For the use only of a Registered Medical Practitioner or a Hospital or a Laboratory

OLEPTAL DT

1. Generic Name

Oxcarbazepine Dispersible Tablets

2. Qualitative & Quantitative Formula

OLEPTAL DT 150

Each dispersible uncoated tablet contains:

Oxcarbazepine I.P…….150mg

Colour: Yellow Oxide of Iron

OLEPTAL DT 300

Each dispersible uncoated tablet contains:

Oxcarbazepine I.P…….300mg

Colour: Yellow Oxide of Iron

OLEPTAL DT 450

Each dispersible uncoated tablet contains:

Oxcarbazepine I.P…….450mg

Colour: Yellow Oxide of Iron

Excipients used are as below:

Ferric oxide yellow, Sodium saccharin, Pineapple flavour, Citric acid anhydrous, Microcrystalline cellullose, Starch, Magnesium stearate, Polyvinyl pyrrolidone, Crosspovidone, Colloidal silicon dioxide, Aspartame.

3. DOSAGE FORM AND STRENGTH

DOSAGE FORM Dispersible Uncoated Tablet

STRENGTH: 150mg, 300mg & 450mg

4. CLINICAL PARTICULARS

4.1 Therapeutic Action

A monotherapy and adjunctive therapy in the treatment of partial seizures in adult patients with epilepsy. Adjunctive therapy in the treatment of partial seizures in children in the group of 4-16 years with epilepsy.

4.2 Posology and Method of Administration

Posology.

In mono- and adjunctive therapy, treatment with OLEPTAL DT is initiated with a clinically effective dose given in two divided doses. The dose may be increased depending on the clinical response of the patient. When other antiepileptic medicinal products are replaced by

OOLEPTAL DT, the dose of the concomitant antiepileptic medicinal product(s) should be reduced gradually on initiation of OLEPTAL DT therapy. In adjunctive therapy, as the total antiepileptic medicinal product load of the patient is increased, the dose of concomitant antiepileptic medicinal product(s) may need to be reduced and/or the OLEPTAL DT dose increased more slowly.

Direction for use: Disperse the tablet in a tablespoonful of boiled and cooled water before administration.

Therapeutic drug monitoring

The therapeutic effect of oxcarbazepine is primarily exerted through the active metabolite 10-monohydroxy derivative (MHD) of oxcarbazepine.

Plasma level monitoring of oxcarbazepine or MHD is not routinely warranted. However, may be useful in situations where an alteration in MHD clearance is to be expected (see section 4.4). In such situations, the dose of OLEPTAL DT may be adjusted (based on plasma levels measured 2-4 hours post dose) to maintain peak MHD plasma levels < 35 mg/L.

Adults

Monotherapy

Recommended initial dose

OLEPTAL DT should be initiated with a dose of 600 mg/day (8-10 mg/kg/day) given in 2 divided doses.

Maintenance dose

If clinically indicated, the dose may be increased by a maximum of 600 mg/day at approximately weekly intervals from the starting dose to achieve the desired clinical response.

Therapeutic effects are seen at doses between 600 mg/day and 2,400 mg/day.

Controlled monotherapy trials in patients not currently being treated with antiepileptic medicinal products showed 1,200 mg/day to be an effective dose; however, a dose of 2,400 mg/day has been shown to be effective in more refractory patients converted from other antiepileptic medicinal products to OLEPTAL DT monotherapy.

Maximum recommended dose

In a controlled hospital setting, dose increases up to 2,400 mg/day have been achieved over 48 hours.

Adjunctive therapy

Recommended initial dose

OLEPTAL DT should be initiated with a dose of 600 mg/day (8-10 mg/kg/day) given in 2 divided doses.

Maintenance dose

If clinically indicated, the dose may be increased by a maximum of 600 mg/day at approximately weekly intervals from the starting dose to achieve the desired clinical response.

Therapeutic responses are seen at doses between 600 mg/day and 2,400 mg/day.

Maximum recommended dose

Daily doses from 600 to 2,400 mg/day have been shown to be effective in a controlled adjunctive therapy trial, although most patients were not able to tolerate the 2,400 mg/day dose without reduction of concomitant antiepileptic medicinal products, mainly because of CNS-related adverse events. Daily doses above 2,400 mg/day have not been studied systematically in clinical trials.

Elderly (65 years old and above)

No special dose recommendations are necessary in elderly patients because therapeutic doses are individually adjusted. Dosage adjustments are recommended in elderly patients with renal impairment (creatinine clearance less than 30 ml/min) (see information below on dosage in renal impairment).

Close monitoring of sodium levels is required in patients at risk of hyponatremia.

Patients with hepatic impairment

No dosage adjustment is required for patients with mild to moderate hepatic impairment. OLEPTAL DT has not been studied in patients with severe hepatic impairment, therefore, caution should be exercised when dosing severely impaired patients (see section 5.2).

Patients with renal impairment

In patients with impaired renal function (creatinine clearance less than 30 ml/min) OLEPTAL DT therapy should be initiated at half the usual starting dose (300 mg/day) and increased, in at least weekly intervals, to achieve the desired clinical response (see section 5.2).

Dose escalation in renally impaired patients may require more careful observation.

Paediatric population

Recommended initial dose

In mono- and adjunctive therapy, OLEPTAL DT should be initiated with a dose of 8-10 mg/kg/day given in 2 divided doses.

Maintenance dose

In adjunctive therapy trials, a maintenance dose of 30-46 mg/kg/day, achieved over two weeks, is shown to be effective and well tolerated in children. Therapeutic effects were seen at a median maintenance dose of approximately 30 mg/kg/day.

Maximum recommended dose

If clinically indicated, the dose may be increased by a maximum of 10 mg/kg/day at approximately weekly intervals from the starting dose, to a maximum dose of 46 mg/kg/day, to achieve the desired clinical response (see section 5.2).

OLEPTAL DT is recommended for use in children of 6 years of age and above. Safety and efficacy have been evaluated in controlled clinical trials involving approximately 230 children aged less than 6 years (down to 1 month). OLEPTAL DT is not recommended in children aged less than 6 years since safety and efficacy have not been adequately demonstrated.

All the above dosing recommendations (adults, elderly and children) are based on the doses studied in clinical trials for all age groups. However, lower initiation doses may be considered where appropriate.

Method of administration

The tablets are scored and can be broken into two halves in order to make it easier for the patient to swallow the tablet. However, the tablet cannot be divided into equal doses. For children, who cannot swallow tablets or where the required dose cannot be administered using tablets, a OLEPTAL DT oral suspension is available.

OLEPTAL DT can be taken with or without food.

4.3 Contraindications

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

4.4 Special Warnings and Precautions for Use

Hypersensitivity

Class I (immediate) hypersensitivity reactions including rash, pruritus, urticaria, angioedema and reports of anaphylaxis have been received in the post-marketing period. Cases of anaphylaxis and angioedema involving the larynx, glottis, lips and eyelids have been reported in patients after taking the first or subsequent doses of OLEPTAL DT. If a patient develops these reactions after treatment with OLEPTAL DT, the drug should be discontinued and an alternative treatment started.

Patients who have exhibited hypersensitivity reactions to carbamazepine should be informed that approximately 25-30 % of these patients may experience hypersensitivity reactions (e.g. severe skin reactions) with OLEPTAL DT.

Hypersensitivity reactions, including multi-organ hypersensitivity reactions, may also occur in patients without a history of hypersensitivity to carbamazepine. Such reactions can affect the skin, liver, blood and lymphatic system or other organs, either individually or together in the context of a systemic reaction (see section 4.8). In general, if signs and symptoms suggestive of hypersensitivity reactions occur, OLEPTAL DT should be withdrawn immediately.

Dermatological effects

Serious dermatological reactions, including Stevens-Johnson syndrome, toxic epidermal necrolysis (Lyell's syndrome) and erythema multiforme, have been reported very rarely in association with the use of OLEPTAL DT. Patients with serious dermatological reactions may require hospitalization, as these conditions may be life-threatening and very rarely be fatal. OLEPTAL DT associated cases occurred in both children and adults. The median time to onset was 19 days. Several isolated cases of recurrence of the serious skin reaction when rechallenged with OLEPTAL DT were reported. Patients who develop a skin reaction with OLEPTAL DT should be promptly evaluated and OLEPTAL DT withdrawn immediately unless the rash is clearly not drug related. In case of treatment withdrawal, consideration should be given to replacing OLEPTAL DT with other antiepileptic drug therapy to avoid withdrawal seizures. OLEPTAL DT should not be restarted in patients who discontinued treatment due to a hypersensitivity reaction.

HLA-B*1502 allele – in Han Chinese, Thai and other Asian populations

HLA-B*1502 in individuals of Han Chinese and Thai origin has been shown to be strongly associated with the risk of developing the severe cutaneous reactions known as Stevens-Johnson syndrome (SJS)/ toxic epidermal necrolysis (TEN) when treated with carbamazepine. The chemical structure of oxcarbazepine is similar to that of carbamazepine, and it is possible that patients who are positive for HLA-B*1502 may also be at risk for SJS/TEN after treatment with oxcarbazepine. There are some data that suggest that such an association exists for

oxcarbazepine. The prevalence of HLA-B*1502 carrier is about 10% in Han Chinese and Thai populations. Whenever possible, these individuals should be screened for this allele before starting treatment with carbamazepine or a chemically-related active substance. If patients of these origins are tested positive for HLA-B*1502 allele, the use of oxcarbazepine may be considered if the benefits are thought to exceed risks.

Because of the prevalence of this allele in other Asian populations (e.g. above 15% in the Philippines and Malaysia), testing genetically at risk populations for the presence of HLA-B*1502 may be considered.

The prevalence of the HLA-B*1502 allele is negligible in e.g. European descent, African, Hispanic populations sampled, and in Japanese and Koreans (< 1%).

Allele frequencies refer to the percentage of chromosomes in the population that carry a given allele. Since a person carries two copies of each chromosome, but even one copy of the HLA-B*1502 allele may be enough to increase the risk of SJS, the percentage of patients who may be at risk is nearly twice the allele frequency.

HLA-A*3101 allele – European descent and Japanese populations

There are some data that suggest HLA-A*3101 is associated with an increased risk of carbamazepine induced cutaneous adverse reactions including SJS, TEN, Drug rash with eosinophilia (DRESS), or less severe acute generalized exanthematous pustulosis (AGEP) and maculopapular rash in people of European descent and the Japanese.

The frequency of the HLA-A*3101 allele varies widely between ethnic populations. HLA-A*3101 allele has a prevalence of 2 to 5% in European populations and about 10% in Japanese population.

The presence of HLA-A*3101 allele may increase the risk for carbamazepine induced cutaneous reactions (mostly less severe) from 5.0% in general population to 26.0% among subjects of European ancestry, whereas its absence may reduce the risk from 5.0% to 3.8%.

HLA-A*3101 alleles – Other descents

The frequency of this allele is estimated to be less than 5% in the majority of Australian, Asian, African and North American populations with some exceptions within 5 to 12%. Frequency above 15% has been estimated in some ethnic groups in South America (Argentina and Brazil), North America (US Navajo and Sioux, and Mexico Sonora Seri) and Southern India (Tamil Nadu) and between 10% to 15% in other native ethnicities in these same regions.

Allele frequencies refer to the percentage of chromosomes in the population that carry a given allele. Since a person carries two copies of each chromosome, but even one copy of the HLA-A*3101 alleles may be enough to increase the risk of SJS, the percentage of patients who may be at risk is nearly twice the allele frequency.

There are insufficient data supporting a recommendation for HLA-A*3101 screening before starting carbamazepine or chemically-related compounds treatment.

If patients of European descent or Japanese origin are known to be positive for HLA-A*3101 alleles, the use of carbamazepine or chemically-related compounds may be considered if the benefits are thought to exceed risks.

Limitation of genetic screening

Genetic screening results must never substitute appropriate clinical vigilance and patient management. Many Asian patients positive for HLA-B*1502 and treated with OLEPTAL DT will not develop SJS/TEN, and patients negative for HLA-B*1502 of any ethnicity can still develop SJS/TEN. The same is true for HLA-A*3101 with respect to risk of SJS, TEN, DRESS, AGEP or maculopapular rash. The development of these severe cutaneous adverse reactions and its related morbidity due to other possible factors such as AED dose, compliance, concomitant medications, co-morbidities, and the level of dermatologic monitoring have not been studied.

Information for healthcare professionals

If testing for the presence of the HLA-B*1502 allele is performed, high-resolution "HLA-B*1502 genotyping" is recommended. The test is positive if either one or two HLA-B*1502 alleles are detected, and negative if no HLA-B*1502 alleles are detected. Similarly, if testing for the presence of the HLA-A*3101 alleles is performed, high resolution "HLA-A*3101 genotyping" is recommended. The test is positive if either one or two HLA-A*3101 alleles are detected, and negative if no HLA-A*3101 alleles are detected.

Risk of seizure aggravation

Risk of seizure aggravation has been reported with OLEPTAL DT. The risk of seizure aggravation is seen especially in children but may also occur in adults. In case of seizure aggravation, OLEPTAL DT should be discontinued.

Hyponatraemia

Serum sodium levels below 125 mmol/l, usually asymptomatic and not requiring adjustment of therapy, have been observed in up to 2.7 % of OLEPTAL DT treated patients. Experience from clinical trials shows that serum sodium levels returned towards normal when the OLEPTAL DT dosage was reduced, discontinued or the patient was treated conservatively (e.g. restricted fluid intake). In patients with pre-existing renal conditions associated with low sodium levels (e.g. inappropriate ADH secretion like syndrome) or in patients treated concomitantly with sodium-lowering medicinal products (e.g. diuretics, desmopressin) as well as NSAIDs (e.g. indometacin), serum sodium levels should be measured prior to initiating therapy. Thereafter, serum sodium levels should be measured after approximately two weeks and then at monthly intervals for the first three months during therapy, or according to clinical need. These risk factors may apply especially to elderly patients. For patients on OLEPTAL DT therapy when starting on sodium-lowering medicinal products, the same approach for sodium checks should be followed. In general, if clinical symptoms suggestive of hyponatraemia occur on OLEPTAL DT therapy (see section 4.8), serum sodium measurement may be considered. Other patients may have serum sodium levels assessed as part of their routine laboratory studies.

All patients with cardiac insufficiency and secondary heart failure should have regular weight measurements to determine occurrence of fluid retention. In case of fluid retention or worsening of the cardiac condition, serum sodium levels should be checked. If hyponatraemia is observed, water restriction is an important counter-measurement. As oxcarbazepine may, very rarely, lead to impairment of cardiac conduction, patients with pre-existing conduction disturbances (e.g. atrioventricular-block, arrhythmia) should be followed carefully.

Hypothyroidism

Hypothyroidism is an adverse reaction (with "not known" frequency, see section 4.8) of oxcarbazepine. Considering the importance of thyroid hormones in children's development

after birth, thyroid function monitoring is recommended in the pediatric age group while on OLEPTAL DT therapy.

Hepatic function

Very rare cases of hepatitis have been reported, which in most cases resolved favourably. When a hepatic event is suspected, liver function should be evaluated and discontinuation of OLEPTAL DT should be considered. Caution should be exercised when treating patients with severe hepatic impairment (see section 4.2 and 5.2).

Renal function

In patients with impaired renal function (creatinine clearance less than 30 mL/min), caution should be exercised during OLEPTAL DT treatment especially with regard to the starting dose and up titration of the dose. Plasma level monitoring of MHD may be considered

Haematological effects

Very rare reports of agranulocytosis, aplastic anemia and pancytopenia have been seen in patients treated with OLEPTAL DT during post-marketing experience (see section 4.8).

Discontinuation of the medicinal product should be considered if any evidence of significant bone marrow depression develops.

Suicidal behaviour

Suicidal ideation and behaviour have been reported in patients treated with antiepileptic agents in several indications. A meta-analysis of randomized placebo controlled trials of antiepileptic medicines 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 oxcarbazepine.

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 sign of suicidal ideation or behaviour emerge.

Hormonal contraceptives

Female patients of childbearing age should be warned that the concurrent use of OLEPTAL DT with hormonal contraceptives may render this type of contraceptive ineffective. Additional non-hormonal forms of contraception are recommended when using OLEPTAL DT.

Alcohol

Caution should be exercised if alcohol is taken in combination with OLEPTAL DT therapy, due to a possible additive sedative effect.

Withdrawal

As with all antiepileptic medicinal products, OLEPTAL DT should be withdrawn gradually to minimise the potential of increased seizure frequency.

Monitoring of plasma levels

Although correlations between dosage and plasma levels of oxcarbazepine, and between plasma levels and clinical efficacy or tolerability are rather tenuous, monitoring of the plasma levels may be useful in the following situations in order to rule out noncompliance or in situations where an alteration in MHD clearance is to be expected, including:

• changes in renal function.

• pregnancy

• concomitant use of liver enzyme-inducing medicines.

4.5 Drugs Interactions

Enzyme induction

Oxcarbazepine and its pharmacologically active metabolite (the monohydroxy derivative, MHD) are weak inducers *in vitro* and *in vivo* of the cytochrome P450 enzymes CYP3A4 and CYP3A5 responsible for the metabolism of a very large number of medicines, for example, immunosuppressants (e.g. ciclosporin, tacrolimus), oral contraceptives (see below), and some other antiepileptic medicinal products (e.g. carbamazepine) resulting in a lower plasma concentration of these medicinal products (see table below summarizing results with other antiepileptic medicinal products).

In vitro, oxcarbazepine and MHD are weak inducers of UDP-glucuronyl transferases (effects on specific enzymes in this family are not known). Therefore, *in vivo* oxcarbazepine and MHD may have a small inducing effect on the metabolism of medicinal products which are mainly eliminated by conjugation through the UDP-glucuronyl transferases. When initiating treatment with OLEPTAL DT or changing the dose, it may take 2 to 3 weeks to reach the new level of induction.

In case of discontinuation of OLEPTAL DT therapy, a dose reduction of the concomitant medications may be necessary and should be decided upon by clinical and/or plasma level monitoring. The induction is likely to gradually decrease over 2 to 3 weeks after discontinuation.

Hormonal contraceptives: OLEPTAL DT was shown to have an influence on the two components, ethinylestradiol (EE) and levonorgestrel (LNG), of an oral contraceptive. The mean AUC values of EE and LNG were decreased by 48-52 % and 32-52% respectively. Therefore, concurrent use of OLEPTAL DT with hormonal contraceptives may render these contraceptives ineffective (see section 4.4). Another reliable contraceptive method should be used.

Enzyme inhibition

Oxcarbazepine and MHD inhibit CYP2C19. Therefore, interactions could arise when co-administering high doses of OLEPTAL DT with medicinal products that are mainly metabolised by CYP2C19 (e.g. phenytoin). Phenytoin plasma levels increased by up to 40 % when OLEPTAL DT was given at doses above 1,200 mg/day (see table below summarizing results with other anticonvulsants). In this case, a reduction of co-administered phenytoin may be required (see section 4.2).

Antiepileptic and enzyme inducing medicinal products

Potential interactions between OLEPTAL DT and other antiepileptic medicinal products were assessed in clinical studies. The effect of these interactions on mean AUCs and C_{min} are summarised in the following table.

Summary of antiepileptic medicinal product interactions with OLEPTAL DT

Antiepileptic medicinal product	Influence of OLEPTAL DT on antiepileptic medicinal product	Influence of antiepileptic medicinal product on MHD
Co-administered	Concentration	Concentration
Carbamazepine	0 - 22 % decrease (30 % increase of carbamazepine-epoxide)	40 % decrease
Clobazam	Not studied	No influence
Felbamate	Not studied	No influence
Lamotrigine	No influence	No influence
Phenobarbitone	14 - 15 % increase	30 - 31 % decrease
Phenytoin	0 - 40 % increase	29 - 35 % decrease
Valproic acid	No influence	0 – 18 % decrease

Strong inducers of cytochrome P450 enzymes and/or UGT (i.e. rifampicin, carbamazepine, phenytoin and phenobarbitone) have been shown to decrease the plasma/serum levels of MHD (29-49 %) in adults; in children 4 to 12 years of age, MHD clearance increased by approximately 35% when given one of the three enzyme-inducing antiepileptic medicinal products compared to monotherapy. Concomitant therapy of OLEPTAL DT and lamotrigine has been associated with an increased risk of adverse events (nausea, somnolence, dizziness and headache). When one or several antiepileptic medicinal products are concurrently administered with OLEPTAL DT, a careful dose adjustment and/or plasma level monitoring may be considered on a case by case basis, notably in paediatric patients treated concomitantly with lamotrigine.

No auto induction has been observed with OLEPTAL DT.

Other medicinal product interactions

Cimetidine, erythromycin, viloxazine, warfarin and dextropropoxyphene had no effect on the pharmacokinetics of MHD.

The interaction between oxcarbazepine and MAOIs is theoretically possible based on a structural relationship of oxcarbazepine to tricyclic antidepressants.

Patients on tricyclic antidepressant therapy were included in clinical trials and no clinically relevant interactions have been observed.

The combination of lithium and oxcarbazepine might cause enhanced neurotoxicity.

4.6 Use in Special Populations (Such as Pregnant Women, Lactating Women, Paediatric Patients, Geriatric Patients Etc.)

Women of childbearing potential and contraceptive measures

OLEPTAL DT may result in a failure of the therapeutic effect of oral contraceptive medicines containing ethinylestradiol (EE) and levonorgestrel (LNG) (see section 4.4 and 4.5). Women of child bearing potential should be advised to use highly effective contraception (preferably non-hormonal; e.g. intrauterine implants) while on treatment with OLEPTAL DT.

Pregnancy

Risk related to epilepsy and antiepileptic medicinal products in general:

In the treated population, an increase in malformations has been noted with polytherapy, particularly in polytherapy including valproate.

Moreover, effective anti-epileptic therapy must not be interrupted, since the aggravation of the illness is detrimental to both the mother and the foetus.

Risk related to oxcarbazepine:

There is moderate amount of data on pregnant women (300-1000 pregnancy outcomes). However, the data on oxcarbazepine associated with congenital malformation is limited. There is no increase in the total rate of malformations with OLEPTAL DT as compared with the rate observed in the general population (2-3%). Nevertheless, with this amount of data, a moderate teratogenic risk cannot be completely excluded.

Taking these data into consideration:

• If women receiving OLEPTAL DT become pregnant or plan to become pregnant, the use of this product should be carefully re-evaluated. Minimum effective doses should be given, and monotherapy whenever possible should be preferred at least during the first three months of pregnancy.

• During pregnancy, an effective antiepileptic oxcarbazepine treatment must not be interrupted, since the aggravation of the illness is detrimental to both the mother and the foetus.

Monitoring and prevention:

Some antiepileptic medicinal products may contribute to folic acid deficiency, a possible contributory cause of foetal abnormality. Folic acid supplementation is recommended before and during pregnancy. As the efficacy of this supplementation is not proved, a specific antenatal diagnosis should be offered even for women with a supplementary treatment of folic acid.

Data from a limited number of women indicate that plasma levels of the active metabolite of oxcarbazepine, the 10-monohydroxy derivative (MHD), may gradually decrease throughout pregnancy. It is recommended that clinical response should be monitored carefully in women receiving OLEPTAL DT treatment during pregnancy to ensure that adequate seizure control is maintained. Determination of changes in MHD plasma concentrations should be considered. If dosages have been increased during pregnancy, postpartum MHD plasma levels may also be considered for monitoring.

In the newborn child:

Bleeding disorders in the newborn have been reported with hepatic inductor antiepileptic medicines. As a precaution, vitamin K_1should be administered as a preventive measure in the last few weeks of pregnancy and to the newborn.

Breast-feeding

Oxcarbazepine and its active metabolite (MHD) are excreted in human breast milk. A milk-to-plasma concentration ratio of 0.5 was found for both. The effects on the infant exposed to OLEPTAL DT by this route are not known. Therefore, OLEPTAL DT should not be used during breast-feeding.

Fertility

There are no human data on fertility.

In rats, oxcarbazepine had no effects on fertility. Effects on reproductive parameters in female rats were observed for MHD at doses comparable to those in human

4.7 Effects On Ability to Drive and Use Machines

Adverse reactions such as dizziness, somnolence, ataxia, diplopia, blurred vision, visual disturbances, hyponatremia and depressed level of consciousness were reported with OLEPTAL DT (for complete list of ADRs see section 4.8), especially at the start of treatment or in connection with dose adjustments (more frequently during the up titration phase). Patients should therefore exercise due caution when driving a vehicle or operating machinery.

4.8 Undesirable Effects

Summary of the safety profile

The most commonly reported adverse reactions are somnolence, headache, dizziness, diplopia, nausea, vomiting and fatigue occurring in more than 10% of patients.

The safety profile is based on adverse events from clinical trials assessed as related to OLEPTAL DT. In addition, clinically meaningful reports on adverse experiences from named patient programs and postmarketing experience were taken into account.

Adverse reactions (Table 1) are listed by MedRA system organ class.

Within each system organ class, the adverse reactions are ranked by frequency, with the most frequent first. Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness. In addition, the corresponding frequency category, using the following convention (CIOMS III) is also provided for each adverse reaction: 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).

Table 1 Adverse reactions

Blood and lymphatic system disorders	
Uncommon	leucopenia.
Very rare	thrombocytopenia.
Not known	bone marrow depression, aplastic anemia, agranulocytosis, pancytopenia, neutropenia.
Immune system disorders	

Very rare	hypersensitivity[#]
Not known	anaphylactic reactions
Endocrine disorders	
Common	weight increased.
Not known	hypothyroidism.
Metabolism and nutrition disorders	
Common	hyponatraemia[†].
Not known	Inappropriate ADH secretion like syndrome with signs and symptoms of lethargy, nausea, dizziness, decrease in serum (blood) osmolality, vomiting, headache, confusional state or other neurological signs and symptoms.
Psychiatric disorders	
Common	agitation (e.g. nervousness), affect lability, confusional state, depression, apathy.
Nervous system disorders	
Very common	somnolence, headache, dizziness.
Common	ataxia, tremor, nystagmus, disturbance in attention, amnesia.
Not known	Speech disorders (including dysarthria); more frequent during up titration of OLEPTAL DT dose.
Eye disorders	
Very common	diplopia.
Common	vision blurred, visual disturbance.
Ear and labyrinth disorders	
Common	vertigo.

Cardiac disorders	
Very rare	atrioventricular block, arrhythmia.
Vascular disorders	
Not known	hypertension.
Gastrointestinal disorders	
Very common	vomiting, nausea.
Common	diarrhoea, abdominal pain, constipation.
Very rare	pancreatitis and/or lipase and/or amylase increase.
Hepato-biliary disorders	
Very rare	hepatitis.
Skin and subcutaneous tissue disorders	
Common	rash, alopecia, acne.
Uncommon	urticaria.
Very rare Not known	Stevens-Johnson syndrome, toxic epidermal necrolysis (Lyell's syndrome), angioedema, erythema multiforme. Drug Rash with Eosinophilia and Systemic Symptoms (DRESS)**, Acute Generalized Exanthematous Pustulosis (AGEP)**
Musculoskeletal, connective tissue and bone disorders	
Very rare	systemic lupus erythematosus.
Not known	There have been reports of decreased bone mineral density, osteopenia, osteoporosis and fractures in patients on long-term therapy with OLEPTAL DT. The mechanism by which OLEPTAL DT affects bone metabolism has not been identified.

General disorders and administration site conditions	
Very common	fatigue.
Common	asthenia.
Investigations	
Uncommon	hepatic enzymes increased, blood alkaline phosphatase increased.
Not known	decrease in T4 (with unclear clinical significance).
Injury, poisoning and procedural complications	
Not known	Fall

Description of selected adverse reactions

[#]Hypersensitivity (including multi-organ hypersensitivity) characterised by features such as rash, fever. Other organs or systems may be affected such as blood and lymphatic system (e.g. eosinophilia, thrombocytopenia, leucopenia, lymphadenopathy, splenomegaly), liver (e.g. hepatitis, abnormal liver function tests), muscles and joints (e.g. joint swelling, myalgia, arthralgia), nervous system (e.g. hepatic encephalopathy), kidneys (e.g. renal failure, nephritis interstitial, proteinuria), lungs (e.g. pulmonary oedema, asthma, bronchospasms, interstitial lung disease, dyspnea), angioedema.

[†] Serum sodium levels below 125 mmol/l have been observed in up to 2.7 % of OLEPTAL DT treated patients with frequency common. In most cases, the hyponatraemia is asymptomatic and does not require adjustment of therapy,

Very rarely, the hyponatraemia is associated with signs and symptoms such as seizures, encephalopathy, depressed level of consciousness, confusion, (see also Nervous system disorders for further undesirable effects), vision disorders (e.g. blurred vision), hypothyroidism, vomiting, and nausea. Low serum sodium levels generally occurred during the first 3 months of treatment with OLEPTAL DT, although there were patients who first developed a serum sodium level <125 mmol/l more than 1 year after initiation of therapy.

***Adverse reactions from spontaneous reports and literature cases (frequency not known):*

The following adverse reactions have been derived from post-marketing experience with OLEPTAL DT via spontaneous case reports and literature cases. Because these reactions are reported voluntarily from a population of uncertain size, it is not possible to reliably estimate their frequency which is therefore categorised as not known.

Paediatric population

In general, the safety profile in children was similar to that observed in the adult population.

Reporting of side effects

If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via any point of contact of Torrent Pharma available at:

http://www.torrentpharma.com/Index.php/site/info/adverse_event_reporting

4.9 Overdose

Isolated cases of overdose have been reported. The maximum dose taken was approximately 48,000 mg.

Symptoms

Electrolyte and fluid balance conditions: hyponatraemia

Eye disorders: diplopia, miosis, blurred vision

Gastrointestinal disorders: nausea, vomiting, hyperkinesia

General disorders and administration site conditions: fatigue

Investigations: respiratory rate depression, QTc prolongation

Nervous system disorders: drowsiness and somnolence, dizziness, ataxia and nystagmus, tremor, disturbances in coordination (coordination abnormal), convulsion, headache, coma, loss of consciousness, dyskinesia

Psychiatric disorders: aggression, agitation, confusional state

Vascular disorders: hypotension

Respiratory, thoracic and mediastinal disorders: dyspnoea

Management

There is no specific antidote. Symptomatic and supportive treatment should be administered as appropriate. Removal of the medicinal product by gastric lavage and/or inactivation by administering activated charcoal should be considered.

5. PHARMACOLOGICAL PROPERTIES

5.1 Mechanism of Action

The pharmacological activity of oxcarbazepine is primarily exerted through the metabolite (MHD) (see section 5.2). The mechanism of action of oxcarbazepine and MHD is thought to be mainly based on the blockade of voltage-sensitive sodium channels, thus resulting in stabilisation of hyperexcited neural membranes, inhibition of repetitive neuronal firing, and diminishment of propagation of synaptic impulses. In addition, increased potassium conductance and modulation of high-voltage activated calcium channels may also contribute to the anticonvulsant effects. No significant interactions with brain neurotransmitter or modulator receptor sites were found.

5.2 Pharmacodynamic Properties

Oxcarbazepine and its active metabolite (MHD), are potent and efficacious anticonvulsants in animals. They protected rodents against generalised tonic-clonic and, to a lesser degree, clonic seizures, and abolished or reduced the frequency of chronically recurring partial seizures in

Rhesus monkeys with aluminum implants. No tolerance (i.e. attenuation of anticonvulsive activity) against tonic-clonic seizures was observed when mice and rats were treated daily for 5 days or 4 weeks, respectively, with oxcarbazepine or MHD.

In a reported prospective, open-label, multicentre, non-comparative, 24-week observational post marketing study has been conducted in India. Out of a study population of 816 patients, 256 pediatric patients (1 month to 19 years) with generalised tonic-clonic seizures (either secondary or primary) were treated with oxcarbazepine monotherapy. The initial oxcarbazepine dose for all patients > 6 years was 8-10 mg/kg/day given in 2 divided doses. For the 27 subjects aged 1 month to 6 years, the dose range for the initial dose was 4.62 - 27.27 mg/kg/day and 4.29 - 30.00 mg/kg/day maintenance dose. The primary endpoint was reduction in seizure frequency from baseline at week 24. In the age group 1 month to 6 years (n=27) the number of seizures changed from 1 [range] [1-12] to 0 [0-2], in the age group 7 years to 12 years (n=77) the frequency changed from 1 [1-22] to 0 [0-1] and in the age group 13-19 years (n=152), the frequency changed from 1 [1-32] to 0 [0-3]. No specific safety concerns in the pediatric patients were identified. Data supporting benefit/risk from the study regarding children under the age of 6 are inconclusive.

Based on the data from the randomized controlled trials, the use of oxcarbazepine is not recommended in children below the age of 6 since safety and efficacy have not been adequately demonstrated.

Paediatric population

In a reported two randomised, rater-blinded, dose-controlled efficacy studies (Study 2339 and Study 2340) were conducted in paediatric patients aged 1 month to <17 years of age (n=31 patients aged 6 to <17 years; n=189 patients aged <6 years old). In addition, a number of open-label studies that enrolled children were conducted. In general, the safety profile of oxcarbazepine in younger children (<6 years old) was similar to that in older children (≥6 years old). However, in some studies in younger children (<4 years old) and older children (≥4 years old), a ≥ 5-fold difference in the proportion of patients with convulsions (7.9% vs. 1.0%, respectively) and status epilepticus (5% vs. 1%, respectively) was observed.

5.3 Pharmacokinetic Properties

Absorption

Following oral administration of OLEPTAL DT, oxcarbazepine is completely absorbed and extensively metabolised to its pharmacologically active metabolite (MHD).

After single dose administration of 600 mg OLEPTAL DT to healthy male volunteers under fasted conditions, the mean C_{max} value of MHD was 34 μmol/l, with a corresponding median t_{max} of 4.5 hours.

In a mass balance study in man, only 2 % of total radioactivity in plasma was due to unchanged oxcarbazepine, approximately 70 % was due to MHD, and the remainder attributable to minor secondary metabolites which were rapidly eliminated.

Food has no effect on the rate and extent of absorption of oxcarbazepine, therefore, OLEPTAL DT can be taken with or without food.

Distribution

The apparent volume of distribution of MHD is 49 litres.

Approximately 40 % of MHD, is bound to serum proteins, predominantly to albumin. Binding was independent of the serum concentration within the therapeutically relevant range. Oxcarbazepine and MHD do not bind to alpha-1-acid glycoprotein.

Oxcarbazepine and MHD cross the placenta. Neonatal and maternal plasma MHD concentrations were similar in one case.

Biotransformation

Oxcarbazepine is rapidly reduced by cytosolic enzymes in the liver to MHD, which is primarily responsible for the pharmacological effect of OLEPTAL DT. MHD is metabolised further by conjugation with glucuronic acid. Minor amounts (4 % of the dose) are oxidised to the pharmacologically inactive metabolite (10, 11-dihydroxy derivative, DHD).

Elimination

Oxcarbazepine is cleared from the body mostly in the form of metabolites which are predominantly excreted by the kidneys. More than 95 % of the dose appears in the urine, with less than 1 % as unchanged oxcarbazepine. Faecal excretion accounts for less than 4 % of the administered dose. Approximately 80 % of the dose is excreted in the urine either as glucuronides of MHD (49 %) or as unchanged MHD (27 %), whereas the inactive DHD accounts for approximately 3 % and conjugates of oxcarbazepine account for 13 % of the dose.

Oxcarbazepine is rapidly eliminated from the plasma with apparent half-life values between 1.3 and 2.3 hours. In contrast, the apparent plasma half-life of MHD averaged 9.3 ± 1.8 h.

Dose proportionality

Steady-state plasma concentrations of MHD are reached within 2 - 3 days in patients when OLEPTAL DT is given twice a day. At steady-state, the pharmacokinetics of MHD are linear and show dose proportionality across the dose range of 300 to 2,400 mg/day.

Special populations

Patients with hepatic impairment

The pharmacokinetics and metabolism of oxcarbazepine and MHD were evaluated in healthy volunteers and hepatically-impaired subjects after a single 900 mg oral dose. Mild to moderate hepatic impairment did not affect the pharmacokinetics of oxcarbazepine and MHD. OLEPTAL DT has not been studied in patients with severe hepatic impairment.

Patients with renal impairment

There is a linear correlation between creatinine clearance and the renal clearance of MHD. When OLEPTAL DT is administered as a single 300 mg dose, in renally impaired patients (creatinine clearance < 30 mL/min) the elimination half-life of MHD is prolonged by 60-90 % (16 to 19 hours) with a two-fold increase in AUC compared to adults with normal renal function (10 hours).

Children

The pharmacokinetics of OLEPTAL DT were evaluated in clinical trials in paediatric patients taking OLEPTAL DT in the dose range 10-60 mg/kg/day. Weight-adjusted MHD clearance decreases as age and weight increases approaching that of adults. The mean weight-adjusted clearance in children 4 to 12 years of age is approximately 40% higher than that of adults. Therefore, MHD exposure in these children is expected to be about two-thirds that of adults

when treated with a similar weight-adjusted dose. As weight increases, for patients 13 years of age and above, the weight-adjusted MHD clearance is expected to reach that of adults.

Pregnancy

Data from a limited number of women indicate that MHD plasma levels may gradually decrease throughout pregnancy (see section 4.6).

Elderly

Following administration of single (300 mg) and multiple doses (600 mg/day) of OLEPTAL DT in elderly volunteers (60 - 82 years of age), the maximum plasma concentrations and AUC values of MHD were 30 % - 60 % higher than in younger volunteers (18 - 32 years of age). Comparisons of creatinine clearances in young and elderly volunteers indicate that the difference was due to age-related reductions in creatinine clearance. No special dose recommendations are necessary because therapeutic doses are individually adjusted.

Gender

No gender related pharmacokinetic differences have been observed in children, adults, or the elderly.

6. NONCLINICAL PROPERTIES

6.1 Animal Toxicology or Pharmacology

Preclinical data indicated no special hazard for humans based on safety pharmacology and genotoxicity studies with oxcarbazepine and the pharmacologically active metabolite, monohydroxy derivative (MHD).

Evidence of nephrotoxicity was noted in repeated dose toxicity rat studies but not in dog or mice studies.

Immunotoxicity

Immunostimulatory tests in mice showed that MHD (and to a lesser extent oxcarbazepine) can induce delayed hypersensitivity.

Mutagenicity

Oxcarbazepine increased mutation frequencies in one Ames test in vitro in the absence of metabolic activation in one of five bacterial strains. Oxcarbazepine and MHD produced increases in chromosomal aberrations and/or polyploidy in the Chinese hamster ovary assay in vitro in the absence of metabolic activation. MHD was negative in the Ames test, and no mutagenic or clastogenic activity was found with either oxcarbazepine or MHD in V79 Chinese hamster cells in vitro. Oxcarbazepine and MHD were both negative for clastogenic or aneugenic effects (micronucleus formation) in an in vivo rat bone marrow assay.

Reproductive toxicity

It is reported that in rats, fertility in both sexes was unaffected by oxcarbazepine at oral doses up to 150 mg/kg/day, at which there is no safety margin. Disruption of estrous cyclicity and reduced numbers of corpora lutea, implantations and live embryos were observed in female animals for MHD at doses comparable to those in humans.

Standard reproductive toxicity studies in rodents and rabbits revealed effects such as increases in the incidence of embryo-foetal mortality and/or some delay in antenatal and/or postnatal growth of the offspring at maternally toxic dose levels. There was an increase in rat foetal

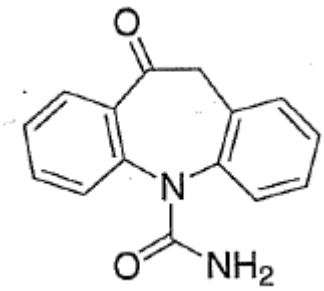
malformations in one of the eight embryo-foetal toxicity studies, which were conducted with either oxcarbazepine or MHD, at doses which also caused maternal toxicity (see section 4.6).

Carcinogenicity

In the carcinogenicity studies, liver (rats and mice), testicular and female genital tract granular cell (rats) tumours were induced in treated animals. The occurrence of liver tumours was most likely a consequence of the induction of hepatic microsomal enzymes; an inductive effect which, although it cannot be excluded, is weak or absent in patients treated with OLEPTAL DT. Testicular tumours may have been induced by elevated luteinizing hormone concentrations. Due to the absence of such an increase in humans, these tumours are considered to be of no clinical relevance. A dose-related increase in the incidence of granular cell tumours of the female genital tract (cervix and vagina) was noted in the rat carcinogenicity study with MHD. These effects occurred at exposure levels comparable with the anticipated clinical exposure. The mechanism for the development of these tumours has not been fully elucidated but could be related to increased estradiol levels specific to the rat. The clinical relevance of these tumours is unclear**.**

7. DESCRIPTION

The chemical name of Carbamazepine is 5-OXO-6*H*-benzo[b][1] benzazepine-11-carboxamide having molecule formula $C_{15}H_{12}N_2O_2$ and its molecular weight is 252.30. The chemical structure is:



Oxcarbazepine is an off-white to yellow crystalline powder.

Product Description:

OLEPTAL DT 150:

Light yellow coloured, round, biconvex uncoated tablets having fruity flavour.

OLEPTAL DT 300:

Light yellow coloured, round, biconvex uncoated tablets having fruity flavour.

OLEPTAL DT 450:

Light yellow coloured, flavoured, round, biconvex uncoated tablets with breakline on one side & plain on other side.

8. PHARMACEUTICAL PARTICULARS

8.1 Incompatibilities

Not applicable.

8.2 Shelf-life

Do not use later than expiry date.

8.3 Packaging information

OLEPTAL DT 150: Available in blister pack of 15 tablets.

OLEPTAL DT 300 & 450: Available in blister pack of 10 tablets.

8.4 Storage and Handing Instructions

Store at a temperature not exceeding 30^{o}C, Protected from light and moisture. Keep out of reach of children.

9. PATIENT COUNSELLING INFORMATION

OLEPTAL DT150 mg

OLEPTAL DT300 mg

OLEPTAL DT450 mg

Oxcarbazepine dispersible Tablets

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.

What is in this leaflet:

9.1. What OLEPTAL DT is and what it is used for

9.2. What you need to know before you take OLEPTAL DT

9.3. How to take OLEPTAL DT

9.4. Possible side effects

9.5. How to store OLEPTAL DT

9.6. Contents of the pack and other information

9.1 What OLEPTAL DT is

OLEPTAL DT contains the active substance oxcarbazepine. OLEPTAL DT belongs to a group of medicines called anticonvulsants or antiepileptics.

What OLEPTAL DT is used for

Medicines such as OLEPTAL DT are the standard treatment for epilepsy. Epilepsy is a brain disorder that causes people to have recurring seizures and convulsions. Seizures happen because of a temporary fault in the brain's electrical activity. Normally brain cells coordinate body movements by sending out signals through the nerves to the muscles in an organised, orderly way. In epilepsy, brain cells send out too many signals in a disorderly fashion. The result can be uncoordinated muscular activity that is called an epileptic seizure. OLEPTAL DT is used to treat partial seizures with or without secondarily

generalised tonic-clonic seizures. Partial seizures involve a limited area of the brain, but may spread to the whole brain and may cause a generalised tonic-clonic seizure. There are two types of partial seizures: simple and complex. In simple partial seizures, the patient remains conscious, whereas in complex partial seizures, patients consciousness is altered. OLEPTAL DT works by keeping the brain's "over excitable" nerve cells under control. This suppresses or reduces the frequency of such seizures. OLEPTAL DT can be used alone or in combination with other antiepileptic medicines.

- Usually, the doctor will try to find the one medicine that works best for you or for your child. However, with more severe epilepsy, a combination of two or more medicines may be needed to control seizures. OLEPTAL DTis for use in adults and in children of 6 years of age and above. If you have any questions about how OLEPTAL DT works or why this medicine has been prescribed for you, ask your doctor.

9.2. What you need to know before you take OLEPTAL DT

Follow all your doctor's instructions carefully, even if they differ from the general information contained in this leaflet.

Monitoring during your treatment with OLEPTAL DT Before and during your treatment with OLEPTAL DT, your doctor may perform blood tests to determine the dose for you. Your doctor will tell you when to have the tests.

Do not take OLEPTAL DT

- if you are allergic to oxcarbazepine or any of the other ingredients of this medicine (listed in section 6) or if you are allergic to eslicarbazepine. If this applies to you, tell your doctor before taking OLEPTAL DT. If you think you may be allergic, ask your doctor for advice.

Warnings and precautions

Talk to your doctor or pharmacist before taking OLEPTAL DT:

- if you have ever shown unusual sensitivity (rash or any other signs of allergy) to carbamazepine or to any other medicines. If you are allergic to carbamazepine, the chances are approximately 1 in 4 (25 %) that you could also have an allergic reaction to oxcarbazepine (OLEPTAL DT).

- if you have kidney disease.

- if you have serious liver disease.

- if you are taking diuretics (medicines used to help the kidneys get rid of salt and water by increasing the amount of urine produced).

- if you have heart disease, shortness of breath and/or swelling of the feet or legs due to fluid build-up.

- if your blood level of sodium is low as shown by blood tests (see section 4 Possible side effects).

- if you are a woman taking a hormonal contraceptive (such as "the birth-control pill"), OLEPTAL DT may stop your contraceptive from working. Use a different or extra (non-hormonal) method of contraception while taking OLEPTAL DT. This should help to prevent an unwanted pregnancy. Tell your doctor immediately if you get irregular vaginal bleeding or spotting. If you have any questions about this, ask your doctor or health professional.

The risk of serious skin reactions in patients of Han Chinese or Thai origin associated with carbamazepine or chemically-related compounds may be predicted by testing a blood sample of these patients. Your doctor should be able to advise if a blood test is necessary before taking oxcarbazepine.

If you develop any of the following symptoms after starting OLEPTAL DT, tell your doctor immediately or go to the emergency department at your nearest hospital:

- if you experience an allergic reaction after starting OLEPTAL DT. Symptoms include swelling of lips, eyelids, face, throat, mouth, or sudden breathing problems, fever with swollen glands, rash or skin blistering.
- if you notice symptoms of hepatitis, such as jaundice (yellowing of skin or the whites of the eyes).
- if you experience an increase in the frequency of seizures. This is particularly important for children but may also occur in adults.
- if you notice possible symptoms of blood disorders such as tiredness, being short of breath when exercising, looking pale, headache, chills, dizziness, frequent infections leading to fever, sore throat, mouth ulcers, bleeding or bruising more easily than normal, nose bleeds, reddish or purplish patches, or unexplained blotches on the skin.
- a small number of people being treated with antiepileptics such as OLEPTAL DT have had thoughts of harming or killing themselves. If at any time you have these thoughts, immediately contact your doctor.
- if you have a fast or unusually slow heartbeat.

Children and adolescents

In children, your doctor may recommend thyroid function monitoring before therapy and during therapy.

Other medicines and OLEPTAL DT

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines. This applies especially to:

- Hormonal contraceptives, such as the pill (see Warnings and precautions).
- Other antiepileptic and enzyme inducing medicines, such as carbamazepine, phenobarbital, phenytoin or lamotrigine and rifampicin.
- Medicines that reduce the level of sodium in your blood, such as diuretics (used to help the kidneys get rid of salt and water by increasing the amount of urine produced), desmopressin and nonsteroidal anti-inflammatory medicines, such as indometacin.
- Lithium and monoamine oxidase inhibitors (medicines used to treat mood swings and some types of depression).
- Medicines that control the body's immune system, such as ciclosporin and tacrolimus.

OLEPTAL DT with food and drink

OLEPTAL DT can be taken with or without food.

Alcohol may increase the sedative effects of OLEPTAL DT. Avoid alcohol as much as possible and ask your doctor for advice.

Pregnancy, breast-feeding and fertility

Pregnancy

If you are pregnant, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine. It is important to control epileptic seizures during pregnancy. However, there may be a risk to your baby if you take antiepileptic medicines during pregnancy. Your doctor will tell you the benefits and potential risks involved and help you to decide whether you should take OLEPTAL DT.

Do not stop your treatment with OLEPTAL DT during pregnancy without first checking with your doctor.

Breast-feeding

You should not breast-feed while taking OLEPTAL DT. The active substance in OLEPTAL DT passes into breast milk. This could cause side effects for breast-fed babies. Ask your doctor or pharmacist for advice before taking this medicine while you are breast-feeding.

Driving and using machines OLEPTAL DT may make you feel sleepy or dizzy, or may cause blurred vision, double vision, lack of muscle coordination or a depressed level of consciousness, especially when starting treatment or increasing the dose. It is important to discuss with your doctor whether you can drive a vehicle or operate machines while taking this medicine.

9.3. How to take OLEPTAL DT

Always take OLEPTAL DT exactly as your doctor or pharmacist has told you, even if this differs from the information given in this leaflet. Check with your doctor or pharmacist if you are not sure.

How much to take

Dose for adults

The usual starting dose of OLEPTAL DT for adults (including elderly patients) is 600 mg per day.

- Take one 300 mg tablet twice daily or two 150 mg tablets twice daily.
- Your doctor may increase the dose gradually to find the best dose for you. The best results are usually with doses between 600 and 2,400 mg per day.
- If you take another antiepileptic medicine, the dose is the same.
- If you have kidney disease (with impaired kidney function), the starting dose is half the usual starting dose.
- If you have severe liver disease, your doctor may adjust your dose. Dose for children OLEPTAL DT can be taken by children aged 6 years or above. The dosage for children depends on their weight. \
- The starting dose is 8 to 10 milligrams per kilogram of bodyweight per day given in two divided doses. For example, a 30-kg child would start treatment with one 150 mg tablet twice daily.

• Your doctor may increase the dose gradually to find the best dose for your child. The best results are usually with a dose of 30 milligrams per kilogram of bodyweight per day. The maximum dose for a child is 46 milligrams per kilogram of bodyweight per day.

Direction for use: Disperse the tablet in a tablespoonful of boiled and cooled water before administration.

The usual starting dose of OLEPTAL DT for adults (including elderly patients) is 600 mg per day.

- Take one 300 mg tablet twice daily or two 150 mg tablets twice daily.
- Your doctor may increase the dose gradually to find the best dose for you. The best results are usually with doses between 600 and 2,400 mg per day.
- If you take another antiepileptic medicine, the dose is the same.
- If you have kidney disease (with impaired kidney function), the starting dose is half the usual starting dose.
- If you have severe liver disease, your doctor may adjust your dose.

Dose for children

OLEPTAL DT can be taken by children aged 6 years or above.

The dosage for children depends on their weight.

- The starting dose is 8 to 10 milligrams per kilogram of bodyweight per day given in two divided doses. For example, a 30-kg child would start treatment with one 150 mg tablet twice daily.
- Your doctor may increase the dose gradually to find the best dose for your child. The best results are usually with a dose of 30 milligrams per kilogram of bodyweight per day. The maximum dose for a child is 46 milligrams per kilogram of bodyweight per day.

How to take OLEPTAL DT

- Swallow the tablets with a little water.
- If necessary, the tablets can be broken in half to help swallow them. Do not break the tablets to take only half of the dose. The score line was not designed for dividing the tablet into equal doses.
- For small children who cannot swallow tablets, or who cannot be given the necessary dose in tablet form, OLEPTAL DTis available as an oral suspension.

When and for how long to take OLEPTAL DT

Take OLEPTAL DT twice a day, every day, at about the same time of day, unless the doctor tells you otherwise. This will have the best effect on controlling epilepsy. It will also help you to remember when to take the tablet(s).

Your doctor will tell you how long your or your child’s treatment with OLEPTAL DTwill last. The length of treatment will depend on your or your child’s seizure type. Treatment may be needed for many years to control the seizures. Do not change the dose or stop treatment without talking to your doctor.

If you take more OLEPTAL DT than you should

If you have taken more tablets than your doctor prescribed, contact the nearest hospital or your doctor immediately. Symptoms of overdose with OLEPTAL DT may include:

- drowsiness, dizziness, problems with coordination and/or involuntary movement of the eyes, muscular twitching or significant worsening of convulsions, headache, loss of consciousness, coma,
- feeling sick (nausea), being sick (vomiting), increased uncontrolled movements,
- lethargy, double vision, narrowing of black part of the eye, blurred vision,
- tiredness,
- short and shallow breathing (respiratory rate depression),
- irregular heart beat (QTc prolonged interval),
- trembling, headache, coma, decreased consciousness, uncontrollable movements of mouth, tongue and limbs,
- aggression, agitation, confusion,
- low blood pressure,
- breathlessness.

If you forget to take OLEPTAL DT

If you have forgotten one dose, take it as soon as you remember. However, if it is time for your next dose,

do not take the missed dose. Go back to your regular dosing timetable. Do not take a double dose to make up for a forgotten dose.

If you are unsure or have forgotten to take several doses, contact your doctor.

If you stop taking OLEPTAL DT

Do not stop taking your medicine unless your doctor tells you to.

To prevent sudden worsening of your seizures, never discontinue your medicine abruptly.

If your treatment is stopped, it should be done gradually as instructed by your doctor.

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

9.4. Possible side effects:

Like all medicines, this medicine can cause side effects, although not everybody gets them. **Tell your doctor immediately or go to the emergency department at your nearest hospital if you get any of the following side effects**:

The following are signs of very rare (may affect up to 1 in 10,000 people), but potentially serious side effects that may require urgent medical treatment. The doctor will also decide whether Oleptal DT has to be stopped immediately and how to continue further medical care.

• Swelling of the lips, eyelids, face, throat or mouth, accompanied by difficulty in breathing, speaking or swallowing (signs of anaphylactic reactions and angioedema) or other signs of hypersensitivity reactions such as skin rash, fever, and pain in the muscles and joints.

• Severe blistering of the skin and/or mucous membranes of the lips, eyes, mouth, nasal passages or genitals (signs of serious allergic reaction including Lyell's syndrome, Stevens-Johnson syndrome and erythema multiforme).

• Tiredness, shortness of breath when exercising, looking pale, headache, chills, dizziness, frequent infections leading to fever, sore throat, mouth ulcers, bleeding or bruising more easily than normal, nose bleeds, reddish or purplish patches, or unexplained blotches on the skin (signs of a decrease in the number of blood platelets or decrease in the number of blood cells).
• Red blotchy rash mainly on face which may be accompanied by fatigue, fever, feeling sick (nausea) or loss of appetite (signs of systemic lupus erythematosus).

• Lethargy, confusion, muscle twitching or significant worsening of convulsions (possible symptoms of low sodium levels in the blood) (see Warnings and precautions).

• Flu-like symptoms with jaundice (yellowing of the skin or the whites of the eyes) (signs of hepatitis).

• Severe upper stomach (abdominal) pain, being sick (vomiting), loss of appetite (signs of inflammation of the pancreas).

• Weight gain, tiredness, hair loss, muscle weakness, feeling cold (signs of under active thyroid gland).

Tell your doctor as soon as possible if you get any of the following side effects, they may require medical attention:

Common (may affect up to 1 in 10 people):

• trembling; coordination problems; involuntary movement of the eyes; anxiety and nervousness; depression, mood swing; rash. Very rare (may affect up to 1 in 10,000 people):

• irregular heart beat or a very fast or slow heart rate.

Other side effects that may occur:

These are usually mild to moderate side effects of Oleptal DT. Most of these effects are transient and usually diminish over time.

Very common (may affect more than 1 in 10 people): • tiredness; headache; dizziness; drowsiness; feeling sick (nausea); being sick (vomiting); double vision.

Common (may affect up to 1 in 10 people):

• weakness; memory disturbances; impaired concentration; apathy; agitation; confusion; blurred vision; visual disturbance; constipation; diarrhoea; stomach (abdominal) pain; acne; hair loss, balance disturbances; weight increased.

Uncommon (may affect up to 1 in 100 people):

• hives. You may also have raised levels of liver enzymes while taking Oleptal DT.

Not known (frequency cannot be estimated from the available data):

• high blood pressure, speech disorder.

• there have been reports of bone disorders including osteopenia and osteoporosis (thinning of the bone) and fractures. Check with your doctor or pharmacist if you are on long-term antiepileptic medication, have a history of osteoporosis or take steroids.

Reporting of side effects

If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via any point of contact of Torrent Pharma available at:

http://www.torrentpharma.com/Index.php/site/info/adverse_event_reporting

9.5. How to store OLEPTAL DT

Store at a temperature not exceeding 30°C, Protected from light and moisture. Keep out of reach of children.

9.6. Contents of the pack and other information

What OLEPTAL DT contains

- The active substance is Oxcarbazepine
- **Other ingredients are:**

Ferric oxide yellow, Sodium saccharin, Pineapple flavour, Citric acid anhydrous, Microcrystalline cellullose, Starch, Magnesium stearate, Polyvinyl pyrrolidone, Crosspovidone, Colloidal silicon dioxide, Aspartame.

10. DETAILS OF MANUFACTURER

TORRENT PHARMACEUTICALS LTD.
32 No., Middle Camp, NH-10,
East District, Gangtok, Sikkim-737 135.
OR
Manufactured By:
Ravenbhel Biotech
EPIP, SIDCO, Kartholi, Bari-Brahmana, Jammu-181133

11. DETAILS OF PERMISSION OR LICENCE NUMBER WITH DATE

M/563/2010 issued on 24.04.2015

Ravenbhel Biotech

JK/01/11-12/192 issued on 10-10.2020

12. DATE OF REVISION

Nov/2020

MARKETED BY

TORRENT PHARMACEUTICALS LTD.

IN/OLEPTAL DT 150,300,450 mg/Nov-20/05/PI