SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Maxgalin 75

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each capsule contains
Pregabalin……..75 mg

Excipient(s) of known effect
Mannitol

For the full list of excipients, see **section 6.1**

3. PHARMACEUTICAL FORM

Capsules
Description: Hard gelatin capsules of size '4' with red opaque cap and white opaque body imprinted with 'rbx' on cap and 'PG75' on body containing white to off white powder.

4. CLINICAL PARTICULARS [1]

4.1 Therapeutic indications

Neuropathic pain

Maxgalin 75 is indicated for the treatment of peripheral and central neuropathic pain in adults.

Epilepsy

Maxgalin 75 is indicated as adjunctive therapy in adults with partial seizures with or without secondary generalisation.

Generalised anxiety disorder

Maxgalin 75 is indicated for the treatment of Generalised Anxiety Disorder (GAD) in adults.

4.2 Posology and method of administration

Maxgalin 75 is available at the strengths of 75 mg only and may not be suitable for all dosage recommendations mentioned below; other approved strengths or dosage forms should be considered in such cases.

Posology

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

Neuropathic pain

Maxgalin 75 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

Maxgalin 75 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.

Maxgalin 75 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 (CL_{cr}), as indicated in Table below deter

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

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 below).

Table: Pregabalin dose adjustment based on renal function

Creatinine clearance (CL_{cr}) (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 pregabalin in children below the age of 12 years and in adolescents (12-17 years of age) have not been reported. Currently available data are described in **sections 4.8 and 5.2** but no recommendation on posology can be made.

Elderly

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

METHOD OF ADMINISTRATION

Maxgalin 75 may be taken with or without food.

Maxgalin 75 is for oral use only.

4.3 Contraindications

Hypersensitivity to pregabalin or to any of the excipients of this product.

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 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.

Severe cutaneous adverse reactions (SCARs)

SCARs including Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN), which can be life-threatening or fatal, have been reported rarely in association with pregabalin treatment. At the time of prescription patients should be advised of the signs and symptoms and monitored closely for skin reactions. If signs and symptoms suggestive of these reactions appear, pregabalin should be withdrawn immediately and an alternative treatment considered (as appropriate).

Dizziness, somnolence, loss of consciousness, confusion, and mental impairment Pregabalin treatment has been reported to be associated with dizziness and somnolence, which could increase the occurrence of accidental injury (fall) in the 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

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. The incidence of visual acuity reduction and visual field changes was reported to be greater in

pregabalin-treated patients than in placebo-treated patients; the incidence of fundoscopic changes was reported to be greater in placebo-treated patients.

Visual adverse reactions have also been reported during post marketing study 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 anti-epileptic medicinal productsThere are insufficient data reported for the withdrawal of concomitant anti-epileptic medicinal products, once seizure control with pregabalin in the add-on situation has been reached, in order to reach monotherapy on pregabalin.

Congestive heart failure
There have been reports of congestive heart failure in some patients receiving pregabalin. These reactions are mostly reported 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 reported to be 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
Severe respiratory depression has been reported 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 behavior
Suicidal ideation and behaviour have been reported in patients treated with anti-epileptic agents in several indications. A small increased risk of suicidal ideation and behaviour have been reported with anti-epileptic drugs. The mechanism of this risk is not known. Cases of suicidal ideation and behaviour have been reported in patients treated with pregabalin in the post-marketing experience (see **section 4.8**). A reported epidemiological study (comparing treatment periods with non-treatment periods within an individual) showed evidence of an increased risk of new onset of suicidal behaviour and death by suicide in patients treated with pregabalin.

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

Reduced lower gastrointestinal tract function
There are postmarketing 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 reported 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 [a OR], 1.68 [95% CI, 1.19 - 2.36]). This increased risk was reported at low doses of pregabalin (≤ 300 mg, a OR 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
Pregabalin can cause drug dependence, which may occur at

therapeutic doses. Cases of abuse and misuse have been reported. Patients with a history of substance abuse may be at higher risk for pregabalin misuse, abuse and dependence, and pregabalin should be used with caution in such patients. Before prescribing pregabalin, the patient's risk of misuse, abuse or dependence should be carefully evaluated.

Patients treated with pregabalin should be monitored for symptoms of pregabalin misuse, abuse or dependence, such as development of tolerance, dose escalation and drug-seeking behaviour.

Withdrawal symptoms
After discontinuation of short-term and long-term treatment with pregabalin, withdrawal symptoms have been reported in some patients. The following events have been reported: insomnia, headache, nausea, anxiety, diarrhoea, flu syndrome, nervousness, depression, suicidal ideation, pain, convulsion, hyperhidrosis and dizziness, suggestive of physical dependence (see **section 4.8**). The patient should be informed about this at the start of the treatment. If pregabalin should be discontinued, it is recommended this should be done gradually over a minimum of 1 week independent of the indication (see **section 4.2**).

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, reported information suggested that the incidence and severity of withdrawal symptoms may be dose-related.

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

Women of childbearing potential/Contraception
Pregabalin use in the first trimester of pregnancy may cause major birth defects in the unborn child. Pregabalin should not be used during pregnancy unless the benefit to the mother clearly outweighs the potential risk to the foetus. Women of childbearing potential have to use effective contraception during treatment (see **section 4.6**).

Excipients

Sodium

Maxgalin 75 contains sodium. It contains less than 1 mmol sodium (23 mg) per hard capsule. Patients on low sodium diets can be informed that this medicinal product is essentially 'sodium-free'.

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.

Reported *in vivo* studies and population pharmacokinetic analysis
No clinically relevant pharmacokinetic interactions were reported between pregabalin and phenytoin, carbamazepine, valproic acid, lamotrigine, gabapentin, lorazepam, oxycodone or ethanol. Oral antidiabetics, diuretics, insulin, phenobarbital, tiagabine and topiramate reportedly 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 medicinal products
Pregabalin may potentiate the effects of ethanol and lorazepam.
In the reported post marketing 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 reported in elderly volunteers. Interaction studies have only been reported in adults.

4.6 Fertility, pregnancy and lactation

Women of childbearing potential / Contraception

Women of childbearing potential have to use effective contraception during treatment (see **section 4.4**).

Pregnancy
Reproductive toxicity has been reported in animals (see **section 5.3**).

Pregabalin has been reported to cross the placenta in rats (see **section 5.2**). Pregabalin may cross the human placenta.

Major congenital malformations
Data reported from a Nordic observational study of pregnancies exposed to pregabalin in the first trimester showed a higher prevalence of major congenital malformations (MCM) among the paediatric population (live or stillborn) exposed to pregabalin compared to the unexposed population (5.9% vs. 4.1%).

The risk of MCM among the paediatric population exposed to pregabalin in the first trimester was slightly higher compared to unexposed population (adjusted prevalence ratio and 95% confidence interval: 1.14 (0.96-1.35)), and compared to population exposed to lamotrigine (1.29 (1.01–1.65)) or to duloxetine (1.39 (1.07–1.82)).

The analyses on specific malformations showed higher risks for malformations of the nervous system, the eye, orofacial clefts, urinary malformations and genital malformations, but numbers were small and estimates imprecise.

Pregabalin 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 reported on the effects of pregabalin on female fertility.

No effects on sperm motility have been reported when healthy males

were exposed to pregabalin at a dose of 600 mg/day for 3 months.

Adverse reproductive and developmental effects have been reported in male and female rats. The clinical relevance of these findings is unknown (see **section 5.3**).

4.7 Effects on ability to drive and use machines

Pregabalin may have minor or moderate influence on the ability to drive and use machines. Pregabalin 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

The most commonly reported adverse reactions of pregabalin were dizziness and somnolence. Adverse reactions were usually mild to moderate in intensity. In reported studies, the discontinuation rate due to adverse reactions was 12% for patients receiving pregabalin and 5% for patients receiving placebo. The most commonly reported adverse reactions that led to discontinuation of pregabalin treatment include dizziness and somnolence.

In the table below all adverse reactions 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 reported to be increased (see **section 4.4)**.

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

Table: 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, suicidal behaviour, suicidal ideation
Not known	*Drug dependence*
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, parkinsonism
Eye disorders	
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

System Organ Class	**Adverse drug reactions**
	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	*Toxic epidermal necrolysis, 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	

System Organ Class	**Adverse drug reactions**
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 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 reported in some patients. The following reactions have been reported: insomnia, headache, nausea, anxiety, diarrhoea, flu syndrome, convulsions, nervousness, depression, suicidal ideation, 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, reported information suggest that the incidence and severity of withdrawal symptoms may be dose-related (see **sections 4.2 and 4.4**).

Paediatric population

The pregabalin safety profile reported in paediatrics was similar to that reported in adults with epilepsy. The most common adverse events reported in the studies with pregabalin treatment were somnolence, pyrexia, upper respiratory tract infection, increased appetite, weight increased, and nasopharyngitis (see **sections 4.2 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 side effects or safety related issues to: pharmacovigilance.africasme@sunpharma.com and also via pharmacy and poisons board, Pharmacovigilance Electronic Reporting System (PvERS) https://pv.pharmacyboardkenya.org' and For product defects, packaging issues, or any quality concerns, contact: Complaintdesk.Tandalja@sunpharma.com.

4.9 Overdose

The most commonly reported adverse reactions 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.

Treatment of pregabalin overdose should include general supportive measures and may include haemodialysis if necessary (see **section**

4.2).

5. PHARMACOLOGICAL PROPERTIES [1]

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Anti-epileptics, other anti-epileptics 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 (2- protein) of voltage-gated calcium channels in the central nervous system.

5.2 Pharmacokinetic properties

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

Absorption

Pregabalin has been reported to be 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 has been reported to be ≥90% and 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

Pregabalin has been reported to cross the blood brain barrier in mice, rats and monkeys. Pregabalin has also been reported 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. There was no indication of racemisation of pregabalin S-enantiomer to the R-enantiomer.

Elimination

Pregabalin has been reported to be 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 reported to be directly proportional to creatinine clearance.

Dose adjustment in patients with reduced renal function or undergoing haemodialysis is necessary (see **section 4.2**).

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 reported single-dose data. Therefore, there is no need for routine monitoring of plasma concentrations of pregabalin.

Gender

It has been reported that gender does not have a clinically significant influence on the plasma concentrations of pregabalin.

Renal impairment

Pregabalin clearance has been reported to be 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**).

Hepatic impairment

No specific pharmacokinetic studies were reported 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 reported 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 was reported 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 reported to be 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.

It has been reported 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 reported to be similar in paediatric and adult patients.

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

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**).

Breast-feeding mothers

The pharmacokinetics of 150 mg pregabalin given every 12 hours (300 mg daily dose) was reported in 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 reported to be approximately 7% of the total daily maternal dose on a mg/kg basis.

5.3 Preclinical safety data

In reported 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 have been reported, including hypoactivity, hyperactivity and ataxia. An increased incidence of retinal atrophy commonly observed in aged albino rats has been reported 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 reported 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 reported at exposures sufficiently in excess of therapeutic exposure. Adverse effects on male reproductive organs and sperm parameters were reversible and reported 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 have been reported to be considered of little or no clinical relevance.

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

No tumours have been reported 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 has been reported at exposures similar to the mean human exposure, but an increased incidence of haemangiosarcoma was reported 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 reported 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 reported 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 have been reported at 5-fold the human therapeutic exposure. Reduced acoustic startle response has been reported 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 :

Capsules content: Mannitol, purified talc
Capsules shell: Gelatin, titanium dioxide, sodium lauryl sulphate

6.2 Incompatibilities

Not applicable

6.3 Shelf life

24 Months

6.4 Special precautions for storage

Store up to 30°C, protected from light

6.5 Nature and contents of container

MAXGALIN CAPSULES are available in strips of 10 tablets

6.6 Special precautions for disposal and other handling

No special requirement

7. MARKETING AUTHORISATION HOLDER AND MANUFACTURING SITE ADDRESS

MA Holder:
Sun Pharmaceutical Industries Limited
Sun House, Plot No. 201 B/1, Western Express Highway,
Goregaon (E) Mumbai - 400 063, Maharashtra, India.

Manufactured at:
Sun Pharmaceutical Industries Limited
Village Ganguwala, Paonta Sahib, District Sirmour,

Himachal Pradesh – 173025, India.

8. MARKETING AUTHORISATION NUMBER

H2011/21483/171

9. DATE OF FIRST REGISTRATION/ RENEWAL OF THE REGISTRATION

Date of First Registration: 17-May-2012

10. DATE OF REVISION OF THE TEXT

June 2026

REFERENCES

1. Summary of Product Characteristics of Lyrica Capsules, Upjohn UK Limited, February 2024.

Information compiled in June 2026

LYRICA *is the registered trademark of* ***UPJOHN UK LIMITED*** *and is not the trademark of Sun Pharmaceutical Industries Ltd. The maker of this brand is not affiliated with and does not endorse Sun Pharmaceutical Industries Ltd. or its products.*