Summary of Product Characteristics

1.Name of the finished pharmaceutical product
Carbamazepine tablet 200mg

2.Qualitative and quantitative composition for excipients
The composition of Carbamazepine tablet 200mg table:

3.Pharmaceutical form
Tablet

4.Clinical particulars
4.1 Therapeutic indications
Epilepsy
Carbamazepine is indicated for use as an anticonvulsant drug. Evidence supporting efficacy of Tegretol as an anticonvulsant was derived from active drug-controlled studies that enrolled patients with the following seizure types: 1. Partial seizures with complex symptomatology (psychomotor, temporal lobe). Patients with these seizures appear to show greater improvement than those with other types. 2.
Generalized tonic-clonic seizures (grand mal). 3. Mixed seizure patterns which include the above, or other partial or generalized seizures. Absence seizures (petit mal) do not appear to be controlled by Tegretol (see PRECAUTIONS, General).
Trigeminal Neuralgia
Carbamazepine is indicated in the treatment of the pain associated with true trigeminal neuralgia. Beneficial results have also been reported in glossopharyngeal neuralgia.
This drug is not a simple analgesic and should not be used for the relief of trivial ached or pains.

4.2 Posology and method of administration
Oral tablets

Epilepsy:
Adults and children over 12 years of age-initial: 200mg twice a day for tablets. Increase at weekly intervals by adding up to 200mg/day until the optimal response is obtained. Dosage generally should not exceed 1000mg daily in children 12 to 15 years of age, and 1200mg daily in patients above 15 years of age. Doses up to 1600mg daily have been used in adults in rare instances. ***Maintenance:*** Adjust dosage to the minimum effective level, usually 800 to 1200 mg daily.
Children 6 to 12 years of age-Initial: 100 mg twice a day for tablets. Increase at weekly intervals by adding up to 100 mg/day until the optimal response is obtained. Dosage

generally should not exceed 1000 mg daily. ***Maintenance:*** Adjust dosage to the minimum effective level, usually 400 to 800 mg daily

Children under 6 years of age-initial: 10 to 20 mg/kg/day twice a day or three times a day as tablets,. Increase weekly to achieve optimal clinical response administered three times a day or four times a day. Maintenance: Ordinarily, optimal clinical response is achieved at daily doses below 35 mg/kg. If satisfactory clinical response has not been achieved, plasma levels should be measured to determine whether or not they are in the therapeutic range. No recommendation regarding the safety of carbamazepine for use at doses above 35 mg/kg/24 hours can be made.

Trigeminal Neuralgia

Initial: On the first day, either 100 mg twice a day for tablets, for a total daily dose of 200 mg. This daily dose may be increased by up to 200 mg/day using. increments of 100 mg every 12 hours for tablets, only as needed to achieve freedom from pain. Do not exceed 1200 mg daily. ***Maintenance:*** Control of pain can be maintained in most patients with 400 to 800 mg daily. However, some patients may be maintained on as little as 200 mg daily, while others may require as much as 1200 mg daily. At least once every 3 months throughout the treatment period, attempts should be made to reduce the dose to the minimum effective level or even to discontinue the drug

Usage in Pregnancy: Carbamazepine can cause fetal harm when administered to a pregnant woman.

4.3 Contraindications

Carbamazepine should not be used in patients with a history of previous bone marrow depression, hypersensitivity to the drug, or known sensitivity to any of the tricyclic compounds, such as amitriptyline, desipramine, imipramine, protriptyline, nortriptyline, etc. Likewise, on theoretical grounds its use with monoamine oxidase (MAO) inhibitors is not recommended. Before administration of Tegretol, MAO inhibitors should be discontinued for a minimum of 14 days, or longer if the clinical situation permits.

Coadministration of carbamazepine and nefazodone may result in insufficient plasma concentrations of nefazodone and its active metabolite to achieve a therapeutic effect. Coadministration of carbamazepine with nefazodone is contraindicated.

4.4 Special warnings and special precautions for use

Serious Dermatologic Reactions

Serious and sometimes fatal dermatologic reactions, including toxic epidermal necrolysis (TEN) and Stevens - Johnson syndrome (SJS), have been reported with Tegretol treatment. The risk of these events is estimated to be about 1 to 6 per 10,000 new users in countries with mainly Caucasian populations. However, the risk in some Asian countries is estimated to be about 10 times higher. Tegretol should be discontinued at the first sign of a rash, unless the rash is clearly not drug-related. If signs or symptoms suggest SJS/TEN, use of this drug should not be resumed and alternative therapy should be considered.

4.5 Interaction with other FPPs and other forms of interaction

1. Cyclophosphamide is an inactive prodrug and is converted to its active metabolite

in part by CYP3A. The rate of metabolism and the leukopenic activity of cyclophosphamide are reportedly increased by chronic coadministration of CYP3A4 inducers. There is a potential for increased cyclophosphamide toxicity when coadministered with carbamazepine.

2. Concomitant administration of carbamazepine and lithium may increase the risk of neurotoxic side effects.

3. Concomitant use of carbamazepine and isoniazid has been reported to increase isoniazid-induced hepatotoxicity.

4. Alterations of thyroid function have been reported in combination therapy with other anticonvulsant medications.

5. Concomitant use of Tegretol with hormonal contraceptive products (e.g., oral, and levonorgestrel subdermal implant contraceptives) may render the contraceptives less effective because the plasma concentrations of the hormones may be decreased. Breakthrough bleeding and unintended pregnancies have been reported. Alternative or back-up methods of contraception should be considered.

6. Resistance to the neuromuscular blocking action of the nondepolarizing neuromuscular blocking agents pancuronium, vecuronium, rocuronium and cisatracurium has occurred in patients chronically administered carbamazepine. Whether or not carbamazepine has the same effect on other non- depolarizing agents is unknown. Patients should be monitored closely for more rapid recovery from neuromuscular blockade than expected, and infusion rate requirements may be higher.

7 Concomitant use of carbamazepine with rivaroxaban, apixaban, dabigatran, and edoxaban (direct acting oral anticoagulants) is expected to result in decreased plasma concentrations of these anticoagulants that may be insufficient to achieve the intended therapeutic effect. In general, coadministration of carbamazepine with rivaroxaban, apixaban, dabigatran, and edoxaban should be avoided.

5.Pharmcological properties

5.1. Pharmacodynamics properties

General effects

Carbamazepine treats seizures and the symptoms of trigeminal neuralgia by inhibiting sodium channels. In bipolar 1 disorder, carbamazepine has been found to decrease mania symptoms in a clinically significant manner according to the Young Mania Rating Scale (YMRS). Carbamazepine has a narrow therapeutic index.

A note on genetic variation and carbamazepine use

In studies of Han Chinese ancestry patients, a pronounced association between the HLA-B*1502 genotype and Steven Johnson syndrome and/or toxic epidermal necrolysis (SJS/TEN) resulting from carbamazepine use was observed.

5.2. Pharmacokinetic properties

The bioavailability of carbamazepine is in the range of 75-85% of an ingested dose.3 After one 200 mg oral extended-release dose of carbamazepine in a pharmacokinetic study, the Cmax carbamazepine was measured to be 1.9 ± 0.3 mcg/mL. The Tmax was 19 ± 7 hours. After several doses of 800 mg every 12 hours, the peak concentrations of carbamazepine were measured to be 11.0 ± 2.5 mcg/mL. The Tmax was reduced to 5.9

± 1.8 hours. Extended-release carbamazepine demonstrated linear pharmacokinetics over a range of 200–800 mg.

Effect of food on absorption

A meal containing high-fat content increased the rate of absorption of one 400 mg dose but not the AUC of carbamazepine. The elimination half-life remained unchanged between fed and fasting state. The pharmacokinetics of an extended-release carbamazepine dose was demonstrated to be similar when administered in the fasted state or with food. Based on these findings, food intake is unlikely to exert significant effects on carbamazepine absorption.

Carbamazepine is largely metabolized in the liver. CYP3A4 hepatic enzyme is the major enzyme that metabolizes carbamazepine to its active metabolite, carbamazepine-10,11-epoxide, which is further metabolized to its trans-diol form by the enzyme epoxide hydrolase. Other hepatic cytochrome enzymes that contribute to the metabolism of carbamazepine are CYP2C8, CYP3A5, and CYP2B6. Carbamazepine also undergoes hepatic glucuronidation by UGT2B7 enzyme and several other metabolic reactions occur, resulting in the formation of minor hydroxy metabolites and quinone metabolites. Interestingly, carbamazepine induces its own metabolism. This leads to enhanced clearance, reduced half-life, and a reduction in serum levels of carbamazepine.

5.3. Preclinical safety data

None stated.

6. Pharmaceutical particulars

6.1 List of excipients

Excipients for Potassium chloride tablet 600mg:

Excipients
Microcrystalline cellulose PH102
sodium carboxymethyl cellulose
Magnesium stearate
Silicon dioxide
Croscarmellose sodium

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

36 months from the date of manufacture.

6.4 Special precautions for storage

Do not store above 30℃. Protect from moisture. Keep out of the reach and sight of children.

6.5 Nature and contents of container

12 tablets in a blister, and such 10 or 2 blisters in a carton

6.6 Instructions for use and handling

Keep out of reach of children.

7.Marketing authorization holder

Name: Humanwell Pharmaceutical Ethiopia PLC.
Address: Tuleffa kebele, Bulga Town, North Shewa Zone,Amhara region, Ethiopia
Tel: +251 18903393, +251 902888222
E-mail:chengpeng@renfu.com.cn

E-mail: tangyuzhong@renfu.com.cn chengpeng@renfu.com.cn

8.Numbers in the national register of finished pharmaceutical products

Not applicable.

9.Date of first authorization/renewal of the authorization

Not applicable.

10.Date of revision the text

Not applicable.