Levipram® IV

Levetiracetam

FORMS AND PRESENTATION
Levipram® IV; 500mg/100ml; solution for infusion; 1 pouch of 100 ml.
Levipram® IV; 1000mg/100ml; solution for infusion; 1 pouch of 100 ml.
Levipram® IV; 1500mg/100ml; solution for infusion; 1 pouch of 100 ml.

COMPOSITION
Levipram® IV 500mg/100ml:
Each ml contains 5 mg of levetiracetam.
Each pouch of 100 ml contains 500 mg of levetiracetam.
Levipram® IV 1000mg/100ml:
Each ml contains 10 mg of levetiracetam.
Each pouch of 100 ml contains 1000 mg of levetiracetam.
Levipram® IV 1500mg/100ml:
Each ml contains 15 mg of levetiracetam.
Each pouch of 100 ml contains 1500 mg of levetiracetam.
Excipients: Sodium Chloride, Glacial Acetic Acid, Sodium Acetate Trihydrate, Water for Injection.

PHARMACOLOGICAL PROPERTIES
Pharmacodynamic properties
Pharmacotherapeutic group: antiepileptics, other antiepileptics, ATC code: N03AX14.
The active substance, levetiracetam, is a pyrrolidone derivative (S-enantiomer of a-ethyl-2oxo-1-pyrrolidine acetamide), chemically unrelated to existing antiepileptic active substances.
Mechanism of action
The mechanism of action of levetiracetam still remains to be fully elucidated.
In vitro and in vivo experiments suggest that levetiracetam does not alter basic cell characteristics and normal neurotransmission.
In vitro studies show that levetiracetam affects intraneuronal Ca^{2+} levels by partial inhibition of N-type Ca^{2+} currents and by reducing the release of Ca^{2+} from intraneuronal stores. In addition, it partially reverses the reductions in GABA- and glycine-gated currents induced by zinc and ß-carbolines. Furthermore, levetiracetam has been shown in in vitro studies to bind to a specific site in rodent brain tissue. This binding site is the synaptic vesicle protein 2A believed to be involved in vesicle fusion and neurotransmitter exocytosis. Levetiracetam and related analogues show a rank order of affinity for binding to the synaptic vesicle protein 2A which correlates with the potency of their anti-seizure protection in the mouse audiogenic model of epilepsy. This finding suggests that the interaction between levetiracetam and the synaptic vesicle protein 2A seems to contribute to the antiepileptic mechanism of action of the medicinal product.
Pharmacodynamic effects
Levetiracetam induces seizure protection in a broad range of animal models of partial and primary generalized seizures without having a pro-convulsant effect. The primary metabolite is inactive.
In man, an activity in both partial and generalized epilepsy conditions (epileptiform discharge/photoparoxysmal response) has confirmed the broad spectrum pharmacological profile of levetiracetam.
Pharmacokinetic properties
The pharmacokinetic profile has been characterized following oral administration. A single dose of 1500 mg levetiracetam diluted in 100 ml of a compatible diluent and infused intravenously over 15 minutes is bioequivalent to 1500 mg levetiracetam oral intake, given as three 500 mg tablets.
The intravenous administration of doses up to 4000 mg diluted in 100 ml of 0.9 % sodium chloride infused over 15 minutes and doses up to 2500 mg diluted in 100 ml of 0.9 % sodium chloride infused over 5 minutes was evaluated. The pharmacokinetic and safety profiles did not identify any safety concerns.
Levetiracetam is a highly soluble and permeable compound. The pharmacokinetic profile is linear with low intra- and inter-subject variability. There is no modification of the clearance after repeated administration. The time independent pharmacokinetic profile of levetiracetam was also confirmed following 1500 mg intravenous infusion for 4 days with b.i.d dosing.
There is no evidence for any relevant gender, race or circadian variability. The pharmacokinetic profile is comparable in healthy volunteers and in patients with epilepsy.
Adults and adolescents
Distribution
Peak plasma concentration (Cmax) observed in 17 subjects following a single intravenous dose of 1500 mg infused over 15 minutes was 51 ± 19 µg/ml (arithmetic average ± standard deviation).
No tissue distribution data are available in humans.
Neither levetiracetam nor its primary metabolite are significantly bound to plasma proteins (<10 %). The volume of distribution of levetiracetam is approximately 0.5 to 0.7 l/kg, a value close to the total body water volume.
Biotransformation
Levetiracetam is not extensively metabolized in humans. The major metabolic pathway (24 % of the dose) is an enzymatic hydrolysis of the acetamide group. Production of the primary metabolite, ucb L057, is not supported by liver cytochrome P450 isoforms. Hydrolysis of the acetamide group was measurable in a large number of tissues including blood cells. The metabolite ucb L057 is pharmacologically inactive.
Two minor metabolites were also identified. One was obtained by hydroxylation of the pyrrolidone ring (1.6 % of the dose) and the other one by opening of the pyrrolidone ring (0.9 % of the dose). Other unidentified components accounted only for 0.6 % of the dose.
No enantiomeric interconversion was evidenced in vivo for either levetiracetam or its primary metabolite.
In vitro, levetiracetam and its primary metabolite have been shown not to inhibit the major human liver cytochrome P450 isoforms (CYP3A4, 2A6, 2C9, 2C19, 2D6, 2E1 and 1A2), glucuronyl transferase (UGT1A1 and UGT1A6) and epoxide hydroxylase activities. In addition, levetiracetam does not affect the in vitro glucuronidation of valproic acid.
In human hepatocytes in culture, levetiracetam had little or no effect on CYP1A2, SULT1E1 or UGT1A1. Levetiracetam caused mild induct ion of CYP2B6 and CYP3A4. The in vitro data and in vivo interact ion data on oral contraceptives, digoxin and warfarin indicate that no significant enzyme inducer ion is expected in vivo. Therefore, the interaction of Levetiracetam with other substances, or vice versa, is unlikely.
Elimination
The plasma half-life in adults was 7±1 hours and did not vary either with dose, route of administration or repeated administration. The mean total body clearance was 0.96 ml/ min/kg.
The major route of excretion was via urine, accounting for a mean 95 % of the dose (approximately 93 % of the dose was excreted within 48 hours). Excretion via faeces accounted for only 0.3 % of the dose.
The cumulative urinary excretion of levetiracetam and its primary metabolite accounted for 66% and 24 % of the dose, respectively during the first 48 hours.
The renal clearance of levetiracetam and ucb L057 is 0.6 and 4.2 ml/ min/kg respectively indicating that levetiracetam is excreted by glomerular filtration with subsequent tubular reabsorption and that the primary metabolite is also excreted by active tubular secret ion in addition to glomerular filtration. Levetiracetam elimination is correlated to creatinine clearance.
Elderly
In the elderly, the half-life is increased by about 40 % (10 to 11 hours). This is related to the decrease in renal function in this population.
Renal impairment
The apparent body clearance of both levetiracetam and of its primary metabolite is correlated to the creatinine clearance. It is therefore recommended to adjust the maintenance daily dose of Levetiracetam, based on creatinine clearance in patients with moderate and severe renal impairment.
In anuric end-stage renal disease adult subjects the half-life was approximately 25 and 3.1 hours during interdialytic and intradialytic periods, respectively.
The fractional removal of levetiracetam was 51 % during a typical 4-hour dialysis session.
Hepatic impairment
In subjects with mild and moderate hepatic impairment, there was no relevant modification of the clearance of levetiracetam. In most subjects with severe hepatic impairment, the clearance of levetiracetam was reduced by more than 50 % due to a concomitant renal impairment.
Pediatric population
Children (4 to 12 years)
The pharmacokinetics in pediatric patients has not been investigated after intravenous administration. However, based on the pharmacokinetic characteristics of levetiracetam, the pharmacokinetics in adults after intravenous administration and the pharmacokinetics in children after oral administration, the exposure (AUC) of levetiracetam is expected to be similar in pediatric patients aged 4 to 12 years after intravenous and oral administration.
Following single oral dose administration (20 mg/kg) to epileptic children (6 to 12 years), the half-life of levetiracetam was 6.0 hours. The apparent body weight adjusted clearance was approximately 30 % higher than in epileptic adults.
Following repeated oral dose administration (20 to 60 mg/kg/day) to epileptic children (4 to 12 years), levetiracetam was rapidly absorbed. Peak plasma concentration was observed 0.5 to 1.0 hour after dosing. Linear and dose proportional increases were observed for peak plasma concentrations and area under the curve. The elimination half-life was approximately 5 hours.
The apparent body clearance was 1.1 ml/ min/kg.

INDICATIONS
Levipram® IV is indicated as monotherapy in the treatment of partial onset seizures with or without secondary generalization in adults and adolescents from 16 years of age with newly diagnosed epilepsy.
Levipram® IV is indicated as adjunctive therapy:
• in the treatment of partial onset seizures with or without secondary generalization in adults, adolescents and children from 4 years of age with epilepsy.
• in the treatment of myoclonic seizures in adults and adolescents from 12 years of age with Juvenile Myoclonic Epilepsy.
• in the treatment of primary generalized tonic-clonic seizures in adults and adolescents from 12 years of age with Idiopathic Generalized Epilepsy.
Levipram® IV is an alternative for patients when oral administration is temporarily not feasible.

CONTRAINDICATIONS
Hypersensitivity to the active substance or other pyrrolidone derivatives or to any of the listed excipients.

PRECAUTIONS
Renal impairment
The administration of levetiracetam to patients with renal impairment may require dose adjustment. In patients with severely impaired hepatic function, assessment of renal function is recommended before dose selection.
Suicide
Suicide, suicide attempt, suicidal ideation and behavior have been reported in patients treated with anti-epileptic agents (including levetiracetam). A meta-analysis of randomized placebo-controlled trials of anti-epileptic medicinal products has shown a small increased risk of suicidal thoughts and behavior. The mechanism of this risk is not known.
Therefore patients should be monitored for signs of depression and/or suicidal ideation and behaviors and appropriate treatment should be considered. Patients (and caregivers of patients) should be advised to seek medical advice should signs of depression and/or suicidal ideation or behavior emerge.
Pediatric population
Available data in children did not suggest impact on growth and puberty. However, long term effects on learning, intelligence, growth, endocrine function, puberty and childbearing potential in children remain unknown.

Excipients:
Levipram® IV 5 mg/ml contains 9.84 mg of sodium per ml.
Levipram® IV 10 mg/ml contains 9.14 mg of sodium per ml.
Levipram® IV 15 mg/ml contains 7.04 mg of sodium per ml.
To be taken into consideration by patients on a controlled sodium diet.

Effects on ability to drive and use machines
Levetiracetam has minor or moderate influence on the ability to drive and use machines.
Due to possible different individual sensitivity, some patients might experience somnolence or other central nervous system related symptoms, especially at the beginning of treatment or following a dose increase. Therefore, caution is recommended in those patients when performing skilled tasks, e.g. driving vehicles or operating machinery. Patients are advised not to drive or use machines until it is established that their ability to perform such activities is not affected.

FERTILITY, PREGNANCY AND LACTATION
Pregnancy
Post-marketing data from several prospective pregnancy registries have documented outcomes in over 1000 women exposed to levetiracetam monotherapy during the first trimester of pregnancy. Overall, these data do not suggest a substantial increase in the risk for major congenital malformations, although a teratogenic risk cannot be completely excluded. Therapy with multiple antiepileptic medicinal products is associated with a higher risk of congenital malformations than monotherapy and therefore monotherapy should be considered.
Studies in animals have shown reproductive toxicity.
Levetiracetam is not recommended during pregnancy and in women of childbearing potential not using contraception unless clinically necessary. Decrease in levetiracetam plasma concentrations has been observed during pregnancy. This decrease is more pronounced during the third trimester (up to 60% of baseline concentration before pregnancy). Appropriate clinical management of pregnant women treated with levetiracetam should be ensured. Discontinuation of antiepileptic ±treatments may result in exacerbation of the disease which could be harmful to the mother and the foetus.
Breastfeeding
Levetiracetam is excreted in human breast milk. Therefore, breast-feeding is not recommended. However, if levetiracetam treatment is needed during breast feeding, the benefit/risk of the treatment should be weighed considering the importance of breast feeding.
Fertility
No impact on fertility was detected in animal studies. No clinical data are available, potential risk for human is unknown.

DRUG INTERACTIONS
Antiepileptic medicinal products
Pre-marketing data from clinical studies conducted in adults indicate that levetiracetam did not influence the serum concentrations of existing antiepileptic medicinal products (phenytoin, carbamazepine, valproic acid, phenobarbital, lamotrigine, gabapent in and primidone) and that these antiepileptic medicinal products did not influence the pharmacokinetics of levetiracetam.
As in adults, there is no evidence of clinically significant medicinal product interactions in pediatric patients receiving up to 60 mg/kg/day levetiracetam.
A retrospective assessment of pharmacokinetic interactions in children and adolescents with epilepsy (4 to 17 years) confirmed that adjunctive therapy with orally administered levetiracetam did not influence the steady-state serum concentrations of concomitantly administered carbamazepine and valproate. However, data suggested a 20 % higher levetiracetam clearance in children taking enzyme- inducing antiepileptic medicinal products. Dose adjustment is not required.
Probenecid
Probenecid (500 mg four times daily), a renal tubular secretion blocking agent, has been shown to inhibit the renal clearance of the primary metabolite, but not of levetiracetam. Nevertheless, the concentration of this metabolite remains low.
Oral contraceptives and other pharmacokinetics interactions
Levetiracetam 1,000 mg daily did not influence the pharmacokinetics of oral contraceptives (ethinyl- estradiol and levonorgestrel); endocrine parameters (luteinizing hormone and progesterone) were not modified. Levetiracetam 2,000 mg daily did not influence the pharmacokinetics of digoxin and warfarin; prothrombin times were not modified. Co-administration with digoxin, oral contraceptives and warfarin did not influence the pharmacokinetics of levetiracetam.
Alcohol
No data on the interaction of levetiracetam with alcohol are available.

ADVERSE EFFECTS
The frequency of the adverse reactions reported is defined as follows: 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) and very rare (<1/10,000).
Infections and infestations: Nasopharyngitis (very common); infection (rare).
Blood and lymphatic system disorders: Thrombocytopenia, leukopenia (uncommon); Pancytopenia, neutropenia, agranulocytosis (rare).
Immune system disorders: Drug reaction with eosinophilia and systemic symptoms (DRESS), hypersensitivity (including angioedema and anaphylaxis) (rare).
Metabolism and nutrition disorders: Anorexia (common); weight decreased, weight increase (uncommon); Hyponatraemia (rare).
Psychiatric disorders: Depression, hostility/ aggression, anxiety, insomnia, nervousness/irritability (common); Suicide attempt, suicidal ideation, psychotic disorder, abnormal behavior, hallucination, anger, confusional state, panic attack, affectlability/mood swings, agitation (uncommon); Completed suicide, personality disorder, thinking abnormal (rare).
Nervous system disorders: Somnolence, headache (very common); Convulsion, balance disorder, dizziness, lethargy, tremor (common); amnesia, memory impairment, coordination abnormal/ataxia, paraesthesia, disturbance in attention (uncommon); Choreoathetosis, dyskinesia, hyperkinesia (rare).
Eye disorders: Diplopia, vision blurred (uncommon).
Ear and labyrinth disorders: Vertigo (common).
Respiratory, thoracic and mediastinal disorders: Cough (common).
Gastrointestinal disorders: Abdominal pain, diarrhea, dyspepsia, vomiting, nausea (common); Pancreatitis (rare).
Hepatobiliary disorders: Liver function test abnormal (uncommon); Hepatic failure, hepatitis (rare).
Skin and subcutaneous tissue disorders: Rash (common); Alopecia, eczema, pruritus, (uncommon); Toxic epidermal necrolysis, Stevens-Johnson syndrome, erythema multiforme (rare).
Musculoskeletal and connective tissue disorders: Muscular weakness, myalgia (uncommon).
General disorders and administration: Athenia/fatigue (common).
Injury, poisoning and procedural complications: Injury (uncommon).

DOSAGE AND ADMINISTRATION
Posology
Monotherapy for adults and adolescents from 16 years of age:
The recommended starting dose is 250 mg twice daily which should be increased to an initial therapeutic dose of 500 mg twice daily after two weeks. The dose can be further increased by 250 mg twice daily every two weeks depending upon the clinical response. The maximum dose is 1500 mg twice daily.
Add-on therapy for adults (≥ 18 years) and adolescents (12 to 17 years) weighing 50 kg or more:
The initial therapeutic dose is 500 mg twice daily. This dose can be started on the first day of treatment.
Depending upon the clinical response and tolerability, the daily dose can be increased up to 1500 mg twice daily. Dose changes can be made in 500 mg twice daily increases or decreases every two to four weeks.
Duration of treatment
There is no experience with administration of intravenous levetiracetam for longer period than 4 days.
Discontinuation
In accordance with current clinical practice, if levetiracetam has to be discontinued it is recommended to withdraw it gradually (e.g. in adults and adolescents weighing more than 50 kg: 500 mg decreases twice daily every two to four weeks; in children and adolescents weighing less than 50 kg: dose decrease should not exceed 10 mg/kg twice daily every two weeks).
Special populations
Elderly (65 years and older)
Adjustment of the dose is recommended in elderly patients with compromised renal function (see "Renal impairment" below).
Renal impairment
The daily dose must be individualized according to renal function.
For adult patients, refer to the following table and adjust the dose as indicated. To use this dosing table, an estimate of the patient's creatinine clearance (CLcr) in ml/ min is needed. The CLcr in ml/ min maybe estimated from serum creatinine (mg/dl) determination, for adults and adolescents weighing 50 kg or more, the following formula:

$$CLcr(ml/min) = \frac{[140 - age(years)] \times weight\ (kg)}{72 \times serum\ creatinine\ (mg/dl)} \quad (\times 0.85 \text{ for women})$$

Then CLcr is adjusted for body surface area (BSA) as follows:

$$CLcr(ml/min/1.73m^2) = \frac{CLcr(ml/min)}{BSA\ subject\ (m^2)} \times 1.73$$

Dosing adjustment for adult and adolescents patients weighing more than 50 kg with impaired renal function

Group	Creatinine clearance (ml/min/1.73 m²)	Dose and frequency
Normal	> 80	500 to 1,500 mg twice daily
Mild	50-79	500 to 1,000 mg twice daily
Moderate	30-49	250 to 750 mg twice daily
Severe	< 30	250 to 500 mg twice daily
End-stage renal disease patients undergoing dialysis[1]	--	500 to 1,000 mg once daily[2]

(1) A 750 mg loading dose is recommended on the first day of treatment with levetiracetam.
(2) Following dialysis, a 250 to 500 mg supplemental dose is recommended.

For children with renal impairment, levetiracetam dose needs to be adjusted based on the renal function as levetiracetam clearance is related to renal function. This recommendation is based on a study in adult renally impaired patients.
The CLcr in ml/ min/1.73 m² may be estimated from serum creatinine (mg/dl) determination using, for young adolescents and children using the following formula (Schwartz formula):

$$CLcr(ml/min/1.73m^2) = \frac{Height\ (cm) \times ks}{Serum\ creatinine\ (mg/dl)}$$

Ks=0.55 in children to less than 13 years and in adolescent female; ks=0.7 in adolescent male.
Dosing adjustment for children and adolescents patients weighing less than 50 kg with impaired renal function:
Normal Group (Creatinine clearance: > 80 ml/min/1.73 m²):
Dose and frequency in Children from 4 years and adolescents weighing less than 50 kg
• 5 mg/ml: 10 to 30 mg/kg (2 to 6 ml/kg) twice daily
• 10 mg/ml: 10 to 30 mg/kg (1 to 3 ml/kg) twice daily
• 15 mg/ml: 10 to 30 mg/kg (0.66 to 2 ml/kg) twice daily
Mild Group (Creatinine clearance: 50 - 79 ml/min/1.73 m²):
Dose and frequency in Children from 4 years and adolescents weighing less than 50 kg
• 5 mg/ml: 10 to 20 mg/kg (2 to 4 ml/kg) twice daily
• 10 mg/ml: 10 to 20 mg/kg (1 to 2 ml/kg) twice daily
• 15 mg/ml: 10 to 20 mg/kg (0.66 to 1.33 ml/kg) twice daily
Moderate Group (Creatinine clearance: 30-49 ml/min/1.73 m²):
Dose and frequency in Children from 4 years and adolescents weighing less than 50 kg
• 5 mg/ml: 5 to 15 mg/kg (1 to 3 ml/kg) twice daily
• 10 mg/ml: 5 to 15 mg/kg (0.5 to 1.5 ml/kg) twice daily
• 15 mg/ml: 5 to 15 mg/kg (0.33 to 1 ml/kg) twice daily
Severe Group (Creatinine clearance: < 30 ml/min/1.73 m²):
Dose and frequency in Children from 4 years and adolescents weighing less than 50 kg
• 5 mg/ml: 5 to 10 mg/kg (1 to 2 ml/kg) twice daily
• 10 mg/ml: 5 to 10 mg/kg (0.5 to 1 ml/kg) twice daily
• 15 mg/ml: 5 to 10 mg/kg (0.33 to 0.66 ml/kg) twice daily
End-stage renal disease patients undergoing dialysis:
Dose and frequency in Children from 4 years and adolescents weighing less than 50 kg
• 5 mg/ml: 10 to 20 mg/kg (2 to 4 ml/kg) once daily (1) (2)
• 10 mg/ml: 10 to 20 mg/kg (1 to 2 ml/kg) once daily (1) (2)
• 15 mg/ml: 10 to 20 mg/kg (0.66 to 1.33 ml/kg) once daily (1) (2)
(1) A 15 mg/kg loading dose is recommended on the first day of treatment with levetiracetam.
(2) Following dialysis, a 5 to 10 mg/kg supplemental dose is recommended

Hepatic impairment
No dose adjustment is needed in patients with mild to moderate hepatic impairment. In patients with severe hepatic impairment, the creatinine clearance may underestimate the renal insufficiency. Therefore a 50 % reduction of the daily maintenance dose is recommended when the creatinine clearance is < 60 ml/ min/1.73 m2.
Pediatric population
The physician should prescribe the most appropriate pharmaceutical form, presentation and strength according to age, weight and dose.
Monotherapy
The safety and efficacy of levetiracetam in children below and adolescents 16 years as monotherapy treatment have not been established.
There are no data available.
Add-on therapy for children aged 4 to 11 years and adolescents (12 to 17 years) weighing less than 50 kg
The initial therapeutic dose is 10 mg/kg twice daily.
Depending upon the clinical response and tolerability, the dose can be increased up to 30mg/kg twice daily. Dose changes should not exceed increases or decreases of 10 mg/kg twice daily every two weeks. The lowest effective dose should be used.
Dose in children 50 kg or greater is the same as in adults.
Dose recommendations for children and adolescents:

Weight	Starting dose: 10 mg/kg twice daily	Maximum dose: 30 mg/kg twice daily
15 kg[1]	150 mg twice daily	450 mg twice daily
20 kg[1]	200 mg twice daily	600 mg twice daily
25 kg	250 mg twice daily	750 mg twice daily
from 50 kg[2]	500 mg twice daily	1500 mg twice daily

(1) Children 25 kg or less should preferably start the treatment with an oral solution.
(2) Dose in children and adolescents 50 kg or more is the same as in adults.
Add-on therapy for infants and children less than 4 years
The safety and efficacy of Levetiracetam SUN concentrate for solution for infusion in infants and children less than 4 years have not been established.

Method of administration
Levetiracetam therapy can be initiated with either intravenous or oral administration.
Conversion to or from oral to intravenous administration can be done directly without titration.
The total daily dose and frequency of administration should be maintained.
Levipram® IV is for intravenous use only. The ready-to-use solution is for single use only. It does not need to be further diluted and should be administered intravenously over a 15-minutes intravenous infusion.
Attention: Concentration differs from other Levetiracetam containing products for intravenous use.
Medicinal product with particulate matter or discoloration should not be used.

OVERDOSAGE
Symptoms
Somnolence, agitation, aggression, depressed level of consciousness; respiratory depression and coma were observed with levetiracetam overdoses.
Management of overdose
There is no specific antidote for levetiracetam. Treatment of an overdose will be symptomatic and may include hemodialysis. The dialyzer extraction efficiency is 60 % for levetiracetam and 74 % for the primary metabolite.

SPECIAL PRECAUTIONS FOR DISPOSAL AND OTHER HANDLING
This medicinal product is for single use only; any unused solution should be discarded.
Any unused medicinal product or waste material should be disposed of in accordance with local requirements.
From a microbiological point of view, the product should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 24 hours at 2 to 8°C.

STORAGE CONDITIONS
Store below 25°C.
Keep in original pack in intact conditions.

Manufactured by InfoRLife SA, Switzerland
for Benta S.A.L, Lebanon

Date of Revision: July 2018.

This is a medicament
- A medicament is a product which affects your health, and its consumption contrary to instructions is dangerous for you.
- Follow strictly the doctor's prescription, the method of use, and the instructions of the pharmacist who sold the medicament.
- The doctor and the pharmacist are experts in medicine, its benefits and risks.
- Do not by yourself interrupt the period of treatment prescribed for you.
- Do not repeat the same prescription without consulting your doctor.
- Medicament: keep out of reach of children.

Council of Arab Health Ministers
Union of Arab Pharmacists

Benta S.A.L.,
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