1.3.1	Pregabalin
SPC, Labeling and Package Leaflet	Common

SUMMARY OF PRODUCT CHARACTERISTICS

1.3.1	Pregabalin
SPC, Labeling and Package Leaflet	Common

1. NAME OF THE MEDICINAL PRODUCT

<Invented name> 25 mg hard capsules
<Invented name> 50 mg hard capsules
<Invented name> 75 mg hard capsules
<Invented name> 100 mg hard capsules
<Invented name> 150 mg hard capsules
<Invented name> 200 mg hard capsules
<Invented name> 225 mg hard capsules
<Invented name> 300 mg hard capsules

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each hard capsule contains 25 mg, 50 mg, 75 mg, 100 mg, 150 mg, 200 mg, 225 mg or 300 mg pregabalin.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Capsule, hard (capsule)

25 mg hard capsules: The body of the capsule is white colour, the cap of the capsule is white colour. Capsule cap is imprinted with black mark P25. The content of the capsule is white to off white powder. Capsule length: 13.8 – 14.8 mm.
50 mg hard capsules: The body of the capsule is white colour, the cap of the capsule is bright yellow colour. Capsule cap is imprinted with black mark P50. The content of the capsule is white to off white powder. Capsule length: 15.3 – 16.2 mm.
75 mg hard capsules: The body of the capsule is brownish yellow colour, the cap of the capsule is brownish yellow colour. Capsule cap is imprinted with black mark P75. The content of the capsule is white to off white powder. Capsule length: 13.8 – 14.8 mm.
100 mg hard capsules: The body of the capsule is reddish brown colour, the cap of the capsule is reddish brown colour. Capsule cap is imprinted with white mark P100. The content of the capsule is white to off white powder. Capsule length: 15.3 – 16.2 mm.
150 mg hard capsules: The body of the capsule is white colour, the cap of the capsule is yellowish brown colour. Capsule cap is imprinted with black mark P150. The content of the capsule is white to off white powder. Capsule length: 17.2 – 18.3 mm.
200 mg hard capsules: The body of the capsule is brown colour, the cap of the capsule is brown colour. Capsule cap is imprinted with black mark P200. The content of the capsule is white to off white powder. Capsule length: 18.7 – 19.8 mm.
225 mg hard capsules: The body of the capsule is white colour, the cap of the capsule is brown colour. Capsule cap is imprinted with black mark P225. The content of the capsule is white to off white powder. Capsule length: 18.7 – 19.8 mm.
300 mg hard capsules: The body of the capsule is white colour, the cap of the capsule is dark brown colour. Capsule cap is imprinted with white mark P300. The content of the capsule is white to off white powder. Capsule length: 20.0 – 22.1 mm.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Neuropathic pain
<Invented name> is indicated for the treatment of peripheral and central neuropathic pain in adults.

Epilepsy
<Invented name> is indicated as adjunctive therapy in adults with partial seizures with or without secondary generalisation.

Generalised Anxiety Disorder
<Invented name> is indicated for the treatment of Generalised Anxiety Disorder (GAD) in adults.

4.2 Posology and method of administration

Posology
The dose range is 150 to 600 mg per day given in either two or three divided doses.

Neuropathic pain
Pregabalin treatment can be started at a dose of 150 mg per day given as two or three divided doses. Based on individual patient response and tolerability, the dose may be increased to 300 mg per day after an interval of 3 to 7 days, and if needed, to a maximum dose of 600 mg per day after an additional 7-day interval.

Epilepsy
Pregabalin treatment can be started with a dose of 150 mg per day given as two or three divided doses. Based on individual patient response and tolerability, the dose may be increased to 300 mg per day after 1 week. The maximum dose of 600 mg per day may be achieved after an additional week.

Generalised Anxiety Disorder
The dose range is 150 to 600 mg per day given as two or three divided doses. The need for treatment should be reassessed regularly. Pregabalin treatment can be started with a dose of 150 mg per day. Based on individual patient response and tolerability, the dose may be increased to 300 mg per day after 1 week. Following an additional week the dose may be increased to 450 mg per day. The maximum dose of 600 mg per day may be achieved after an additional week.

Discontinuation of pregabalin
In accordance with current clinical practice, if pregabalin has to be discontinued it is recommended this should be done gradually over a minimum of 1 week independent of the indication (see sections 4.4 and 4.8).

Renal impairment
Pregabalin is eliminated from the systemic circulation primarily by renal excretion as unchanged drug. As pregabalin clearance is directly proportional to creatinine clearance (see section 5.2), dose reduction in patients with compromised renal function must be individualised according to creatinine clearance (CLcr), as indicated in Table 1 determined using the following formula:

$$CL_{cr}(ml/min) = \left[\frac{1.23 \times [140 - age\ (years)] \times weight\ (kg)}{serum\ creatinine\ (\mu mol/l)} \right] (\times\ 0.85\ for\ female\ patients)$$

Pregabalin is removed effectively from plasma by haemodialysis (50% of drug in 4 hours). For patients receiving haemodialysis, the pregabalin daily dose should be adjusted based on renal function. In addition to the daily dose, a supplementary dose should be given immediately following every 4 hour haemodialysis treatment (see Table 1).

1.3.1	Pregabalin
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Table 1. Pregabalin dose adjustment based on renal function

Creatinine clearance (CLcr) (ml/min)	Total pregabalin daily dose *		Dose regimen
	Starting dose (mg/day)	Maximum dose (mg/day)	
≥ 60	150	600	BID or TID
≥30 - <60	75	300	BID or TID
≥15 - <30	25 – 50	150	Once daily or BID
<15	25	75	Once daily
Supplementary dosage following haemodialysis (mg)			
	25	100	Single dose+

TID = Three divided doses
BID = Two divided doses
* Total daily dose (mg/day) should be divided as indicated by dose regimen to provide mg/dose
+ Supplementary dose is a single additional dose

Hepatic impairment
No dose adjustment is required for patients with hepatic impairment (see section 5.2).

Paediatric population
The safety and efficacy of <Invented name> in children below the age of 12 years and in adolescents (12-17 years of age) have not been established. Currently available data are described in section 4.8, 5.1 and 5.2 but no recommendation on a posology can be made.

Elderly
Elderly may require a dose reduction of pregabalin due to a decreased renal function (see section 5.2).

Method of administration
<Invented name> may be taken with or without food.
<Invented name> is for oral use only.

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

Diabetic patients
In accordance with current clinical practice, some diabetic patients who gain weight on pregabalin treatment may need to adjust hypoglycaemic medicinal products.

Hypersensitivity reactions
There have been reports in the postmarketing experience of hypersensitivity reactions, including cases of angioedema. Pregabalin should be discontinued immediately if symptoms of angioedema, such as facial, perioral, or upper airway swelling occur.

Dizziness, somnolence, loss of consciousness, confusion, and mental impairment
Pregabalin treatment has been associated with dizziness and somnolence, which could increase the occurrence of accidental injury (fall) in elderly population. There have also been post-marketing reports of loss of consciousness, confusion and mental impairment. Therefore, patients should be advised to exercise caution until they are familiar with the potential effects of the medicinal product.

Vision-related effects
In controlled trials, a higher proportion of patients treated with pregabalin reported blurred vision than did patients treated with placebo which resolved in a majority of cases with continued dosing. In the clinical studies where ophthalmologic testing was conducted, the incidence of visual acuity reduction and visual field changes was greater in pregabalin-treated patients than in placebo-treated patients; the incidence of fundoscopic changes was greater in placebo-treated patients (see section 5.1).

In the post-marketing experience, visual adverse reactions have also been reported, including loss of vision, visual blurring or other changes of visual acuity, many of which were transient. Discontinuation of pregabalin may result in resolution or improvement of these visual symptoms.

Renal failure
Cases of renal failure have been reported and in some cases discontinuation of pregabalin did show reversibility of this adverse reaction.

Withdrawal of concomitant antiepileptic medicinal products
There are insufficient data for the withdrawal of concomitant antiepileptic medicinal products, once seizure control with pregabalin in the add-on situation has been reached, in order to reach monotherapy on pregabalin.

Withdrawal symptoms
After discontinuation of short-term and long-term treatment with pregabalin withdrawal symptoms have been observed in some patients. The following events have been mentioned: insomnia, headache, nausea, anxiety, diarrhoea, flu syndrome, nervousness, depression, pain, convulsion, hyperhidrosis and dizziness, suggestive of physical dependence. The patient should be informed about this at the start of the treatment.

Convulsions, including status epilepticus and grand mal convulsions, may occur during pregabalin use or shortly after discontinuing pregabalin.

Concerning discontinuation of long-term treatment of pregabalin, data suggest that the incidence and severity of withdrawal symptoms may be dose-related.

Congestive heart failure
There have been post-marketing reports of congestive heart failure in some patients receiving pregabalin. These reactions are mostly seen in elderly cardiovascular compromised patients during pregabalin treatment for a neuropathic indication. Pregabalin should be used with caution in these patients. Discontinuation of pregabalin may resolve the reaction.

Treatment of central neuropathic pain due to spinal cord injury
In the treatment of central neuropathic pain due to spinal cord injury the incidence of adverse reactions in general, central nervous system adverse reactions and especially somnolence was increased. This may be attributed to an additive effect due to concomitant medicinal products (e.g. anti-spasticity agents) needed for this condition. This should be considered when prescribing pregabalin in this condition.

Respiratory depression
There have been reports of severe respiratory depression in relation to pregabalin use. Patients with compromised respiratory function, respiratory or neurological disease, renal impairment, concomitant use of CNS depressants and the elderly may be at higher risk of experiencing this severe adverse reaction. Dose adjustments may be necessary in these patients (see section 4.2).

Suicidal ideation and behaviour
Suicidal ideation and behaviour have been reported in patients treated with anti-epileptic agents in several indications. A meta-analysis of randomised placebo controlled studies of anti-epileptic drugs has also shown a small increased risk of suicidal ideation and behaviour. The mechanism of this risk is not known and the available data do not exclude the possibility of an increased risk for pregabalin.

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

Reduced lower gastrointestinal tract function
There are post-marketing reports of events related to reduced lower gastrointestinal tract function (e.g., intestinal obstruction, paralytic ileus, constipation) when pregabalin was co-administered with medications that have the potential to produce constipation, such as opioid analgesics. When pregabalin and opioids will be used in combination, measures to prevent constipation may be considered (especially in female patients and elderly).

Concomitant use with opioids
Caution is advised when prescribing pregabalin concomitantly with opioids due to risk of CNS depression (see section 4.5). In a case-control study of opioid users, those patients who took pregabalin concomitantly with an opioid had an increased risk for opioid-related death compared to opioid use alone (adjusted odds ratio [aOR], 1.68 [95% CI, 1.19 – 2.36]). This increased risk was observed at low doses of pregabalin (≤ 300 mg, aOR 1.52 [95% CI, 1.04 – 2.22]) and there was a trend for a greater risk at high doses of pregabalin (> 300 mg, aOR 2.51 [95% CI 1.24 – 5.06]).

Misuse, abuse potential or dependence
Cases of misuse, abuse and dependence have been reported. Caution should be exercised in patients with a history of substance abuse and the patient should be monitored for symptoms of pregabalin misuse, abuse or dependence (development of tolerance, dose escalation, drug-seeking behaviour have been reported).

Encephalopathy
Cases of encephalopathy have been reported, mostly in patients with underlying conditions that may precipitate encephalopathy.

4.5 Interaction with other medicinal products and other forms of interaction

Since pregabalin is predominantly excreted unchanged in the urine, undergoes negligible metabolism in humans (<2% of a dose recovered in urine as metabolites), does not inhibit drug metabolism *in vitro*, and is not bound to plasma proteins, it is unlikely to produce, or be subject to, pharmacokinetic interactions.

In vivo studies and population pharmacokinetic analysis
Accordingly, in *in vivo* studies no clinically relevant pharmacokinetic interactions were observed between pregabalin and phenytoin, carbamazepine, valproic acid, lamotrigine, gabapentin, lorazepam, oxycodone or ethanol. Population pharmacokinetic analysis indicated that oral antidiabetics, diuretics, insulin, phenobarbital, tiagabine and topiramate had no clinically significant effect on pregabalin clearance.

Oral contraceptives, norethisterone and/or ethinyl oestradiol
Co-administration of pregabalin with the oral contraceptives norethisterone and/or ethinyl oestradiol does not influence the steady-state pharmacokinetics of either substance.

Central nervous system influencing medical products
Pregabalin may potentiate the effects of ethanol and lorazepam. In the postmarketing experience, there are reports of respiratory failure, coma and deaths in patients taking pregabalin and opioids and/or other central nervous system (CNS) depressant medicinal products. Pregabalin appears to be additive in the impairment of cognitive and gross motor function caused by oxycodone.

Interactions and the elderly
No specific pharmacodynamic interaction studies were conducted in elderly volunteers. Interaction studies have only been performed in adults.

4.6 Fertility, pregnancy and lactation

Women of childbearing potential/Contraception in males and females
As the potential risk for humans is unknown, effective contraception must be used in women of child bearing potential.

Pregnancy
There are no adequate data from the use of pregabalin in pregnant women.
Studies in animals have shown reproductive toxicity (see section 5.3). The potential risk for humans is unknown.

<Invented name> should not be used during pregnancy unless clearly necessary (if the benefit to the mother clearly outweighs the potential risk to the foetus).

Breast-feeding
Pregabalin is excreted into human milk (see section 5.2). The effect of pregabalin on newborns/infants is unknown. A decision must be made whether to discontinue breast feeding or to discontinue pregabalin therapy taking into account the benefit of breast- feeding for the child and the benefit of therapy for the woman.

Fertility
There are no clinical data on the effects of pregabalin on female fertility.

In a clinical trial to assess the effect of pregabalin on sperm motility, healthy male subjects were exposed to pregabalin at a dose of 600 mg/day. After 3 months of treatment, there were no effects on sperm motility.

A fertility study in female rats has shown adverse reproductive effects. Fertility studies in male rats have shown adverse reproductive and developmental effects. The clinical relevance of these findings is unknown (see section 5.3).

4.7 Effects on ability to drive and use machines

<Invented name> may have minor or moderate influence on the ability to drive and use machines.
<Invented name> may cause dizziness and somnolence and therefore may influence the ability to drive or use machines. Patients are advised not to drive, operate complex machinery or engage in other potentially hazardous activities until it is known whether this medicinal product affects their ability to perform these activities.

4.8 Undesirable effects

Summary of the safety profile
The pregabalin clinical programme involved over 8900 patients who were exposed to pregabalin, of

whom over 5600 were in double-blind placebo controlled trials. The most commonly reported adverse reactions were dizziness and somnolence. Adverse reactions were usually mild to moderate in intensity. In all controlled studies, the discontinuation rate due to adverse reactions was 12% for patients receiving pregabalin and 5% for patients receiving placebo. The most common adverse reactions resulting in discontinuation from pregabalin treatment groups were dizziness and somnolence.

Tabulated list of adverse reactions

In table 2 below all adverse reactions, which occurred at an incidence greater than placebo and in more than one patient, are listed by class and frequency (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). Within each frequency grouping, undesirable effects are presented in order of decreasing seriousness.

The adverse reactions listed may also be associated with the underlying disease and/or concomitant medicinal products.

In the treatment of central neuropathic pain due to spinal cord injury the incidence of adverse reactions in general, CNS adverse reactions and especially somnolence was increased (see section 4.4).

Additional reactions reported from post-marketing experience are included in italics in the list below.

Table 2. Pregabalin Adverse Drug Reactions

System organ class	Adverse drug reactions
Infections and infestations	
Common	Nasopharyngitis
Blood and lymphatic system disorders	
Uncommon	Neutropaenia
Immune system disorders	
Uncommon	*Hypersensitivity*
Rare	*Angioedema, allergic reaction*
Metabolism and nutrition disorders	
Common	Appetite increased
Uncommon	Anorexia, hypoglycaemia
Psychiatric disorders	
Common	Euphoric mood, confusion, irritability, disorientation, insomnia, libido decreased
Uncommon	Hallucination, panic attack, restlessness, agitation, depression, depressed mood, elevated mood, *aggression*, mood swings, depersonalisation, word finding difficulty, abnormal dreams, libido increased, anorgasmia, apathy
Rare	Disinhibition
Nervous system disorders	
Very common	Dizziness, somnolence, headache
Common	Ataxia, coordination abnormal, tremor, dysarthria, amnesia, memory impairment, disturbance in attention, paraesthesia, hypoaesthesia, sedation, balance disorder, lethargy
Uncommon	Syncope, stupor, myoclonus, *loss of consciousness*, psychomotor hyperactivity, dyskinesia, dizziness postural, intention tremor, nystagmus, cognitive disorder, *mental impairment*, speech disorder, hyporeflexia, hyperaesthesia, burning sensation, ageusia, *malaise*
Rare	*Convulsions*, parosmia, hypokinesia, dysgraphia
Eye disorders	

System organ class	Adverse drug reactions
Common	Vision blurred, diplopia
Uncommon	Peripheral vision loss, visual disturbance, eye swelling, visual field defect, visual acuity reduced, eye pain, asthenopia, photopsia, dry eye, lacrimation increased, eye irritation
Rare	*Vision loss, keratitis*, oscillopsia, altered visual depth perception, mydriasis, strabismus, visual brightness
Ear and labyrinth disorders	
Common	Vertigo
Uncommon	Hyperacusis
Cardiac disorders	
Uncommon	Tachycardia, atrioventricular block first degree, sinus bradycardia, *congestive heart failure*
Rare	*QT prolongation*, sinus tachycardia, sinus arrhythmia
Vascular disorders	
Uncommon	Hypotension, hypertension, hot flushes, flushing, peripheral coldness
Respiratory, thoracic and mediastinal disorders	
Uncommon	Dyspnoea, epistaxis, cough, nasal congestion, rhinitis, snoring, nasal dryness
Rare	*Pulmonary oedema*, throat tightness
Not known	Respiratory depression
Gastrointestinal disorders	
Common	Vomiting, *nausea*, constipation, *diarrhoea*, flatulence, abdominal distension, dry mouth
Uncommon	Gastrooesophageal reflux disease, salivary hypersecretion, hypoaesthesia oral
Rare	Ascites, pancreatitis, *swollen tongue*, dysphagia
Hepatobiliary disorders	
Uncommon	Elevated liver enzymes*
Rare	Jaundice
Very rare	Hepatic failure, hepatitis
Skin and subcutaneous tissue disorders	
Uncommon	Rash papular, urticaria, hyperhidrosis, *pruritus*
Rare	*Stevens Johnson syndrome*, cold sweat
Musculoskeletal and connective tissue disorders	
Common	Muscle cramp, arthralgia, back pain, pain in limb, cervical spasm
Uncommon	Joint swelling, myalgia, muscle twitching, neck pain, muscle stiffness
Rare	Rhabdomyolysis
Renal and urinary disorders	
Uncommon	Urinary incontinence, dysuria
Rare	Renal failure, oliguria, *urinary retention*
Reproductive system and breast disorders	
Common	Erectile dysfunction
Uncommon	Sexual dysfunction, ejaculation delayed, dysmenorrhoea, breast pain
Rare	Amenorrhoea, breast discharge, breast enlargement, *gynaecomastia*
General disorders and administration site conditions	
Common	Oedema peripheral, oedema, gait abnormal, fall, feeling drunk, feeling abnormal, fatigue
Uncommon	Generalised oedema, *face oedema*, chest tightness, pain, pyrexia, thirst, chills, asthenia
Investigations	
Common	Weight increased
Uncommon	Blood creatine phosphokinase increased, blood glucose increased, platelet

System organ class	Adverse drug reactions
	count decreased, blood creatinine increased, blood potassium decreased, weight decreased
Rare	White blood cell count decreased

*Alanine aminotransferase increased (ALT) and aspartate aminotransferase increased (AST)

After discontinuation of short-term and long-term treatment with pregabalin withdrawal symptoms have been observed in some patients. The following reactions have been mentioned: insomnia, headache, nausea, anxiety, diarrhoea, flu syndrome, convulsions, nervousness, depression, pain, hyperhidrosis and dizziness, suggestive of physical dependence. The patient should be informed about this at the start of the treatment. Concerning discontinuation of long-term treatment of pregabalin, data suggest that the incidence and severity of withdrawal symptoms may be dose-related.

Paediatric population
The pregabalin safety profile observed in five paediatric studies (in patients with partial seizures with or without secondary generalization (12-week efficacy and safety study in patients 4 to 16 years of age, n=295; 14-day efficacy and safety study in patients 1 month to younger than 4 years of age, n=175; pharmacokinetic and tolerability study, n=65; and two 1 year open label follow on safety studies, n=54 and n=431) was similar to that observed in the adult studies of patients with epilepsy. The most common adverse events observed in the 12-week study with pregabalin treatment were somnolence, pyrexia, upper respiratory tract infection, increased appetite, weight increased, and nasopharyngitis. The most common adverse events observed in the 14-day study with pregabalin treatment were somnolence, upper respiratory tract infection, and pyrexia (see sections 4.2, 5.1 and 5.2).

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
In the post-marketing experience, the most commonly reported adverse reactions observed when pregabalin was taken in overdose included somnolence, confusional state, agitation, and restlessness. Seizures were also reported.
In rare occasions, cases of coma have been reported.

Management
Treatment of pregabalin overdose should include general supportive measures and may include haemodialysis if necessary (see section 4.2 Table 1).

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Antiepileptics, other antiepileptics; ATC code: N03AX16.

The active substance, pregabalin, is a gamma-aminobutyric acid analogue [(S)-3-(aminomethyl)-5-methylhexanoic acid].

Mechanism of action

Pregabalin binds to an auxiliary subunit (α2-δ protein) of voltage-gated calcium channels in the central nervous system.

Clinical efficacy and safety

Neuropathic pain

Efficacy has been shown in trials in diabetic neuropathy, post herpetic neuralgia and spinal cord injury. Efficacy has not been studied in other models of neuropathic pain.

Pregabalin has been studied in 10 controlled clinical trials of up to 13 weeks with twice a day dosing (BID) and up to 8 weeks with three times a day (TID) dosing. Overall, the safety and efficacy profiles for BID and TID dosing regimens were similar.

In clinical trials up to 12 weeks for both peripheral and central neuropathic pain, a reduction in pain was seen by week 1 and was maintained throughout the treatment period.

In controlled clinical trials in peripheral neuropathic pain 35% of the pregabalin treated patients and 18% of the patients on placebo had a 50% improvement in pain score. For patients not experiencing somnolence, such an improvement was observed in 33% of patients treated with pregabalin and 18% of patients on placebo. For patients who experienced somnolence the responder rates were 48% on pregabalin and 16% on placebo.

In the controlled clinical trial in central neuropathic pain 22% of the Pregabalin treated patients and 7% of the patients on placebo had a 50% improvement in pain score.

Epilepsy

Adjunctive Treatment

Pregabalin has been studied in 3 controlled clinical trials of 12 week duration with either BID or TID dosing. Overall, the safety and efficacy profiles for BID and TID dosing regimens were similar.

A reduction in seizure frequency was observed by Week 1.

Paediatric population

The efficacy and safety of pregabalin as adjunctive treatment for epilepsy in paediatric patients below the age of 12 and adolescents has not been established. The adverse events observed in a pharmacokinetic and tolerability study that enrolled patients from 3 months to 16 years of age (n=65) with partial onset seizures were similar to those observed in adults. Results of a 12-week placebo-controlled study of 295 paediatric patients aged 4 to 16 years and a 14-day placebo-controlled study of 175 paediatric patients aged 1 month to younger than 4 years of age performed to evaluate the efficacy and safety of pregabalin as adjunctive therapy for the treatment of partial onset seizures and two 1 year open label safety studies in 54 and 431 paediatric patients respectively, from 3 months to 16 years of age with epilepsy indicate that the adverse events of pyrexia and upper respiratory infections were observed more frequently than in adult studies of patients with epilepsy (see sections 4.2, 4.8 and 5.2).

In the 12-week placebo-controlled study, paediatric patients (4 to 16 years of age) were assigned to pregabalin 2.5 mg/kg/day (maximum, 150 mg/day), pregabalin 10 mg/kg/day (maximum, 600 mg/day), or placebo. The percentage of subjects with at least a 50% reduction in partial onset seizures as compared to baseline was 40.6% of subjects treated with pregabalin 10 mg/kg/day (p=0.0068 versus placebo), 29.1% of subjects treated with pregabalin 2.5 mg/kg/day (p=0.2600 versus placebo) and 22.6% of those receiving placebo.

In the 14-day placebo-controlled study, paediatric patients (1 month to younger than 4 years of age) were assigned to pregabalin 7 mg/kg/day, pregabalin 14 mg/kg/day, or placebo. Median 24-hour

seizure frequencies at baseline and at the final visit were 4.7 and 3.8 for pregabalin 7 mg/kg/day, 5.4 and 1.4 for pregabalin 14 mg/kg/day, and 2.9 and 2.3 for placebo, respectively. Pregabalin 14 mg/kg/day significantly reduced the log-transformed partial onset seizure frequency versus placebo (p=0.0223); pregabalin 7 mg/kg/day did not show improvement relative to placebo.

Monotherapy (newly diagnosed patients)
Pregabalin has been studied in 1 controlled clinical trial of 56 week duration with BID dosing. Pregabalin did not achieve non-inferiority to lamotrigine based on the 6-month seizure freedom endpoint. Pregabalin and lamotrigine were similarly safe and well tolerated.

Generalised Anxiety Disorder
Pregabalin has been studied in 6 controlled trials of 4-6 week duration, an elderly study of 8 week duration and a long-term relapse prevention study with a double blind relapse prevention phase of 6 months duration.
Relief of the symptoms of GAD as reflected by the Hamilton Anxiety Rating Scale (HAM-A) was observed by Week 1.

In controlled clinical trials (4-8 week duration) 52% of the pregabalin treated patients and 38% of the patients on placebo had at least a 50% improvement in HAM-A total score from baseline to endpoint.

In controlled trials, a higher proportion of patients treated with pregabalin reported blurred vision than did patients treated with placebo which resolved in a majority of cases with continued dosing. Ophthalmologic testing (including visual acuity testing, formal visual field testing and dilated funduscopic examination) was conducted in over 3600 patients within controlled clinical trials. In these patients, visual acuity was reduced in 6.5% of patients treated with pregabalin, and 4.8% of placebo-treated patients. Visual field changes were detected in 12.4% of pregabalin-treated, and 11.7% of placebo-treated patients. Funduscopic changes were observed in 1.7% of pregabalin-treated and 2.1% of placebo-treated patients.

5.2 Pharmacokinetic properties

Pregabalin steady-state pharmacokinetics are similar in healthy volunteers, patients with epilepsy receiving anti-epileptic drugs and patients with chronic pain.

Absorption
Pregabalin is rapidly absorbed when administered in the fasted state, with peak plasma concentrations occurring within 1 hour following both single and multiple dose administration. Pregabalin oral bioavailability is estimated to be ≥90% and is independent of dose. Following repeated administration, steady state is achieved within 24 to 48 hours. The rate of pregabalin absorption is decreased when given with food resulting in a decrease in C_{max} by approximately 25-30% and a delay in t_{max} to approximately 2.5 hours. However, administration of pregabalin with food has no clinically significant effect on the extent of pregabalin absorption.

Distribution
In preclinical studies, pregabalin has been shown to cross the blood brain barrier in mice, rats, and monkeys. Pregabalin has been shown to cross the placenta in rats and is present in the milk of lactating rats. In humans, the apparent volume of distribution of pregabalin following oral administration is approximately 0.56 l/kg. Pregabalin is not bound to plasma proteins.

Biotransformation
Pregabalin undergoes negligible metabolism in humans. Following a dose of radiolabelled pregabalin, approximately 98% of the radioactivity recovered in the urine was unchanged pregabalin. The N-methylated derivative of pregabalin, the major metabolite of pregabalin found in urine, accounted

for 0.9% of the dose. In preclinical studies, there was no indication of racemisation of pregabalin S-enantiomer to the R-enantiomer.

Elimination
Pregabalin is eliminated from the systemic circulation primarily by renal excretion as unchanged drug. Pregabalin mean elimination half-life is 6.3 hours. Pregabalin plasma clearance and renal clearance are directly proportional to creatinine clearance (see section 5.2 Renal impairment). Dose adjustment in patients with reduced renal function or undergoing haemodialysis is necessary (see section 4.2 Table 1).

Linearity/non-linearity
Pregabalin pharmacokinetics are linear over the recommended daily dose range. Inter-subject pharmacokinetic variability for pregabalin is low (<20%). Multiple dose pharmacokinetics are predictable from single-dose data. Therefore, there is no need for routine monitoring of plasma concentrations of pregabalin.

Gender
Clinical trials indicate that gender does not have a clinically significant influence on the plasma concentrations of pregabalin.

Renal impairment
Pregabalin clearance is directly proportional to creatinine clearance. In addition, pregabalin is effectively removed from plasma by haemodialysis (following a 4 hour haemodialysis treatment plasma pregabalin concentrations are reduced by approximately 50%). Because renal elimination is the major elimination pathway, dose reduction in patients with renal impairment and dose supplementation following haemodialysis is necessary (see section 4.2 Table 1).

Hepatic impairment
No specific pharmacokinetic studies were carried out in patients with impaired liver function. Since pregabalin does not undergo significant metabolism and is excreted predominantly as unchanged drug in the urine, impaired liver function would not be expected to significantly alter pregabalin plasma concentrations.

Paediatric population
Pregabalin pharmacokinetics were evaluated in paediatric patients with epilepsy (age groups: 1 to 23 months, 2 to 6 years, 7 to 11 years and 12 to 16 years) at dose levels of 2.5, 5, 10 and 15 mg/kg/day in a pharmacokinetic and tolerability study.

After oral administration of pregabalin in paediatric patients in the fasted state, in general, time to reach peak plasma concentration was similar across the entire age group and occurred 0.5 hours to 2 hours postdose.

Pregabalin C_{max} and AUC parameters increased in a linear manner with increasing dose within each age group. The AUC was lower by 30% in paediatric patients below a weight of 30 kg due to an increased body weight adjusted clearance of 43% for these patients in comparison to patients weighing ≥30 kg.

Pregabalin terminal half-life averaged about 3 to 4 hours in paediatric patients up to 6 years of age, and 4 to 6 hours in those 7 years of age and older.

Population pharmacokinetic analysis showed that creatinine clearance was a significant covariate of pregabalin oral clearance, body weight was a significant covariate of pregabalin apparent oral volume of distribution, and these relationships were similar in paediatric and adult patients.

Pregabalin pharmacokinetics in patients younger than 3 months old have not been studied (see sections 4.2, 4.8 and 5.1).

Elderly
Pregabalin clearance tends to decrease with increasing age. This decrease in pregabalin oral clearance is consistent with decreases in creatinine clearance associated with increasing age. Reduction of pregabalin dose may be required in patients who have age related compromised renal function (see section 4.2 Table 1).

Breast feeding mothers
The pharmacokinetics of 150 mg pregabalin given every 12 hours (300 mg daily dose) was evaluated in 10 lactating women who were at least 12 weeks postpartum. Lactation had little to no influence on pregabalin pharmacokinetics. Pregabalin was excreted into breast milk with average steady state concentrations approximately 76% of those in maternal plasma. The estimated infant dose from breast milk (assuming mean milk consumption of 150 ml/kg/day) of women receiving 300 mg/day or the maximum dose of 600 mg/day would be 0.31 or 0.62 mg/kg/day, respectively. These estimated doses are approximately 7% of the total daily maternal dose on a mg/kg basis.

5.3 Preclinical safety data

In conventional safety pharmacology studies in animals, pregabalin was well-tolerated at clinically relevant doses. In repeated dose toxicity studies in rats and monkeys CNS effects were observed, including hypoactivity, hyperactivity and ataxia. An increased incidence of retinal atrophy commonly observed in aged albino rats was seen after long term exposure to pregabalin at exposures ≥ 5 times the mean human exposure at the maximum recommended clinical dose.

Pregabalin was not teratogenic in mice, rats or rabbits. Foetal toxicity in rats and rabbits occurred only at exposures sufficiently above human exposure. In prenatal/postnatal toxicity studies, pregabalin induced offspring developmental toxicity in rats at exposures >2 times the maximum recommended human exposure.

Adverse effects on fertility in male and female rats were only observed at exposures sufficiently in excess of therapeutic exposure. Adverse effects on male reproductive organs and sperm parameters were reversible and occurred only at exposures sufficiently in excess of therapeutic exposure or were associated with spontaneous degenerative processes in male reproductive organs in the rat. Therefore the effects were considered of little or no clinical relevance.

Pregabalin is not genotoxic based on results of a battery of *in vitro* and *in vivo* tests.

Two-year carcinogenicity studies with pregabalin were conducted in rats and mice. No tumours were observed in rats at exposures up to 24 times the mean human exposure at the maximum recommended clinical dose of 600 mg/day. In mice, no increased incidence of tumours was found at exposures similar to the mean human exposure, but an increased incidence of haemangiosarcoma was observed at higher exposures. The non-genotoxic mechanism of pregabalin-induced tumour formation in mice involves platelet changes and associated endothelial cell proliferation. These platelet changes were not present in rats or in humans based on short term and limited long term clinical data. There is no evidence to suggest an associated risk to humans.

In juvenile rats the types of toxicity do not differ qualitatively from those observed in adult rats. However, juvenile rats are more sensitive. At therapeutic exposures, there was evidence of CNS clinical signs of hyperactivity and bruxism and some changes in growth (transient body weight gain suppression). Effects on the oestrus cycle were observed at 5-fold the human therapeutic exposure.

1.3.1	Pregabalin
SPC, Labeling and Package Leaflet	Common

Reduced acoustic startle response was observed in juvenile rats 1-2 weeks after exposure at >2 times the human therapeutic exposure. Nine weeks after exposure, this effect was no longer observable.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Capsule contents:
Pregelatinised maize starch
Talc (E553b)

Capsule shell:
25 mg hard capsules
Titanium dioxide (E171)
Gelatin
Black printing ink (shellac (E904), black iron oxide (E172), propylene glycol (E1520))

50 mg, 75 mg hard capsules
Titanium dioxide (E171)
Gelatin
Yellow iron oxide (E172)
Black printing ink (shellac (E904), black iron oxide (E172), propylene glycol (E1520))

100 mg hard capsules
Titanium dioxide (E171)
Gelatin
Red iron oxide (E172)
White printing ink (shellac (E904), propylene glycol (E1520), potassium hydroxide (E525), titanium dioxide (E171))

150 mg hard capsules
Titanium dioxide (E171)
Gelatin
Red iron oxide (E172)
Yellow iron oxide (E172)
Black printing ink (shellac (E904), black iron oxide (E172), propylene glycol (E1520))

200 mg, 225 mg hard capsules
Titanium dioxide (E171)
Gelatin
Red iron oxide (E172)
Yellow iron oxide (E172)
Black iron oxide (E172)
Black printing ink (shellac (E904), black iron oxide (E172), propylene glycol (E1520))

300 mg hard capsules
Titanium dioxide (E171)
Gelatin
Red iron oxide (E172)
Yellow iron oxide (E172)
Black iron oxide (E172)
White printing ink (shellac (E904), propylene glycol (E1520), potassium hydroxide (E525), titanium

dioxide (E171))

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

25 mg, 50 mg, 75 mg, 100 mg, 200 mg, 225 mg, 300 mg hard capsules:
3 years
150 mg hard capsules:
5 years

6.4 Special precautions for storage

Do not store above 30°C.

6.5 Nature and contents of container

Blister (PVC/PVDC//Al): 14, 28, 30, 56, 60, 84, 90 or 100 hard capsules, in a box.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements.

7. MARKETING AUTHORISATION HOLDER

To be completed nationally.

8. MARKETING AUTHORISATION NUMBER(S)

To be completed nationally.

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

To be completed nationally.

10. DATE OF REVISION OF THE TEXT

To be completed nationally.

Detailed information on this medicinal product is available on the website of: {name of Member State Agency (link)}

1.3.1	Pregabalin
SPC, Labeling and Package Leaflet	Common

LABELLING

1.3.1	Pregabalin
SPC, Labeling and Package Leaflet	Common

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

BOX

1. NAME OF THE MEDICINAL PRODUCT

<Invented name> 25 mg hard capsules
<Invented name> 50 mg hard capsules
<Invented name> 75 mg hard capsules
<Invented name> 100 mg hard capsules
<Invented name> 150 mg hard capsules
<Invented name> 200 mg hard capsules
<Invented name> 225 mg hard capsules
<Invented name> 300 mg hard capsules

pregabalin

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each hard capsule contains 25 mg pregabalin.
Each hard capsule contains 50 mg pregabalin.
Each hard capsule contains 75 mg pregabalin.
Each hard capsule contains 100 mg pregabalin.
Each hard capsule contains 150 mg pregabalin.
Each hard capsule contains 200 mg pregabalin.
Each hard capsule contains 225 mg pregabalin.
Each hard capsule contains 300 mg pregabalin.

3. LIST OF EXCIPIENTS

4. PHARMACEUTICAL FORM AND CONTENTS

capsule, hard

14 hard capsules
28 hard capsules
30 hard capsules
56 hard capsules
60 hard capsules
84 hard capsules
90 hard capsules
100 hard capsules

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
Oral use

1.3.1	Pregabalin
SPC, Labeling and Package Leaflet	Common

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

Do not store above 30°C.

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

To be completed nationally.

12. MARKETING AUTHORISATION NUMBER(S)

To be completed nationally.

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

To be completed nationally.

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

1.3.1	Pregabalin
SPC, Labeling and Package Leaflet	Common

<Invented name> 25 mg
<Invented name> 50 mg
<Invented name> 75 mg
<Invented name> 100 mg
<Invented name> 150 mg
<Invented name> 200 mg
<Invented name> 225 mg
<Invented name> 300 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

1.3.1	Pregabalin
SPC, Labeling and Package Leaflet	Common

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

BLISTER

1. NAME OF THE MEDICINAL PRODUCT

<Invented name> 25 mg hard capsules
<Invented name> 50 mg hard capsules
<Invented name> 75 mg hard capsules
<Invented name> 100 mg hard capsules
<Invented name> 150 mg hard capsules
<Invented name> 200 mg hard capsules
<Invented name> 225 mg hard capsules
<Invented name> 300 mg hard capsules

multilingual blisters:
<Invented name> 25 mg capsules
<Invented name> 50 mg capsules
<Invented name> 75 mg capsules
<Invented name> 100 mg capsules
<Invented name> 150 mg capsules
<Invented name> 200 mg capsules
<Invented name> 225 mg capsules
<Invented name> 300 mg capsules

pregabalin

2. NAME OF THE MARKETING AUTHORISATION HOLDER

To be completed nationally.

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. OTHER

1.3.1	Pregabalin
SPC, Labeling and Package Leaflet	Common

PACKAGE LEAFLET

Package leaflet: Information for the user

<Invented name> 25 mg hard capsules
<Invented name> 50 mg hard capsules
<Invented name> 75 mg hard capsules
<Invented name> 100 mg hard capsules
<Invented name> 150 mg hard capsules
<Invented name> 200 mg hard capsules
<Invented name> 225 mg hard capsules
<Invented name> 300 mg hard capsules
pregabalin

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

What is in this leaflet

1. What <Invented name> is and what it is used for

<Invented name> belongs to a group of medicines used to treat epilepsy, neuropathic pain and Generalised Anxiety Disorder (GAD) in adults.

Peripheral and central neuropathic pain: <Invented name> is used to treat long lasting pain caused by damage to the nerves. A variety of diseases can cause peripheral neuropathic pain, such as diabetes or shingles. Pain sensations may be described as hot, burning, throbbing, shooting, stabbing, sharp, cramping, aching, tingling, numbness, pins and needles. Peripheral and central neuropathic pain may also be associated with mood changes, sleep disturbance, fatigue (tiredness), and can have an impact on physical and social functioning and overall quality of life.

Epilepsy: <Invented name> is used to treat a certain form of epilepsy (partial seizures with or without secondary generalisation) in adults. Your doctor will prescribe <Invented name> for you to help treat your epilepsy when your current treatment is not controlling your condition. You should take <Invented name> in addition to your current treatment. <Invented name> is not intended to be used alone, but should always be used in combination with other anti-epileptic treatment.

Generalised Anxiety Disorder: <Invented name> is used to treat Generalised Anxiety Disorder (GAD). The symptoms of GAD are prolonged excessive anxiety and worry that are difficult to control. GAD can also cause restlessness or feeling keyed up or on edge, being easily fatigued (tired), having difficulty concentrating or mind going blank, feeling irritable, having muscle tension or sleep disturbance. This is different to the stresses and strains of everyday life.

2. What you need to know before you take <Invented name>

Do not take <Invented name>
- if you are allergic to pregabalin or any of the other ingredients of this medicine (listed in section 6).

Warnings and precautions
Talk to your doctor or pharmacist before taking <Invented name>.
- Some patients taking pregabalin have reported symptoms suggesting an allergic reaction. These symptoms include swelling of the face, lips, tongue, and throat, as well as diffuse skin rash. Should you experience any of these reactions, you should contact your physician immediately.
- Pregabalin has been associated with dizziness and somnolence, which could increase the occurrence of accidental injury (fall) in elderly patients. Therefore, you should be careful until you are used to any effect the medicine might have.
- <Invented name> may cause blurring or loss of vision, or other changes in eyesight, many of which are temporary. You should immediately tell your doctor if you experience any changes in your vision.
- Some patients with diabetes who gain weight while taking <Invented name> may need an alteration in their diabetic medicines.
- Certain side effects may be more common, such as sleepiness, because patients with spinal cord injury may be taking other medicines to treat, for example, pain or spasticity, that have similar side effects to <Invented name> and the severity of these effects may be increased when taken together.
- There have been reports of heart failure in some patients when taking pregabalin; these patients were mostly elderly with cardiovascular conditions. **Before taking this medicine you should tell your doctor if you have a history of heart disease**.
- There have been reports of kidney failure in some patients when taking pregabalin. If while taking <Invented name> you notice decreased urination, you should tell your doctor as stopping the medicine may improve this.
- A small number of people being treated with anti-epileptics such as pregabalin have had thoughts of harming or killing themselves. If at any time you have these thoughts, immediately contact your doctor.
- When <Invented name> is taken with other medicines that may cause constipation (such as some types of pain medicines) it is possible that gastrointestinal problems may occur (e.g., constipation, blocked or paralysed bowel). Tell your doctor if you experience constipation, especially if you are prone to this problem.
- Before taking this medicine you should tell your doctor if you have a history of alcoholism or any drug abuse or dependence. Do not take more medicine than prescribed.
- There have been reports of convulsions when taking pregabalin or shortly after stopping <Invented name>. If you experience a convulsion, contact your doctor immediately.
- There have been reports of reduction in brain function (encephalopathy) in some patients taking pregabalin when they have other conditions. Tell your doctor if you have a history of any serious medical conditions, including liver or kidney disease.
- There have been reports of breathing difficulties. If you have nervous system disorders, respiratory disorders, renal impairment, or you are older than 65, your doctor may prescribe you a different dosing regimen. Contact your doctor if you experience trouble breathing or shallow breaths.

Children and adolescents
The safety and efficacy in children and adolescents (under 18 years of age) has not been established and therefore, pregabalin should not be used in this age group.

Other medicines and <Invented name>
Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines.
<Invented name> and certain other medicines may influence each other (interaction). When taken with certain other medicines which have sedative effects (including opioids), <Invented name> may potentiate these effects and could lead to respiratory failure, coma and death. The degree of dizziness, sleepiness and decreased concentration may be increased if <Invented name> is taken together with medicinal products containing:
- Oxycodone (used as a pain-killer)
- Lorazepam (used for treating anxiety)
- Alcohol

<Invented name> may be taken with oral contraceptives.

<Invented name> with food, drink and alcohol
<Invented name> capsules may be taken with or without food.
It is advised not to drink alcohol while taking <Invented name>.

Pregnancy and breast-feeding and fertility
If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine.
<Invented name> should not be taken during pregnancy or when breast-feeding, unless you are told otherwise by your doctor. Effective contraception must be used by women of child-bearing potential.

Driving and using machines
<Invented name> may cause dizziness, sleepiness and decreased concentration. You should not drive, operate complex machinery or engage in other potentially hazardous activities until you know whether this medicine affects your ability to perform these activities.

3. How to take <Invented name>

Always take this medicine exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.

Your doctor will determine what dose is appropriate for you.
<Invented name> is for oral use only.

Peripheral and central neuropathic pain, epilepsy or Generalised Anxiety Disorder:
- Take the number of capsules as instructed by your doctor.
- The dose, which has been adjusted for you and your condition, will generally be between 150 mg and 600 mg each day.
- Your doctor will tell you to take <Invented name> either twice or three times a day. For twice a day take <Invented name> once in the morning and once in the evening, at about the same time each day. For three times a day take <Invented name> once in the morning, once in the afternoon and once in the evening, at about the same time each day.

If you have the impression that the effect of <Invented name> is too strong or too weak, talk to your doctor or pharmacist.

If you are an elderly patient (over 65 years of age), you should take <Invented name> normally except if you have problems with your kidneys. Your doctor may prescribe a different dosing schedule and/or dose if you have problems with your kidneys.

Swallow the capsule whole with water.

Continue taking <Invented name> until your doctor tells you to stop.

If you take more <Invented name> than you should
Call your doctor or go to the nearest hospital emergency unit immediately. Take your box of <Invented name> capsules with you. You may feel sleepy, confused, agitated, or restless as a result of taking more <Invented name> than you should. Fits have also been reported.

If you forget to take <Invented name>
It is important to take your <Invented name> capsules regularly at the same time each day. If you forget to take a dose, take it as soon as you remember unless it is time for your next dose. In that case, just carry on with the next dose as normal. Do not take a double dose to make up for a forgotten dose.

If you stop taking <Invented name>
Do not stop taking <Invented name> unless your doctor tells you to. If your treatment is stopped it should be done gradually over a minimum of 1 week.

After stopping long and short-term <Invented name> treatment, you need to know that you may experience certain side effects. These include trouble sleeping, headache, nausea, feeling anxious, diarrhoea, flu-like symptoms, convulsions, nervousness, depression, pain, sweating, and dizziness. These symptoms may occur more commonly or severely if you have been taking <Invented name> for a longer period of time.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

If you experience swollen face or tongue or if your skin turns red and starts to blister or peel you should seek immediate medical advice.

Very common: may affect more than 1 in 10 people:
Dizziness, drowsiness, headache

Common: may affect up to 1 in 10 people:
- Increased appetite.
- Feeling of elation, confusion, disorientation, decrease in sexual interest, irritability.
- Disturbance in attention, clumsiness, memory impairment, loss of memory, tremor, difficulty with speaking, tingling feeling, numbness, sedation, lethargy, insomnia, fatigue, feeling abnormal.
- Blurred vision, double vision.
- Vertigo, problems with balance, fall.
- Dry mouth, constipation, vomiting, flatulence, diarrhoea, nausea, swollen abdomen.
- Difficulties with erection.
- Swelling of the body including extremities.
- Feeling drunk, abnormal style of walking.
- Weight gain.
- Muscle cramp, joint pain, back pain, pain in limb.
- Sore throat.

Uncommon: may affect up to 1 in 100 people:
- Loss of appetite, weight loss, low blood sugar, high blood sugar.
- Change in perception of self, restlessness, depression, agitation, mood swings, difficulty finding words, hallucinations, abnormal dreams, panic attack, apathy, aggression, elevated mood, mental impairment, difficulty with thinking, increase in sexual interest, problems with sexual functioning including inability to achieve a sexual climax, delayed ejaculation.
- Changes in eyesight, unusual eye movement, changes in vision including tunnel vision, flashes of light, jerky movements, reduced reflexes, increased activity, dizziness on standing, sensitive skin, loss of taste, burning sensation, tremor on movement, decreased consciousness, loss of consciousness, fainting, increased sensitivity to noise, feeling unwell.
- Dry eyes, eye swelling, eye pain, weak eyes, watery eyes, eye irritation.
- Heart rhythm disturbances, increased heart rate, low blood pressure, high blood pressure, changes in heartbeat, heart failure.
- Flushing, hot flushes.
- Difficulty breathing, dry nose, nasal congestion.
- Increased saliva production, heartburn, numb around mouth.
- Sweating, rash, chills, fever.
- Muscle twitching, joint swelling, muscle stiffness, pain including muscle pain, neck pain.
- Breast pain.
- Difficulty with or painful urination, incontinence.
- Weakness, thirst, chest tightness.
- Changes in blood and liver test results (blood creatinine phosphokinase increased, alanine amino transferase increased, aspartate aminotransferase increased, platelet count decreased, neutropaenia, increase in blood creatinine, decrease in blood potassium).
- Hypersensitivity, swollen face, itchiness, hives, runny nose, nose bleed, cough, snoring.
- Painful menstrual periods.
- Coldness of hands and feet.

Rare: may affect up to 1 in 1,000 people:
- Abnormal sense of smell, swinging vision, altered perception of depth, visual brightness, vision loss.
- Dilated pupils, cross eyes.
- Cold sweat, tightness of the throat, swollen tongue.
- Inflammation of the pancreas.
- Difficulty in swallowing.
- Slow or reduced movement of the body.
- Difficulty with writing properly.
- Increased fluid in the abdomen.
- Fluid in the lungs
- Convulsions
- Changes in the recording of electrical changes (ECG) in the heart which correspond to heart rhythm disturbances
- Muscle damage.
- Breast discharge, abnormal breast growth, breast growth in males.
- Interrupted menstrual periods.
- Kidney failure, reduced urine volume, urinary retention.
- Decrease in white blood cell count.
- Inappropriate behaviour.
- Allergic reactions (which may include difficulty breathing, inflammation of the eyes (keratitis) and a serious skin reaction characterized by rash, blisters, peeling skin and pain).
- Jaundice (yellowing of the skin and eyes).

Very rare: may affect up to 1 in 10,000 people:
- Liver failure.
- Hepatitis (inflammation of the liver).

Certain side effects may be more common, such as sleepiness, because patients with spinal cord injury may be taking other medicines to treat, for example, pain or spasticity, that have similar side effects to <Invented name> and the severity of these effects may be increased when taken together.

The following adverse reaction has been reported in the postmarketing experience: Trouble breathing, shallow breaths.

Reporting of side effects
If you get any side effects, talk to your 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 <Invented name>

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 packaging after EXP. The expiry date refers to the last day of that month.

Do not store above 30°C.

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 <Invented name> contains
- The active substance is pregabalin. Each hard capsule contains 25 mg, 50 mg, 75 mg, 100 mg, 150 mg, 200 mg, 225 mg or 300 mg pregabalin.
- The other ingredients are pregelatinised maize starch, talc (E553b) in capsule contents.
- The other ingredients of 25 mg hard capsules are titanium dioxide (E171), gelatin, black printing ink (shellac (E904), black iron oxide (E172), propylene glycol (E1520)) in capsule shell.
- The other ingredients of 50 mg and 75 mg hard capsules are titanium dioxide (E171), gelatin, yellow iron oxide (E172), black printing ink (shellac (E904), black iron oxide (E172), propylene glycol (E1520)) in capsule shell.
- The other ingredients of 100 mg hard capsules are titanium dioxide (E171), gelatin, red iron oxide (E172), white printing ink (shellac (E904), propylene glycol (E1520), potassium hydroxide (E525), titanium dioxide (E171)) in capsule shell.
- The other ingredients of 150 mg hard capsules are titanium dioxide (E171), gelatin, red iron oxide (E172), yellow iron oxide (E172), black printing ink (shellac (E904), black iron oxide (E172), propylene glycol (E1520)) in capsule shell.
- The other ingredients of 200 mg and 225 mg hard capsules are titanium dioxide (E171), gelatin, red iron oxide (E172), yellow iron oxide (E172), black iron oxide (E172), black printing ink (shellac (E904), black iron oxide (E172), propylene glycol (E1520)) in capsule shell.
- The other ingredients of 300 mg hard capsules are titanium dioxide (E171), gelatin, red iron

oxide (E172), yellow iron oxide (E172), black iron oxide (E172), white printing ink (shellac (E904), propylene glycol (E1520), potassium hydroxide (E525), titanium dioxide (E171)) in capsule shell.

What <Invented name> looks like and contents of the pack
Capsule, hard (capsule)
25 mg hard capsules (capsules): The body of the capsule is white colour, the cap of the capsule is white colour. Capsule cap is imprinted with black mark P25. The content of the capsule is white to off white powder. Capsule length: 13.8 – 14.8 mm.
50 mg hard capsules (capsules): The body of the capsule is white colour, the cap of the capsule is bright yellow colour. Capsule cap is imprinted with black mark P50. The content of the capsule is white to off white powder. Capsule length: 15.3 – 16.2 mm.
75 mg hard capsules (capsules): The body of the capsule is brownish yellow colour, the cap of the capsule is brownish yellow colour. Capsule cap is imprinted with black mark P75. The content of the capsule is white to off white powder. Capsule length: 13.8 – 14.8 mm.
100 mg hard capsules (capsules): The body of the capsule is reddish brown colour, the cap of the capsule is reddish brown colour. Capsule cap is imprinted with white mark P100. The content of the capsule is white to off white powder. Capsule length: 15.3 – 16.2 mm.
150 mg hard capsules (capsules): The body of the capsule is white colour, the cap of the capsule is yellowish brown colour. Capsule cap is imprinted with black mark P150. The content of the capsule is white to off white powder. Capsule length: 17.2 – 18.3 mm.
200 mg hard capsules (capsules): The body of the capsule is brown colour, the cap of the capsule is brown colour. Capsule cap is imprinted with black mark P200. The content of the capsule is white to off white powder. Capsule length: 18.7 – 19.8 mm.
225 mg hard capsules (capsules): The body of the capsule is white colour, the cap of the capsule is brown colour. Capsule cap is imprinted with black mark P225. The content of the capsule is white to off white powder. Capsule length: 18.7 – 19.8 mm.
300 mg hard capsules (capsules): The body of the capsule is white colour, the cap of the capsule is dark brown colour. Capsule cap is imprinted with white mark P300. The content of the capsule is white to off white powder. Capsule length: 20.0 – 22.1 mm.

<Invented name> is available in boxes of 14, 28, 30, 56, 60, 84, 90 or 100 hard capsules in blister packs.
Not all pack sizes may be marketed.

Marketing Authorisation Holder
To be completed nationally.

Manufacturer
To be completed nationally.

This medicinal product is authorised in the Member States of the EEA under the following names:
To be completed nationally.

This leaflet was last revised in
To be completed nationally.

Detailed information on this medicine is available on the website of {name of Member State Agency (link)}