Olmec 20 mg - 40 mg
Olmesartan medoxomil

Coated tablets

Made in Argentina - Rx Only

FORMULAS:
Each coated tablet of **OLMEC 20 mg** contains: Olmesartan medoxomil 20 mg. Excipients: cellactose, sodium starch glycolate, magnesium stearate, hydroxypropyl methylcellulose, polyethylene glycol 6000, titanium dioxide q.s.
Each coated tablet of **OLMEC 40 mg** contains: Olmesartan medoxomil 40 mg. Excipients: cellactose, sodium starch glycolate, magnesium stearate, hydroxypropyl methylcellulose, polyethylene glycol 6000, titanium dioxide q.s.

THERAPEUTIC ACTION:
Antihypertensive.

INDICATIONS:
Olmesartan is indicated for the treatment of hypertension. It may be used alone or combined with other antihypertensive agents.

PHARMACOLOGICAL ACTION:
Olmesartan is an AT1 angiotensin II receptor subtype selective antagonist. Angiotensin II is formed from angiotensin I in a reaction catalyzed by angiotensin converting enzyme (ACE). Angiotensin II is the principal pressor agent of the renin-angiotensin system and it plays a significant role in the physiopathology of arterial hypertension, with effects that include vasoconstriction, stimulation of synthesis and release of aldosterone, cardiac stimulation and renal reabsorption of sodium. Olmesartan blocks the vasoconstrictor effects of angiotensin II, by blocking selectively the binding of angiotensin II to the AT1 receptor in the vascular smooth muscle. Its action is, therefore, independent of the pathways for angiotensin II synthesis. Repeated administration of up to 80 mg olmesartan medoxomil had minimal influence on aldosterone levels and no effect on serum potassium. In clinical trials, the blood pressure lowering effect was maintained throughout a 24-hour period, with olmesartan once daily. There was no evidence of tachyphylaxis during the long-term treatment with olmesartan or rebound effect following abrupt withdrawal of olmesartan medoxomil after one year of treatment. The antihypertensive effect of olmesartan was similar in men and women and in patients older and younger than 65. Olmesartan proved to have an additional blood pressure lowering effect when added to hydrochlorothiazide.

PHARMACOKINETICS:
Olmesartan medoxomil is rapidly and completely bioactivated by hydrolysis to olmesartan during absorption from the gastrointestinal tract. Olmesartan appears to be eliminated in a biphasic manner with a terminal elimination half-life of approximately 13 hours. Olmesartan shows linear pharmacokinetics following single oral doses of up to 320 mg and multiple oral doses of up to 80 mg. Steady-state levels of olmesartan are achieved within 3 to 5 days and no accumulation in plasma occurs with once-daily dosing. The absolute bioavailability of olmesartan is approximately 26%. After oral administration the peak plasma concentration (Cmax) is reached after 1 to 2 hours. Food does not affect the bioavailability of olmesartan. Following the rapid and complete conversion of olmesartan medoxomil to olmesartan during absorption, there is virtually no further metabolism of olmesartan. Total plasma clearance of olmesartan is 1.3 L/h, with a renal clearance of 0.6 L/h. Approximately 35% to 50% of the absorbed dose is recovered in urine while the remaining dose is eliminated in feces via the bile. The volume of distribution of olmesartan is approximately 17 L. Olmesartan is highly bound to plasma proteins (99%) and does not penetrate red blood cells.

Special Populations:
Pediatrics: The pharmacokinetics of olmersartan has not been investigated in patients < 18.
Geriatrics (> 65): Overall, maximum plasma concentrations of olmesartan were similar in young adults and the elderly. Modest accumulation of olmesartan was observed in the elderly with repeated dosing; AUC was 33% higher in elderly patients, corresponding to an approximate 30% reduction in renal clearance.
Gender: Minor differences were observed in the pharmacokinetics of olmesartan in women compared to men. AUC and Cmax were 10-15% higher in women than in men.
Renal insufficiency: In patients with renal insufficiency, serum concentrations of olmesartan were elevated compared to subjects with normal renal function. After repeated dosing, the AUC approximately tripled in patients with severe renal impairment (creatinine clearance < 20 mL/min). The pharmacokinetics of olmesartan in patients undergoing hemodyalisis has not been studied.
Hepatic insufficiency: Increases in AUC and Cmax were observed in patients with moderate hepatic impairment compared to those in matched controls, with an increase in AUC of about 60%.

DOSAGE AND ADMINISTRATION:
Doses must be individualized. The initial usually recommended olmesartan dose, when used as monotherapy is 20 mg once daily. For those patients requiring a more significant reduction in blood pressure following 2 weeks of treatment, the dose of olmesartan may be increased to 40 mg. Doses over 40 mg do not appear to be more effective. Twice-daily doses do not offer any advantage over the same total dose administered once daily. It is not necessary to make adjustments to the initial dose in elderly subjects with moderate to severe renal insufficiency (creatinine clearance < 40 mL/min) or with moderate to severe hepatic insufficiency. For those patients with probable intravascular volume reduction (i.e. patients treated with diuretics, especially those with renal function reduction), the treatment with olmesartan should be initiated under strict medical supervision and special attention should be given to the use of a lower initial dose. Olmesartan may be administered with or without food. If blood pressure cannot be controlled with olmesartan alone, a diuretic agent may be added to the treatment. Olmesartan may be administered with other antihypertensive agents.

CONTRAINDICATIONS:
Hypersensitivity to any component contained in the product. Pregnancy.

WARNINGS:
Pregnancy: Category C (first quarter) and D (second and third quarter). There is no clinical experience with the use of olmesartan in pregnant women. Those drugs which act directly on the renin-angiotensin system may cause morbidity and fetal death when administered to pregnant women. When pregnancy is detected, olmesartan should be discontinuated as soon as possible. The use of drugs acting directly on the renin-angiotensin system during the second and third quarter of pregnancy has been associated to fetal and neonatal damages. When female patients become pregnant, physicians should make the patient interrupt the use of olmesartan as soon

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as possible, and they should inform them about the possible risks for the fetus (see below). Rarely (probably less than 1/1000 pregnancies) no alternative will be found to a drug acting on the renin-angiotensin system. In such cases, the mother should be informed about the possible risks to the fetus (blood pressure alterations, renal disorders, congenic craneofacial and pulmonary malformations; open arterial duct, intrauterine growth delay and death) and ultrasound studies should be performed to examine the intra-amniotic environment.

Lactation: It is not yet known whether olmesartan is eliminated through human milk, however, olmesartan is found in low concentrations in nursing rat's milk. As a result of the potential adverse effects on the nursing infant, a decision should be made regarding the interruption of breastfeeding or the discontinuation of the drug, considering the importance of the drug for the mother.

Pediatric Use: The safety and efficacy of Olmesartan in pediatric patients has not been established.

Geriatric Use: No general differences have been observed regarding the efficacy or safety between older and younger subjects, however, a higher sensitivity should not be discarded in some elderly subjects. Hypotension in patients with hypovolemia or sodium loss. In those patients with an active renin-angiotensin system, such as patients with hypovolemia and/or sodium loss (i.e., those treated with high doses of diuretics), a symptomatic hypotension may appear following the beginning of olmesartan treatment, which should be initiated under strict medical surveillance. In case of hypotension, the patient should adopt supine position, and if necessary, he/she should be administered an intravenous infusion of saline solution. A transient hypotension response should not be considered as a contraindication to continue with the treatment, which may generally be continued without any difficulty whatsoever once blood pressure has been stabilized.

PRECAUTIONS:

General precautions: *Renal insufficiency:* In those patients whose renal function may depend on the activity of the renin-angiotensin-aldosterone system activity (i.e., patients with severe cardiac insufficiency), the treatment with angiotensin converting enzyme inhibitors and angiotensin receptors antagonists has been associated to oliguria and/or progressive azoemia and (rarely) with acute renal insufficiency and/or death. Similar results may be anticipated in those patients treated with olmesartan medoxomil. In studies performed with ACE in patients with unilateral or bilateral stenosis in renal arteries, increases in serum creatinine or in blood urea nitrogen have been reported. There are no available data on the long-term use of olmesartan medoxomil in patients with unilateral or bilateral stenosis of the renal arteries, but similar results may be anticipated.

DRUG INTERACTIONS:

No significant drug interactions have been reported in studies involving the joint administration of olmesartan medoxomil with digoxin or warfarin in healthy subjects. The bioavailability of olmesartan was not significantly altered by the joint administration of antacids (aluminum hydroxide, magnesium hydroxide). Olmesartan medoxomil is not metabolized through the cytochrome P450 system and it does not have any effect on cytochrome P450 enzymes; thus, no interactions with drugs, inhibiting, inducing or metabolized by these enzymes are expected.

ADVERSE REACTIONS:

In clinical trials, the treatment with olmesartan has been well tolerated, with an incidence of adverse events similar to that observed in patients treated with placebo. The events were generally mild, transient and had no relation with the olmesartan medoxomil dose. The discontinuation rate due to adverse effects in all the trials performed in hypertensive patients was 2.4% in patients treated with olmesartan, and 2.7% in the control patients. In placebo-controlled trials, the only adverse event observed in > 1% of the patients treated with olmesartan medoxomil and at a higher incidence versus placebo was dizziness (3% vs. 1%). The following adverse events were produced in placebo-controlled clinical trials at an incidence > 1% of the patients treated with olmesartan medoxomil, however, they were also observed at the same or even higher incidence in the patients receiving placebo: back pain, bronchitis, creatinine phosphokinase increase, diarrhea, headache, hematuria, hyperglycemia, hypertriglyceridemia, lesions, flu symptoms, faringytis, rhinitis, sinusytis and upper respiratory tract infections. The incidence of cough was similar in patients treated with placebo and in patients treated with olmesartan. In controlled-clinical trials, no clinically significant changes were observed in standard laboratory parameters with the administration of olmesartan medoxomil. Small reductions were observed in hemoglobine and hematocryte (average reductions of approximately 0.3 g/dL and 0.3 % volume, respectively).

OVERDOSE:

Little information is available in relation to olmesartan overdose in humans. The most frequent kind of overdose would result in hypotension and tachycardia; bradycardia might also appear in case of parasympathic stimulation (vagal). In case of asymptomatic hypotension, support treatment should be administered. The dializability of olmesartan remains unknown.

In case of a possible overdose, seek medical attention in the nearest hospital or toxicology center.

HOW SUPPLIED:

OLMEC 20 mg: packs containing 30 coated tablets.

OLMEC 40 mg: packs containing 30 coated tablets.

KEEP OUT OF THE REACH OF CHILDREN.

STORE IN THE ORIGINAL PACKAGE, PROTECTED FROM LIGTH AND MOISTURE.

STORE BELOW 30°C.

PHOENIX
Compromiso por la Salud

Manufactured by
Laboratorios Phoenix S.A.I.C. y F.
Humahuaca 4065/79 (C1192ACC)
CABA, Argentina
Av. Gral. J. Lemos 2809 (B1614BHD)
Villa de Mayo, Buenos Aires, Argentina
Distributed in Lebanon by Droguerie Phenicia
Achrafieh-Chahrouri Street-Attallah Bldg., Beirut, Lebanon.

Recyclable material

"The sale packaging of this product has its trade name printed in Braille system, in order to allow its identification by blind patients."

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