## 1. NAME OF THE DRUG PRODUCT

**Brand Name: - Aquatix** Pregabalin capsule 300 mg
**Generic Name:** Pregabalin capsule 300 mg

**Strength:** 300 mg

**Dosage form:** Hard gelatin capsule

**Rout of administration:** Oral

## 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

**Label claim:**
Each Hard gelatin capsule contains:
Pregabalin BP 300 mg
Excipients Q.S.
Approved colour used in Empty hard gelatine shell

**UNIT FORMULA:**

| Sr. No | Ingredients | Specifi-cation | Quantity/ capsules | Function |
|---|---|---|---|---|
| 1 | Pregabalin* | BP | 300.00 mg | Active |
| 2 | Lactose | BP | 160.0 mg | Diluent |
| 3 | Starch(SP-Maize starch powder) | BP | 75.00 mg | Diluent |
| 4 | Sodium Lauryl sulphate | BP | 5.00 mg | Disintegrant |
| 5 | Calcium Silicate | USP | 5.00 mg | Filler |
| 6 | Magnesium Stearate | BP | 5.00 mg | Lubricant |
| 7 | Hard Gelatin Capsules Size “0” Colour: Red/white | IH | 01.Nos. | Capsule shell |

## 3. PHARMACEUTICAL FORM

Hard Gelatin Capsule

## 4. CLINICAL PARTICULARS

### 4.1 Therapeutic indications:

Neuropathic pain
Pregabalin Capsules 300Mg is indicated for the treatment of peripheral and central neuropathic pain in adults.
Epilepsy
Pregabalin Capsules 300Mg is indicated as adjunctive therapy in adults with partial seizures with or without secondary generalisation.
Generalised Anxiety Disorder

Pregabalin Capsules 300Mg is indicated for the treatment of Generalised Anxiety Disorder (GAD) in adults.

**4.2 Posology/Dosage 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.

**Method of administration: Oral**

**4.3 Contraindication:**

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

**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 post marketing 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 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.

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.
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.

**4.5 Interaction with other drug 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.
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.
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**

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. The potential risk for humans is unknown.
Pregabalin Capsules 300Mg should not be used during pregnancy unless clearly necessary
Breast-feeding
Pregabalin is excreted into human milk. 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.

**4.7 Effects on ability to drive and use machines**

Pregabalin Capsules 300Mg may have minor or moderate influence on the ability to drive and use machines. Pregabalin Capsules 300Mg may cause dizziness and somnolence and therefore may influence the ability to 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 adverse reactions listed may also be associated with the underlying disease and/or concomitant medicinal products.

| **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, libido decreased, disorientation, insomnia |
| 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*, hypokinesia, parosmia, dysgraphia |
| **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 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 | Flushing, hot flushes, hypotension, hypertension, 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,* dry mouth, constipation, *diarrhoea,* flatulence, abdominal distension |
| Uncommon | Gastrooesophageal reflux disease, salivary hypersecretion, hypoaesthesia oral |
| Rare | Ascites, pancreatitis, dysphagia, *Swollen tongue* |

**4.9 Overdose**

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.
Treatment of pregabalin overdose should include general supportive measures and may include haemodialysis if necessary.

## 5. PHARMACOLOGICAL PROPERTIES

**5.1 Pharmacodynamic properties**

Pharmacotherapeutic group: Other analgesics and antipyretics, ATC code: N02BF02

**Mechanism of action:**

Pregabalin binds to an auxiliary subunit (α 2-δ protein) of voltage-gated calcium channels in the central nervous system.

**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 Cmax by approximately 25-30 % and a delay in tmax 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

## 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.

# 6. PHARMACEUTICAL PARTICULARS

## 6.1 List of excipients:

| Sr. No | Excipients |
|---|---|
| 1 | Lactose BP |
| 2 | Starch (SP-maize starch powder) BP |
| 3 | Sodium Lauryl Sulphate BP |
| 4 | Calcium Silicate USP |
| 5 | Magnesium stearate BP |
| 6 | Hard Gelatin Capsules Size: “O” |

**6.2 Incompatibilities**

Not applicable.

**6.3 Shelf life**

3 Years

**6.4 Special precautions for storage**

Store below $30^{O}$ C in dry & dark place.

**6.5 Nature and contents of container**

An ALU-PVC blister containing 10 capsules such 10 blisters are packed in carton along with pack insert.

**6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product**

No special requirements for disposal.

**7. APPLICANT/HOLDER OF CERTIFICATE OF PRODUCT REGISTRATION**

Aquatix Pharmaceuticals Ltd.
No.7, Sapara Williams Street, Industrial Estate, Ikeja, Lagos

**8. DRUG PRODUCT MANUFACTURER**

KCH Consumer Healthcare
7/9 Sawyer Cres, Gbagada, Lagos 100232, Lagos

**9. NAFDAC REGISTRATION NUMBER(S):** New Registration