk ratio of vigabatrin should be evaluated on an individual patient basis. If new movement disorders occur during treatment with vigabatrin, consideration should be given to dose reduction or a gradual discontinuation of treatment.

Some patients may experience an increase in seizure frequency or the onset of new types of seizures with vigabatrin (see section 4.8). Patients with myoclonic seizures may be particularly susceptible to this effect. New onset myoclonus and exacerbation of existing myoclonus may occur in rare cases. These phenomena may also be the consequence of an overdose, a decrease in plasma concentrations of concomitant antiepileptic treatment, or a paradoxical effect.

Abrupt withdrawal may lead to rebound seizures. If a patient is to be withdrawn from vigabatrin treatment, it is recommended that this is done by gradual dose reduction over a 2- to 4-week period.

Vigabatrin should be used with caution in patients with a history of psychosis, depression or behavioural problems. Psychiatric events (e.g., agitation, depression, abnormal thinking, paranoid reactions) have been reported during vigabatrin treatment. These events occurred in patients with and without a psychiatric history and were usually reversible when vigabatrin doses were reduced or gradually discontinued.

Suicidal ideation and behaviour

Suicidal ideation and behaviour have been reported in patients treated with antiepileptic medicinal products in several indications. A meta-analysis of randomised placebo-controlled trials of antiepileptic medicinal products has also shown a small increased risk of suicidal ideation and behaviour. The mechanism of this effect is not known and the available data do not exclude the possibility of an increased risk for vigabatrin.

Therefore, patients should be monitored for signs of suicidal ideation and behaviour, and appropriate treatment should be considered. Patients (and caregivers of patients) should be advised to seek medical advice immediately should signs of suicidal ideation or behaviour emerge.

Renal impairment

Since vigabatrin is eliminated via the kidneys, caution should be exercised in patients with a creatinine clearance of less than 60 ml/min. These patients should be monitored closely for undesirable effects such as sedation and confusion (see section 4.2).

Interference with serological testing

Vigabatrin may lead to a decrease in measured plasma activity of alanine aminotransferase (ALT) and to a lesser extent, aspartate aminotransferase (AST). The magnitude of suppression for ALT has been reported to vary between 30 % and 100 %. Therefore, these liver tests may be quantitatively unreliable in patients taking vigabatrin (see section 4.8).

Vigabatrin may increase the amount of amino acids in the urine possibly leading to a false positive test for certain rare genetic metabolic disorders (e.g., alpha aminoadipic aciduria).

Risk of medication error

Because both tablet strengths (100 mg and 500 mg) can be used concomitantly there may be confusion between the tablets or tablet halves administered with a risk of incorrect dosing. Special attention should be paid to the tablet size to correctly identify the strength.

Excipients

This medicinal product contains less than 1 mmol sodium (23 mg) per tablet, that is to say essentially ‘sodium-free’.

4.5 Interaction with other medicinal products and other forms of interaction

Interaction studies have only been performed in adults.

As vigabatrin is neither metabolised, nor protein bound and is not an inducer of hepatic cytochrome P450 metabolising-enzymes, interactions with other medicinal products are unlikely. However, during controlled clinical studies, a gradual reduction of 16-33 % in the plasma concentration of phenytoin has been observed. The exact nature of this interaction is presently not understood, however, in the majority of cases it is unlikely to be of therapeutic significance.

The plasma concentrations of carbamazepine, phenobarbital, and sodium valproate have also been monitored during controlled clinical trials and no clinically significant interactions have been detected.

4.6 Fertility, pregnancy and lactation

Pregnancy

This medicinal product is not intended for use in women of child-bearing potential.

Breastfeeding

This medicinal product is not intended for use in women who are breastfeeding.

Fertility

Fertility studies in rats have shown no effect on male and female fertility (see section 5.3).

4.7 Effects on ability to drive and use machines

Kigabeq has major influence on the ability to perform hazardous activities.

In view of the fact that drowsiness has been observed in clinical trials with vigabatrin, patients should be warned of this possibility at the start of treatment.
Visual field defects which can significantly affect the ability to perform hazardous activities have been frequently reported in association with vigabatrin. Patients should be evaluated for the presence of visual field defects (see also section 4.4). Special care should be taken with infants, toddlers and children cycling, climbing or performing any other hazardous activity.

4.8 Undesirable effects

Summary of the safety profile

The most commonly reported adverse reactions related to vigabatrin are visual field defects (ranging from mild to severe and occurring usually after months to years of vigabatrin therapy), psychiatric disorders such as agitation, excitation, aggression, nervousness, depression, paranoid reaction, nervous system disorders such as marked sedation, stupor and confusion. Rarely seen events include suicide attempts, encephalopathy and retinal disorders.

Some patients may experience an increase in seizure frequency, including status epilepticus with vigabatrin. Patients with myoclonic seizures may be particularly susceptible to this effect. New onset myoclonus and exacerbation of existing myoclonus may occur in rare cases.

Tabulated list of adverse reactions

The adverse reactions listed below have been reported during pre- or post-approval use of vigabatrin worldwide. They are not specific to the paediatric population.

~~1~~The adverse reactions are listed below by SOC (System organ class) and by frequency, most frequent reactions first, with the following guidelines: very common (≥ 1/10), common (≥ 1/100 to < 1/10), uncommon (≥ 1/1 000 to < 1/100), rare (≥ 1/10 000 to < 1/1 000), very rare (< 1/10 000), not known (cannot be estimated from the available data).

System organ class	**Very common**	**Common**	**Uncommon**	**Rare**	**Very rare**	**Not known**
Blood and lymphatic system disorders		Anaemia				
Psychiatric disorders		Agitation, aggression, nervousness, depression, paranoid reaction, insomnia	Hypomania, mania, psychotic disorder	Suicide attempt	Hallucination	

Nervous system disorders	Somnolence	Speech disorder, headache, dizziness, paraesthesia, disturbance in attention and memory impairment, mental impairment (thought disturbance), tremor	Coordination abnormal (ataxia)	Encephalopathy	Optic neuritis	Brain MRI abnormalities, intramyelinic oedema (particularly in infants) (see sections 4.4 and 5.3), movement disorders, including dystonia, dyskinesia and hypertonia, either alone or in association with abnormalities in MRI
Eye disorders	Visual field defect	Vision blurred, diplopia, nystagmus		Retinal disorder (such as peripheral retinal atrophy)	Optic atrophy	Reduced visual acuity
Gastrointestinal disorders		Nausea, vomiting, abdominal pain				
Hepatobiliary disorders					Hepatitis	
Skin and subcutaneous tissue disorders		Alopecia	Rash	Angioedema, urticaria		
Musculoskeletal and connective tissue disorders	Arthralgia					
General disorders and administration site conditions	Fatigue	Oedema, irritability				
Investigations		Weight increased				

Description of selected adverse reactions

Visual field defects

Epidemiology of VFD in patients with refractory partial epilepsy was observed in an observational, open-label, multicentre, comparative, parallel group, Phase IV study, including 734 patients, at least 8 years old, with refractory partial epilepsy for at least one year.

Patients were split in three treatment groups: patients currently treated with vigabatrin (group I), patients previously exposed to vigabatrin (group II) and patients never exposed to vigabatrin (group III).

The following table presents the main findings at inclusion and the first and last conclusive evaluations in the evaluable population (n = 524):

	Children (from 8 to 12 years old)			Adolescents and adults (> 12 years old)		
	Group I [1]	Group II [2]	Group III	Group I [3]	Group II [4]	Group III
	N = 38	N = 47	N = 41	N = 150	N = 151	N = 97
Visual field defect with non-identified aetiology:						
- *Observed at inclusion*	1 (4.4 %)	3 (8.8 %)	2 (7.1 %)	31 (34.1 %)	20 (19.2 %)	1 (1.4 %)
- *Observed at first conclusive evaluation*	4 (10.5 %)	6 (12.8 %)	2 (4.9 %)	59 (39.3 %)	39 (25.8 %)	4 (4.1 %)
- *Observed at last conclusive evaluation*	10 (26.3 %)	7 (14.9 %)	3 (7.3 %)	70 (46.7 %)	47 (31.1 %)	5 (5.2 %)

[1] Median treatment duration: 44.4 months, mean daily dose 1.48 g
[2] Median treatment duration: 20.6 months, mean daily dose 1.39 g
[3] Median treatment duration: 48.8 months, mean daily dose 2.10 g
[4] Median treatment duration: 23.0 months, mean daily dose 2.18 g

Psychiatric disorders

Psychiatric reactions have been reported during vigabatrin therapy. These reactions occurred in patients with and without a psychiatric history and were usually reversible when vigabatrin doses were reduced or gradually discontinued (see section 4.4). Depression was a common psychiatric reaction in clinical trials but seldom required discontinuation of vigabatrin.

Encephalopathy

Rare reports of encephalopathic symptoms such as marked sedation, stupor and confusion in association with non-specific slow wave activity on electroencephalogram have been described soon after the initiation of vigabatrin treatment. Such reactions have been fully reversible following dose reduction or discontinuation of vigabatrin (see section 4.4).

Investigations

Laboratory data indicate that vigabatrin treatment does not lead to renal toxicity. Decreases in ALT and AST, which are considered to be a result of inhibition of these aminotransferases by vigabatrin, have been observed. Chronic treatment with vigabatrin may be associated with a slight decrease in haemoglobin which rarely attains significance.

Abnormal MRI signals

Asymptomatic and transient MRI abnormalities in the brain have been observed in some infants treated with vigabatrin for infantile spasms. The clinical significance of these MRI abnormalities is unknown. As routine MRI surveillance of this paediatric population is not recommended, the frequency of MRI abnormalities cannot be reliably estimated from the available data. Movement disorders either alone or in association with abnormalities in MRI have been reported in patients treated with vigabatrin for infantile spasms but their frequency is not known.

Paediatric population

Psychiatric disorders

Very common: excitation, agitation

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system listed in Appendix V.

4.9 Overdose

Symptoms

Vigabatrin overdose has been reported. When provided, doses were most commonly between 7.5 to 30 g; however, ingestions up to 90 g have been reported. Nearly half of the cases involved multiple substance ingestions. When reported, the most common symptoms included drowsiness or coma. Other less frequently reported symptoms included vertigo, headache, psychosis, respiratory depression or apnoea, bradycardia, hypotension, agitation, irritability, confusion, abnormal behaviour, and speech disorder.

Management

There is no specific antidote. The usual supportive measures should be employed. Measures to remove unabsorbed medicinal product should be considered. Activated charcoal has been shown to not significantly adsorb vigabatrin in an *in vitro* study. The effectiveness of haemodialysis in the treatment of vigabatrin overdose is unknown. In isolated case reports in renal failure patients receiving therapeutic doses of vigabatrin, haemodialysis reduced vigabatrin plasma concentrations by 40 % to 60 %.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Antiepileptics, fatty acid derivatives, ATC code: N03AG04

Mechanism of action

Vigabatrin is a selective irreversible inhibitor of GABA transaminase, the enzyme responsible for the breakdown of GABA (gamma aminobutyric acid). Vigabatrin increases the concentration of GABA, the major inhibitory neurotransmitter in the brain.

Clinical efficacy and safety

Controlled and long-term clinical trials have shown that vigabatrin is an effective anticonvulsant agent when given as first line treatment in patients with infantile spasms and as add-on therapy in patients with epilepsy not controlled satisfactorily by conventional therapy. This efficacy is particularly marked in patients with seizures of partial origin.

5.2 Pharmacokinetic properties

Adults

Absorption

Vigabatrin is a water soluble compound and it is rapidly and completely absorbed from the gastrointestinal tract. Food administration does not alter the extent of vigabatrin absorption. Time to reach maximum plasma concentrations (t_{max}) is approximately 1 hour.

Distribution

Vigabatrin is widely distributed with an apparent volume of distribution slightly greater than total body water. Binding to plasma proteins is negligible. Plasma and cerebrospinal fluid concentrations are linearly related to dose over the recommended dose range.

Biotransformation

Vigabatrin is not significantly metabolised. No metabolites have been identified in plasma.

Elimination

Vigabatrin is eliminated via renal excretion with a terminal half-life of 5-8 hours. Oral clearance (Cl/F) of vigabatrin is approximately 7 L/h (i.e. 0.10 L/h/kg). Approximately 70 % of a single oral dose was recovered as unchanged vigabatrin in the urine in the first 24 hours post-dose.

Pharmacokinetic/pharmacodynamic relationship(s)

There is no direct correlation between plasma concentration and efficacy. The duration of the effect of the medicinal product is dependent on the GABA transaminase re-synthesis rate.

Paediatric population

Pharmacokinetic properties of vigabatrin have been investigated in groups of six neonates (age 15-26 days), six infants (age 5-22 months) and six children (age 4.6-14.2 years) with refractory epilepsy.

After administration of a single 37-50 mg/kg dose of an oral solution vigabatrin t_{max} was approximately 2.5 hours in neonates and infants, and 1 hour in children. Mean terminal half-life of vigabatrin was about 7.5 hours in neonates, 5.7 hours in infants and 5.5 hours in children. The mean Cl/F of active S-enantiomer of vigabatrin in infants and children was 0.591 L/h/kg and 0.446 L/h/kg respectively.

5.3 Preclinical safety data

Animal safety studies carried out in the rat, mouse, dog and monkey have indicated that vigabatrin has no significant adverse reactions on the liver, kidney, lung, heart or gastrointestinal tract.

In the brain, microvacuolation due to intramyelinic oedema has been observed in white matter tracts of rat, mouse and dog at doses of 30-50 mg/kg/day. In the monkey these lesions are minimal or

equivocal. In both rat and dog they were reversible on stopping vigabatrin treatment and even regressed with continued treatment.

Vigabatrin-associated retinotoxicity has been observed in 80-100 % of albino rats at the dose of 300 mg/kg/day orally, but not in pigmented rats, dogs or monkeys. The retinal changes in albino rats were characterised as focal or multifocal disorganisation of the outer nuclear layer while the other layers of retina were not affected.

Animal experiments have shown that vigabatrin has no negative influence on fertility or pup development. No teratogenicity was seen in rats in doses up to 150 mg/kg (3 times the human dose) or in rabbits in doses up to 100 mg/kg. However, in rabbits, a slight increase in the incidence of cleft palate at doses of 150-200 mg/kg was seen.

Studies with vigabatrin revealed no evidence of mutagenic or carcinogenic effects.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Crospovidone type B
Mannitol
Sodium stearyl fumarate

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

4 years
Use immediately following preparation of the oral solution.
After first opening: 100 days

6.4 Special precautions for storage

This medicinal product does not require any special storage conditions.

6.5 Nature and contents of container

Kigabeq 100 mg soluble tablets

High density polyethylene bottle closed with a child resistant tamper evident polypropylene screw cap.
Pack size: 100 soluble tablets.

Kigabeq 500 mg soluble tablets

High density polyethylene bottle closed with a child resistant tamper evident polypropylene screw cap.
Pack size: 50 soluble tablets.

6.6 Special precautions for disposal and other handling

Dissolution of soluble tablet

Fill a drinking glass with one or two teaspoons of water (approximately 5 or 10 ml), according to the age of the child. Add the prescribed number of Kigabeq tablets or tablet halves to the water. Wait until

the tablet(s) fully disintegrate; tablets generally disintegrate in less than one minute but disintegration can be fastened by gently hand stirring the oral solution.
The resulting solution is whitish and cloudy. This is normal and due to presence of water-insoluble excipients.

7. MARKETING AUTHORISATION HOLDER

ORPHELIA Pharma SAS
85 boulevard Saint-Michel
75005 PARIS
France

8. MARKETING AUTHORISATION NUMBER(S)

EU/1/18/1302/001
EU/1/18/1302/002

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 20 September 2018
Date of latest renewal: 04 July 2023

10. DATE OF REVISION OF THE TEXT

Detailed information on this medicinal product is available on the website of the European Medicines Agency http://www.ema.europa.eu.

ANNEX II

A. MANUFACTURER(S) RESPONSIBLE FOR BATCH RELEASE

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

A. MANUFACTURERS RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturers responsible for batch release

Farmea
10, rue Bouché Thomas
ZAC d'Orgemont
F-49000 Angers
France

Centre Spécialités Pharmaceutiques
76-78 avenue du Midi
63800 Cournon d'Auvergne
France

Biocodex
1 avenue Blaise Pascal
60000 Beauvais
France

The printed package leaflet of the medicinal product must state the name and address of the manufacturer responsible for the release of the concerned batch.

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

Medicinal product subject to restricted medical prescription (see Annex I: Summary of Product Characteristics, section 4.2).

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

- **Periodic safety update reports**

The requirements for submission of periodic safety update reports for this medicinal product are set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC and any subsequent updates published on the European medicines web-portal.

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

- **Risk Management Plan (RMP)**

The MAH shall perform the required pharmacovigilance activities and interventions detailed in the agreed RMP presented in Module 1.8.2 of the marketing authorisation and any agreed subsequent updates of the RMP.

An updated RMP should be submitted:

- At the request of the European Medicines Agency;

- Whenever the risk management system is modified, especially as the result of new information being received that may lead to a significant change to the benefit/risk profile or as the result of an important (pharmacovigilance or risk minimisation) milestone being reached.

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

CARTON CONTAINING 1 BOTTLE OF 100 SOLUBLE TABLETS OF KIGABEQ 100 MG

1. NAME OF THE MEDICINAL PRODUCT

Kigabeq 100 mg soluble tablets
vigabatrin
For children aged 1 month to less than 7 years

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each soluble tablet contains 100 mg vigabatrin.

3. LIST OF EXCIPIENTS

4. PHARMACEUTICAL FORM AND CONTENTS

Soluble tablets

100 soluble tablets

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
Oral and gastric use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

ORPHELIA Pharma SAS
85 boulevard Saint-Michel
75005 PARIS
France

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/18/1302/001

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Kigabeq 100 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGING

LABEL FOR BOTTLE CONTAINING 100 SOLUBLE TABLETS OF KIGABEQ 100 MG

1. NAME OF THE MEDICINAL PRODUCT

Kigabeq 100 mg soluble tablets
vigabatrin
For children aged 1 month to less than 7 years

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each soluble tablet contains 100 mg vigabatrin.

3. LIST OF EXCIPIENTS

4. PHARMACEUTICAL FORM AND CONTENTS

Soluble tablets

100 soluble tablets

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
Oral and gastric use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

ORPHELIA Pharma SAS

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/18/1302/001

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

17. UNIQUE IDENTIFIER – 2D BARCODE

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

CARTON CONTAINING 1 BOTTLE OF 50 SOLUBLE TABLETS OF KIGABEQ 500 MG

1. NAME OF THE MEDICINAL PRODUCT

Kigabeq 500 mg soluble tablets
vigabatrin
For children aged 1 month to less than 7 years

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each soluble tablet contains 500 mg vigabatrin.

3. LIST OF EXCIPIENTS

4. PHARMACEUTICAL FORM AND CONTENTS

Soluble tablets

50 soluble tablets

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
Oral and gastric use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

ORPHELIA Pharma SAS
85 boulevard Saint-Michel
75005 PARIS
France

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/18/1302/002

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Kigabeq 500 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON IMMEDIATE PACKAGING

LABEL FOR BOTTLE CONTAINING 50 SOLUBLE TABLETS OF KIGABEQ 500 MG

1. NAME OF THE MEDICINAL PRODUCT

Kigabeq 500 mg soluble tablets
vigabatrin
For children aged 1 month to less than 7 years

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each soluble tablet contains 500 mg vigabatrin.

3. LIST OF EXCIPIENTS

4. PHARMACEUTICAL FORM AND CONTENTS

Soluble tablets

50 soluble tablets

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
Oral and gastric use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

ORPHELIA Pharma SAS
85 boulevard Saint-Michel
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France

12. MARKETING AUTHORISATION NUMBER(S)

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13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

17. UNIQUE IDENTIFIER – 2D BARCODE

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

B. PACKAGE LEAFLET

Package leaflet: Information for the user

Kigabeq 100 mg soluble tablets
For children aged 1 month to less than 7 years

Kigabeq 500 mg soluble tablets
For children aged 1 month to less than 7 years

vigabatrin

Read all of this leaflet carefully before you give this medicine to your child because it contains important information.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your child's doctor or pharmacist.
- This medicine has been prescribed for your child. Do not pass it on to others. It may harm them, even if their signs of illness are the same as your child's.
- If your child gets any side effects, talk to your child's doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Kigabeq is and what it is used for

Kigabeq contains vigabatrin and it is used for treating infants and children aged from 1 month to less than 7 years. It is used to treat infantile spasms (West's syndrome) or, together with other epilepsy medicines to treat partial epilepsy that is not controlled well enough with current treatment.

2. What you need to know before your child takes Kigabeq

Do not give Kigabeq:
- if your child is allergic to vigabatrin or any of the other ingredients of this medicine (listed in section 6).

Warnings and precautions
Talk to your child's doctor before you give Kigabeq if your child:
- has or has had depression or any other psychiatric illness in the past
- has had any kidney problems as he/she could develop symptoms like sedation or confusion
- has had any eye problems.

Visual field loss (loss of sight from the edges of your child's field of vision) may occur during treatment with vigabatrin. You should discuss this possibility with the doctor before your child begins treatment and the doctor will tell you how to detect this side effect. This visual field loss may be severe and permanent, so it must be detected early to avoid progression. Worsening of visual field loss may continue after stopping treatment. It is important that you tell the doctor promptly if there is any

change in your child's vision. The doctor will check your child's visual field before your child starts taking vigabatrin and carry on checking it at regular intervals during the treatment.

If your child develops symptoms like sleepiness, reduced consciousness and movements (stupor) or confusion, tell your child's doctor who may reduce the dose or stop Kigabeq treatment.

A small number of people being treated with epilepsy medicines such as vigabatrin have had thoughts of harming or killing themselves. Look for symptoms suggestive of such thoughts: disturbed sleep, loss of appetite or weight, isolation, loss of interest for favorite activities.
If at any time your child has had these symptoms, immediately contact child's doctor.

Movement disorders can occur in young infants treated for infantile spasms (West's syndrome). If you see unusual movements in your child, tell your child's doctor who may change the treatment.

Tell your child's doctor if your child has had or is going to perform laboratory tests because this medicine may lead to abnormal results.

You must speak to your child's doctor if your child's condition does not improve within a month of starting vigabatrin.

Children
Do not give this medicine to children less than 1 month of age or more than 7 years of age.

Other medicines and Kigabeq
Tell your child's doctor if the child is taking, has recently taken or might take any other medicines. Kigabeq should not be used in combination with other medicines that may have side effects related to the eye.

Pregnancy and breast-feeding
This medicine is not intended for use in women of child-bearing potential or in breast-feeding women.

Driving and using machines
Your child should not ride a bicycle, climb or take part in hazardous activity if the child has symptoms like drowsiness or dizziness with Kigabeq. Visual disorders, which can affect the ability to cycle, climb or take part in hazardous activity, have occurred in some patients taking this medicine.

Kigabeq contains sodium
This medicine contains less than 1 mmol sodium (23 mg) per tablet, that is to say essentially 'sodium-free'.

3. How to give Kigabeq

Always give this medicine to your child exactly as the doctor has told you. Check with the doctor or pharmacist if you are not sure.

Dose
Never change the dose yourself. The doctor works out the dose individually for your child, taking account of the child's body weight.

Kigabeq is available as 100 mg or 500 mg tablets which can be given together to make up the right dose for your child. Always check the label and the size of the tablets to make sure you are giving the right dose.

In infantile spasms (West's Syndrome), the recommended starting dose is 50 milligrams per kilogram bodyweight daily. In resistant partial epilepsy (focal onset seizures), the recommended starting dose is

40 milligrams per kilogram daily. The doctor will adjust the dose during treatment as necessary. If your child has kidney problems, the doctor may prescribe a smaller dose.

The following table gives the number of Kigabeq tablets to give to your child according to the dose prescribed by your child's doctor.

Dose (mg per day)	**Number of tablets (strength) Morning**	**Number of tablets (strength) Evening**
150	Half a tablet (100 mg)	One tablet (100 mg)
200	One tablet (100 mg)	One tablet (100 mg)
250	One tablet (100 mg)	One and a half tablets (100 mg)
300	One and a half tablets (100 mg)	One and a half tablets (100 mg)
350	One and a half tablets (100 mg)	Two tablets (100 mg)
400	Two tablets (100 mg)	Two tablets (100 mg)
450	Two tablets (100 mg)	Two and a half tablets (100 mg)
500	Half a tablet (500 mg) or two and a half tablets (100 mg)	Half a tablet (500 mg) or two and a half tablets (100 mg)
550	Two and a half tablets (100 mg)	Three tablets (100 mg)
600	Three tablets (100 mg)	Three tablets (100 mg)
650	Three tablets (100 mg)	Three and a half tablets (100 mg)
700	Three and a half tablets (100 mg)	Three and a half tablets (100 mg)
750	Half a tablet (500 mg)	One tablet (500 mg)
800	Four tablets (100 mg)	Four tablets (100 mg)
850	Four tablets (100 mg)	Four and a half tablets (100 mg)
900	Four and a half tablets (100 mg)	Four and a half tablets (100 mg)
950	Four and a half tablets (100 mg)	One tablet (500 mg)
1 000	One tablet (500 mg)	One tablet (500 mg)
1 100	One tablet (500 mg)	One tablet (500 mg) and one tablet (100 mg)
1 200	One tablet (500 mg) and one tablet (100 mg)	One tablet (500 mg) and one tablet (100 mg)
1 300	One tablet (500 mg) and one tablet (100 mg)	One tablet (500 mg) and two tablets (100 mg)
1 400	One tablet (500 mg) and two tablets (100 mg)	One tablet (500 mg) and two tablets (100 mg)
1 500	One and a half tablets (500 mg)	One and a half tablets (500 mg)

How to give this medicine

Ask your child's doctor to show you how to give this medicine. Check with the doctor or pharmacist if you are not sure.

Kigabeq is to be given by mouth and may be taken before or after meals. The tablet can be cut into equal halves.

Use only water to prepare solution.

- Pour one or two teaspoonfuls (about 5 to 10 ml) of water into a drinking glass or beaker
- Add the right dose of Kigabeq tablets (as whole or half tablets) to the water
- Wait until the tablet has broken down completely. This takes less than a minute but you can speed it up by stirring the mixture gently by hand
- The mixture will be whitish and cloudy. This is normal and the cloudiness is because the tablet contains some excipients that do not dissolve completely
- Give the mixture straightway to your child direct from the drinking glass or beaker
- If your child cannot drink from the glass or beaker then you can use an oral syringe to gently squirt the mixture into your child's mouth, taking care not to cause choking: sit just in front and below your child in order that he/she has the head leaning forward and administer the mixture against his cheek

- Rinse the glass or beaker with one or two teaspoonfuls (about 5 to 10 ml) of water and give this to your child to make sure that the child receives all the medicine
- If the child cannot swallow, the mixture can be given through a gastric tube, using a suitable syringe. The tube should be rinsed with 10 ml of water

If your child takes too much Kigabeq
If your child accidentally takes too many Kigabeq tablets, tell the doctor immediately or go to your nearest hospital or poison information centre. Possible signs of overdose include drowsiness or reduced level of consciousness.

If you forget to give your child Kigabeq
If you forget to give your child a dose, give the dose as soon as you remember. If it is almost time for the next dose, just give one dose. Do not give a double dose to make up for a forgotten tablet.

If you stop giving Kigabeq to your child
Do not stop giving this medicine without talking to your child's doctor. If the doctor decides to stop the treatment you will be advised to gradually reduce the dose. Do not stop suddenly as this may cause your child's seizures to occur again.
If you have any further questions on the use of this medicine, ask the doctor or pharmacist.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.
Some patients may have more seizures (fits) whilst taking Kigabeq. If this happens, contact your child's doctor immediately.

Serious side effects
Get medical advice immediately if your child has the following:
Very common side effects (may affect more than 1 in 10 people)
- Visual field changes – About 33 out of 100 patients treated with vigabatrin may have changes in the visual field (narrow visual field). This visual field defect can range from mild to severe. It is usually detected after months or years of treatment with vigabatrin. The changes in the visual field may be permanent, so it is important to detect them early to avoid progression. If your child has visual disturbances, contact your child's doctor or hospital immediately.

Other side effects include:
Very common side effects (may affect more than 1 in 10 people)
- excitation or restlessness
- tiredness and pronounced sleepiness
- joint pain

Common side effects (may affect up to 1 in 10 people)
- headache
- weight gain
- shaking (tremor)
- swelling (oedema)
- dizziness
- sensation of numbness or tingling (pins and needles)
- reduced concentration and memory
- psychological problems including aggression, nervousness, irritability, depression, thought disturbance, feeling suspicious without reason (paranoia) and insomnia. These side effects usually stop when vigabatrin doses are reduced or the medicine is gradually discontinued. However, do not decrease the dose without first talking to your child's doctor. Contact the doctor if your child has these psychological effects
- nausea (feeling sick), vomiting and abdominal pain
- blurred vision, double vision and uncontrolled movement of the eye, which may cause dizziness

- speech disorder
- decrease in the number of red blood cells (anaemia)
- unusual hair loss or thinning (alopecia)

Uncommon side effects (may affect up to 1 in 100 people)
- lack of coordination or fumbling
- more severe psychological problems such as feeling elated or over-excited, which causes unusual behaviour, and feeling detached from reality
- skin rash

Rare side effects (may affect up to 1 in 1 000 people)
- serious allergic reaction, which causes swelling of the face or throat. If your child has these symptoms, you should tell his/her doctor immediately
- hives or nettle rash
- marked sedation (sleepiness), stupor and confusion (encephalopathy). These side effects usually stop when doses are reduced or the medicine is gradually discontinued. However, do not decrease the dose without first talking to your child's doctor. Contact the doctor if your child has these effects
- suicide attempt
- other eye problems such as retinal disorder, causing, for example, poor vision at night and difficulty adjusting from bright to dim areas, sudden or unexplained loss of vision, sensitivity to light

Very rare side effects (may affect up to 1 in 10 000 people)
- other eye problems such as pain in eyes (optic neuritis) and loss of vision, including colour vision (optic atrophy)
- hallucinations (feeling, seeing or hearing things that are not there)
- liver problems

Not known (frequency cannot be estimated from the available data)
- movement disorders and abnormalities in magnetic resonance imaging (MRI) brain scans in young infants treated for infantile spasms
- swelling in the protective layer of nerve cells in part of the brain as observed in MRI pictures, particularly in infants
- decreased sharpness of vision

Reporting of side effects
If your child gets any side effects, talk to your child's doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects, you can help provide more information on the safety of this medicine.

5. How to store Kigabeq

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the carton and the bottle. The expiry date refers to the last day of that month. This medicine should be used within 100 days after first opening.

This medicinal product does not require any special storage conditions.

The solution should be administered immediately after preparation.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Kigabeq contains
- The active substance is vigabatrin.
- One soluble tablet of Kigabeq 100 mg contains 100 mg vigabatrin
- One soluble tablet of Kigabeq 500 mg contains 500 mg vigabatrin
- The other ingredients are: crospovidone type B, mannitol, sodium stearyl fumarate.

What Kigabeq looks like and contents of the pack
Kigabeq are white oval scored soluble tablets.

100 mg tablet size: 9.4 x 5.3 mm
500 mg tablet size: 16.0 x 9.0 mm

The solution in water is whitish and cloudy.

Pack sizes:
Kigabeq 100 mg is supplied in packs of 100 soluble tablets.
Kigabeq 500 mg is supplied in packs of 50 soluble tablets

Marketing Authorisation Holder
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75005 PARIS
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49000 Angers
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76-78 avenue du Midi
63800 Cournon d'Auvergne
France

Biocodex
1 avenue Blaise Pascal
60000 Beauvais
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For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder:

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This leaflet was last revised in

Other sources of information

Detailed information on this medicine is available on the European Medicines Agency web site: http://www.ema.europa.eu