Oloduo film-coated tablet

(Olmesartan medoxomil, Rosuvastatin Calcium)

COMPOSITION

Each tablet of Oloduo film-coated tablet 40/20 mg contains

Olmesartan medoxomil ..... 40.0 mg

Rosuvastatin calcium ..... 20.80 mg

(As Rosuvastatin 20 mg)

Each tablet of Oloduo film-coated tablet 20/10 mg contains

Olmesartan medoxomil ..... 20.0 mg

Rosuvastatin calcium ..... 10.40 mg

(As Rosuvastatin 10 mg)

DESCRIPTION

White to light yellow film-coated tablet

INDICATIONS & USAGE

Patients receiving olmesartan and rosuvastatin from separate tablets may receive Oloduo containing the same component doses.
This drug should not be used as initial therapy.

- Olmesartan medoxomil
  Treatment of essential hypertension

- Rosuvastatin
  - Rosuvastatin is indicated for patients with primary hypercholesteroleaemia (type IIa, including heterozygous familial hypercholesterolaemia) or mixed dyslipidaemia (type IIb) as an adjunct to diet when response to diet and exercise is inadequate.
  - Rosuvastatin reduces elevated LDL-cholesterol, total cholesterol, triglycerides and ApoB, and increases HDL-cholesterol

DOSAGE & ADMINISTRATION

This drug should be administered to adults

Usual adult dose

Treatment should not be initiated with this combination
The recommended dosage of Oloduo is one tablet daily.

General considerations

Olmesartan/rosuvastatin is a combination product targeting concomitant cardiovascular conditions hypertension and dyslipidemia.
The dosage range for olmesartan/rosuvastatin is 20 mg/10 mg to a maximum dose of 40 mg/20 mg once daily. Before treatment, the patient should be placed on a standard cholesterol lowering diet that should continue during treatment.
As a component of multiple risk factor intervention, olmesartan/rosuvastatin should be used in addition to non-pharmacological measures, including an appropriate diet, exercise and weight reduction in obese patients, smoking cessation, and to treat underlying medical problems, when the response to these measures have been inadequate.

Replacement Therapy

For convenience, patients receiving olmesartan medoxomil and rosuvastatin from separate tablets may be switched to Oloduo tablet containing the same components dose.
The dosage should be individualized according to patients, depending on the effect and tolerance of each drug.
In patients whose blood pressure is not adequately controlled at 20 mg once daily, the dose can be increased to a maximum of 40 mg daily.
The antihypertensive effect of olmesartan medoxomil is substantially present within 2 weeks of initiating therapy and is maximal by about 8 weeks after initiating therapy. This should be borne in mind when considering changing the dose regimen for any patient.

Elderly (65 years or over)

The maximum dose in elderly patients is 20 mg olmesartan medoxomil once daily, owing to limited experience of higher dosages in this patient group.
No adjustment of dosage is generally required in elderly people.

Renal impairment

The maximum dose in patients with mild to moderate renal impairment (creatinine clearance of 20-60 mL/min) is 20 mg olmesartan medoxomil once daily owing to limited experience of higher dosages in this patient group. The use of olmesartan medoxomil in patients with severe renal impairment (creatinine clearance < 20 mL/min) is not recommended, since there is only limited experience in this patient group.
For rosuvastatin, no dose adjustment is necessary in patients with mild to moderate renal impairment. The use of rosuvastatin is contraindicated in patients with severe renal impairment. Special caution should be exercised in giving 20 mg of rosuvastatin to patients with moderate renal impairment.

Hepatic impairment

The use of Oloduo is not recommended in patients with hepatic impairment, since there is only limited experience in this patient group.

Children and adolescents

The safety and efficacy of Oloduo have not been established in children and adolescents up to 18 years of age.

Method of administration

In order to assist compliance, it is recommended that Oloduo tablets be taken at about the same time each day, with or without food. The tablet should be swallowed with a sufficient amount of fluid. The tablet should not be chewed.

WARNING

Use of drugs that act on the renin-angiotensin system during the second and third trimesters of pregnancy reduces fetal renal function and increases fetal and neonatal morbidity and death. When pregnancy is detected, discontinue drug as soon as possible (see CONTRAINDICATIONS and PREGNANCY AND LACTATION).

CONTRAINDICATIONS

1) Patients with hypersensitivity to this drug or any component of drug.
2) Women during pregnancy, while breast-feeding, and having potential of child-bearing not using appropriate contraceptive measures.
3) Patients with kidney dialysis (There is no experience)(creatinine clearance (CLcr)<30mL/min)
4) Patients with biliary obstruction
5) Do not co-administer aliskiren with this drug in patients with diabetes.
6) Patients with active liver disease including unexplained persistent elevations of serum transaminase levels and any serum transaminase elevation exceeding 3 times upper limit of normal
7) Patients with myopathy
8) Patients receiving concomitant cyclosporine
9) The 40 mg dose is contraindicated in patients with pre-disposing factors for myopathy/rhabdomyolysis. Such factors include:
   - Moderate renal impairment (creatinine clearance < 60 ml/min)
   - Hypothyroidism
   - Personal or family history of hereditary muscular disorders
   - Previous history of muscular toxicity with another HMG-CoA reductase inhibitor or fibrate
   - Alcohol abuse
   - Situations where an increase in plasma levels may occur
   - Concomitant use of fibrates
10) Since this drug contains lactose, patients with hereditary problems such as galactose intolerance, the Lapp lactase deficiency, or glucose-galactose malabsorption should not take this medicine.

PRECAUTIONS

1) Hypotension in Volume- or Salt-Depleted Patients
   In patients with an activated renin-angiotensin system, such as volume- or salt-depleted patients (e.g., those being treated with high doses of diuretics), symptomatic hypotension may occur after initiation of treatment with this drug therefore, appropriate measurements need to be taken before administration. Treatment should start under close medical super vision. If hypotension does occur, the patient should be placed in the supine position and, if necessary, given an intravenous infusion of normal saline. A transient hypotensive response is not a contraindication to further treatment. When blood pressure has been stabilized, therapy usually can be continued without difficulty.

2) Other conditions with stimulation of the renin-angiotensin-aldosteron system
   In patients whose vascular tone and renal function depend predominantly on the activity of the renin-angiotensin aldosterone system (e.g. patients with severe congestive heart failure or underlying renal disease, including renal artery stenosis), treatment with other drugs that affect this system has been associated with acute hypotension, azotaemia, oliguria or, rarely,

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acute renal failure. The possibility of similar effects cannot be excluded with angiotensin II receptor antagonists.

3) Renal impairment and kidney transplantation
When this drug is used in patients with impaired renal function, periodic monitoring of serum potassium and creatinine levels is recommended. Use of this drug is not recommended in patients with severe renal impairment (creatinine clearance less than 20 mL/min). There is no study of the administration of this drug in patients with a recent kidney transplant.

4) Sprue-like Enteropathy
Severe, chronic diarrhea with substantial weight loss has been reported in patients taking olmesartan medoxomil months to years after drug initiation. Intestinal biopsies of patients often demonstrated villous atrophy. If a patient develops these symptoms during treatment with this drug, exclude other etiologies. Consider discontinuation of olmesartan medoxomil in cases where no other etiology is identified.

5) Hepatic impairment
There is currently limited experience in patients with mild to moderate hepatic impairment and no experience in patients with severe hepatic impairment, therefore use of this drug in these patient groups is not recommended.

6) Hyperkalaemia
As with other angiotensin II antagonists and ACE inhibitors, hyperkalemia may occur during treatment with olmesartan medoxomil, especially in the presence of renal impairment and/or heart failure. Close monitoring of serum potassium levels in at risk patients is recommended.

7) Lithium
As with other angiotensin-II receptor antagonists, the combination of lithium and this drug is not recommended.

8) Aortic or mitral valve stenosis
Obstructive hypertropic cardiomyopathy: as with other vasodilators, special caution is indicated in patients suffering from aortic or mitral valve stenosis, or obstructive hypertropic cardiomyopathy.

9) Patients with Renovascular Hypertension
In studies of ACE inhibitors in patients with unilateral or bilateral renal artery stenosis, increases in serum creatinine or blood urea nitrogen (BUN) have been reported. There has been no long-term use of this drug in patients with unilateral or bilateral renal artery stenosis, but similar results may be expected.

10) Primary aldosteronism
Patients with primary aldosteronism generally will not respond to antihypertensive drugs acting through inhibition of the renin-angiotensin system. Therefore, the use of this drug is not recommended in such patients.

11) This drug may cause dizziness due to antihypertensive effect. Do not drive, use machinery, or do any activity such as high place work that requires alertness.

12) Skeletal muscle effects
As with other HMG-CoA reductase inhibitors, effects on skeletal muscle e.g. myalgia, myopathy and, rarely, rhabdomyolysis have been reported in patients taking this drug.

13) Others
As with all other angiotensin II antagonists, the blood pressure lowering effect of this drug is somewhat less in black patients than in non-black patients, possibly because of a higher prevalence of low-renin status in the black

Creatinine kinase measurement
Creatinine Kinase (CK) should not be measured following strenuous exercise or in the presence of a plausible alternative cause of CK increase which may confound interpretation of the result. If CK levels are significantly elevated at baseline (>5 x ULN) a confirmatory test should be carried out within 5-7 days. If the repeat test confirms a baseline CK > 5 x ULN, treatment should not be started.

Before treatment
As with other HMG-CoA reductase inhibitors, this drug should be prescribed with caution in patients with pre-disposing factors for myopathy/rhabdomyolysis. Such factors include:

- renal impairment
- hypothyroidism
- personal or family history of hereditary muscular disorders
- previous history of muscular toxicity with another HMG-CoA reductase inhibitor or fibrate
- alcohol abuse
- age > 70 years
- situations where an increase in plasma levels may occur
- concomitant use of fibrates

In such patients the risk of treatment should be considered in relation to possible benefit and clinical monitoring is recommended. If CK levels are significantly elevated at baseline (>5x ULN) treatment should not be started.

Whilst on treatment
Patients should be asked to report inexplicable muscle pain, weakness or cramps immediately, particularly if associated with malaise or fever. CK levels should be measured in these patients. Therapy should be discontinued if CK levels are markedly elevated (>5 x ULN) or if muscular symptoms are severe and cause daily discomfort (even if CK levels are less than or equal to 5 x ULN). If symptoms resolve and CK levels return to normal, then consideration should be given to re-introducing this drug or an alternative HMG-CoA reductase inhibitor at the lowest dose with close monitoring. Routine monitoring of CK levels in asymptomatic patients is not warranted.

There have been very rare reports of an immune-mediated necrotizing myopathy clinically characterized by persistent proximal muscle weakness and elevated serum creatinine kinase during treatment or following discontinuation of statins, including rosuvastatin. Additional neuromuscular and serologic testing may be necessary. Treatment with immunosuppressive agents may be required.

The incidence of myositis and myopathy increase in patients receiving other HMG-CoA reductase inhibitors together with fibric acid derivatives including gemfibrozil, ciclosporin, nicotinic acid, azole antifungals, protease inhibitors and macrolide antibiotics. Gemfibrozil increases the risk of myopathy when given concomitantly with some HMG-CoA reductase inhibitors. The benefit of further alterations in lipid levels by the combined use of this drug with fibrates or niacin should be carefully weighed against the potential risks of such combinations.

This drug should not be used in any patients with an acute, serious condition suggestive of myopathy or predisposing to the development of renal failure secondary to rhabdomyolysis (e.g. sepsis, hypotension, major surgery, trauma, severe metabolic, endocrine and electrolyte disorders; or uncontrolled seizures).

14) Renal effects: Proteinuria, detected by dipstick testing and mostly tubular in origin, has been observed in patients taking this drug. Proteinuria has not been shown to be predictive of acute or progressive renal disease. An assessment of renal function should be considered during routine follow-up of patients treated with this drug.

15) Liver effects
As with other HMG-CoA reductase inhibitors, this drug should be used with caution in patients who consume excessive quantities of alcohol and/or have a history of liver disease. It is recommended that liver function tests be carried out prior to, and 3 months following, the initiation of treatment. This drug should be discontinued or the dose reduced if the level of serum transaminases is greater than 3 times the upper limit of normal. In patients with secondary hypercholesterolaemia caused by hypothyroidism or nephrotic syndrome, the underlying disease should be treated prior to initiating therapy with this drug.

16) Diabetes mellitus
As with other HMG-CoA reductase inhibitors, increases in HbAlc and serum glucose levels have been observed in patients treated with rosuvastatin, and in some instances these increases may exceed the threshold for the diagnosis of diabetes mellitus, primarily in patients already at high risk for developing diabetes.

17) Race
Pharmacokinetic studies show an increase in exposure in Asian subjects compared with Caucasians.

ADVERSE REACTIONS

- **Olmesartan medoxomil**
The frequencies of adverse events are ranked according to the following: common (≥ 1/100, < 1/10), uncommon (≥ 1/1000, < 1/100), rare (≥ 1/10,000, < 1/1000), very rare (1/10,000; not known (cannot be estimated from the available data)

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The adverse events listed include all adverse events reported commonly and other adverse events of potential clinical relevance.

- **Central nervous disorders**:
  Common: Dizziness
  Uncommon: Vertigo
- **Cardiovascular disorders**:
  Rare: Hypotension
- **Myo/endo/pericardial and valve disorders**:
  Uncommon: Angina pectoris
- **Respiratory system disorders**:
  Common: Bronchitis, cough, pharyngitis, rhinitis
- **Gastro-intestinal disorders:**
  Common: Abdominal pain, diarrhea, dyspepsia, gastroenteritis, nausea
- **Skin and appendages disorders:**
  Uncommon: Rash
- **Musculoskeletal disorders:**
  Common: Arthritis, back pain, skeletal pain
- **Urinary system disorders:**
  Common: Haematuria, urinary tract infection
- **General disorders:**
  Common: Chest pain, fatigue, influenza-like symptoms, peripheral oedema, pain
- **Post-launch experience**
  In addition, as with other angiotensin II antagonists, headache has been observed, in very rare hypersensitivy reactions (pruritus, urticaria, angiodema), peripheral oedema, vomiting, diarrhea, sprue-like enteropathy, anaphylactic reaction, acute renal failure, hyperkalemia, rhabdomyolysis, increased blood creatinine levels, alopecia, myalgia and asthenic condition such as asthenia, fatigue, lethargy, malaise have been reported.
- **Laboratory parameters**
  The incidence was somewhat higher on olmesartan medoxomil for hypertriglyceridaemia and for raised creatine phosphokinase.
  Laboratory adverse events reported with olmesartan medoxomil included:
  - **Metabolic and nutritional disorders:**
    Common: Increased creatinine phosphokinase, hypertriglyceridaemia, hyperuricaemia
    Rare: Hyperkalaemia
  - **Liver and biliary disorders:**
    Common: Liver enzyme elevations

● **Rosuvastatin**

The adverse events seen with rosuvastatin are generally mild and transient.

- **Immune system disorders**
  Rare: hypersensitivity reactions including angioedema
- **Endocrine disorders**
  Common: diabetes mellitus
- **Nervous system disorder**
  Common: headache, dizziness
- **Gastrointestinal disorders**
  Common: constipation, nausea, abdominal pain
  Rare: pancreatitis
- **Skin and subcutaneous tissue disorders**
  Uncommon: pruritus, rash and urticarial
- **Musculoskeletal, connective tissue and bone disorders**
  Common: myalgia
  Rare: myopathia (including myositis) and rhabdomyolysis
- **General disorders**
  Common: asthenia
- **Renal effects**: proteinuria, detected by dipstick testing and mostly tubular in origin, has been observed in patients treated with rosuvastatin. In most cases, proteinuria decreases or disappears spontaneously on continued therapy and is not predictive acute or progressive renal disease.
- **Skeletal muscle effects**: Rare cases of rhabdomyolysis which were occasionally associated with the impairment of renal function have been reported with rosuvastatin and with other marketed statins.
- **Laboratory effects**: As with other HMG-CoA reductase inhibitors, a dose-related increase in transaminases and CK have been observed in a small number of patients taking rosuvastatin; the majority of cases were mild, asymptomatic and transient. If CK levels are elevated (>5x ULN), treatment should be discontinued. Increases in HcA1c have also been observed in patients treated with rosuvastatin.

Post marketing experience:

In addition to the above, following adverse events have been reported during post marketing experience for rosuvastatin:

- **Haematological disorders:**
  Frequency unknown: thrombocytopenia
- **Hepatobiliary disorders:**
  Very rare: jaundice, hepatitis
  Rare: increased hepatic transaminases
- **Musculoskeletal disorders:**
  Frequency unknown: immune-mediated necrotizing myopathy
  Very rare: arthralgia

As with other HMG-CoA reductase inhibitors, the reporting rate for rhabdomyolysis in post marketing use is higher at the highest marketed dose.

- **Nervous system disorders:**
  Very rare: polyneuropathy, memory loss
  Frequency unknown: peripheral neuropathy.
- **Psychiatric disorders:**
  Frequency unknown: depression, sleep disorders (including insomnia and nightmares)
- **Reproductive system and breast disorders:**
  Frequency unknown: gynaecomastia

GENERAL PRECAUTIONS

● **Olmesartan medoxomil**

Close monitoring of blood pressure and renal function is advised in hepatically-impaired patients who are already receiving diuretics and/or other antihypertensive agents.

● **Rosuvastatin**

1) Interstitial lung disease: Exceptional cases of interstitial lung disease have been reported with some statins, especially with long term therapy. Presenting features can include dyspnoea, non-productive cough and deterioration in general health (fatigue, weight loss and fever). If it is suspected a patient has developed interstitial lung disease, statin therapy should be discontinued.
2) There have been rare postmarketing reports of fatal and non-fatal hepatic failure in patients taking statins, including rosuvastatin. If serious liver injury with clinical symptoms and/or hyperbilirubinemia or jaundice occurs during treatment with this drug, promptly interrupt therapy. If an alternate etiology is not found, do not restart this drug.
3) Increases in HbA1c and fasting serum glucose levels have been reported with HMG-CoA reductase inhibitors, including this drug.
4) Diabetes mellitus: Some evidences suggest that statins as a class raise blood glucose and in some patients, at high risk of future diabetes, may produce a level of hyperglycaemia where formal diabetes care is appropriate. This risk, however, is outweighed by the reduction in vascular risk with statins and therefore should not be a reason for stopping statin treatment. Patients at risk (fasting glucose 5.6 to 6.9 mmol/l, BMI >30 kg/m2, raised triglycerides, hypertension) should be monitored both clinically and biochemically according to national guidelines.

DRUG INTERACTIONS

● **Olmesartan medoxomil**

1) Potassium supplements and potassium sparing diuretics: Based on experience with the use of other drugs that affect the renin-angiotensin system, concomitant use of potassium-sparing diuretics, potassium supplements, salt substitutes containing potassium or other drugs that may increase serum potassium levels (e.g. heparin) may lead to increases in serum potassium.
2) The blood pressure lowering effect can be increased by concomitant use of other antihypertensive medications.
3) Lithium: Reversible increases in serum lithium concentrations and toxicity have been reported during concomitant administration of lithium with angiotensin converting enzyme inhibitors. The same condition is very rarely reported with this drug, therefore use of this drug and lithium in combination is not recommended.
4) Non-steroidal anti-inflammatory drugs (NSAIDs):
   NSAIDs (including aspirin at doses > 3g/day and also COX-2 inhibitors) and angiotensin-II receptor antagonists may act synergistically by decreasing glomerular filtration. The risk of the concomitant use of NSAIDs and angiotensin II antagonists is the occurrence of acute renal failure. Monitoring of renal function at the beginning of treatment should be recommended as well as regular hydration of the patient. Additionally, concomitant treatment can reduce the antihypertensive effect of angiotensin II receptor antagonists, leading to their partial loss of efficacy.
5) Dual Blockade of the Renin-Angiotensin System (RAS)
   Dual blockade of the RAS with angiotensin receptor antagonists, ACE inhibitors or aliskiren is associated with increased risks of hypotension,

hyperkalemia and changes in renal function (including acute renal failure) compared to monotherapy. Monitor blood pressure, renal function and electrolytes in patients on olmesartan and other agents that affect the RAS.

6) Use with aliskiren
Do not co-administer with olmesartan medoxomil in patients with diabetes because dual use is associated with increased risks of hypotension, hyperkalemia, and changes in renal function (including acute renal failure) compared to monotherapy

7) Use with colesevelam hydrochloride
Concurrent administration of bile acid sequestering agent colesevelam hydrochloride reduces the systemic exposure and peak plasma concentration of olmesartan. Administration of olmesartan at least 4 hours prior to colesevelam hydrochloride decreased the drug interaction effect.

8) Protease inhibitors: Although the exact mechanism of interaction is unknown, concomitant protease inhibitor use may strongly increase rosuvastatin exposure. The concomitant use of rosuvastatin and some protease inhibitor combination may be considered after careful consideration of rosuvastatin dose adjustments based on expected increase in rosuvastatin exposure.

9) Other compounds:
After treatment with antacid (aluminium magnesium hydroxide), a modest reduction in bioavailability of olmesartan was observed.

● **Rosuvastatin**

1) Vitamin K antagonists : as with other HMG-CoA reductase inhibitors, the initiation of treatment or dosage up-titration of rosuvastatin in patients treated concomitantly with vitamin K antagonists (e.g. warfarin or another coumarin anticoagulant) may result in an increase in International Normalised Ratio (INR). Discontinuation or down-titration of rosuvastatin may result in a decrease in INR. In such situations, appropriate monitoring of INR is desirable.

2) Rosuvastatin is contraindicated in patients receiving concomitant ciclosporin. Concomitant administration did not affect plasma concentration of ciclosporin.

3) Gemfibrozil and other lipid-lowering products: Gemfibrozil, fenofibrate, other fibrates and lipid lowering doses (≥ 1 g/day) of niacin (nicotinic acid) increase the risk of myopathy when given concomitantly with HMG-CoA reductase inhibitors, probably because they can produce myopathy when given alone.

4) Antacid : the simultaneous dosing of rosuvastatin with an antacid suspension containing aluminium and magnesium hydroxide resulted in a decrease in rosuvastatin plasma concentration. This effect was mitigated when the antacid was dosed 2 hours after rosuvastatin. The clinical relevance of this interaction has not been studied.

5) Cytochrome P450 enzymes : rosuvastatin is a poor substrate for cytochrome P450 isoenzymes. Therefore, drug interactions resulting from cytochrome P450-mediated metabolism are not expected. No clinically relevant interactions have been observed between rosuvastatin and either fluconazole (an inhibitor of CYP2C9 and CYP3A4) or ketoconazole.

6) Erythromycin : the concomitant use of rosuvastatin and erythromycin cause an increase in gut motility caused by erythromycin.

7) Protease inhibitors : although the exact mechanism of interaction is unknown, concomitant protease inhibitor use may strongly increase rosuvastatin exposure.

8) Oral contraceptive/hormone replacement therapy (HRT)
Concomitant use of rosuvastatin and an oral contraceptive resulted in an increase plasma level of ethinyl estradiol and norgestrel. These increased plasma levels should be considered when selecting oral contraceptive doses. There are no pharmacokinetic data available in subjects taking concomitant rosuvastatin and HRT and therefore a similar effect cannot be excluded. However, the combination has been extensively used in women in clinical trials and was well tolerated.

9) Transporter protein inhibitors
Rosuvastatin is a substrate for certain transporter proteins including the hepatic uptake transporter OATP1B1 and efflux transporter BCRP. Concomitant administration of rosuvastatin with medicinal products that are inhibitors of these transporter proteins may result in increased rosuvastatin plasma concentration and an increased risk of myopathy.

10) Ezetimibe : there was an increase in AUC of rosuvastatin when rosuvastatin and ezetimibe was administered in hypercholesterolaemic subjects. A pharmacodynamic interaction, in terms of adverse effects, between rosuvastatin and ezetimibe cannot be ruled out.

11) Fusidic Acid : As with other statins, muscle related events, including rhabdomyolysis, have not been reported in post-marketing experience with rosuvastatin and fusidic acid given concurrently. Patients should be closely monitored and temporary suspension of rosuvastatin treatment may be appropriate.

12) Genotip polymorphisms
Genotypes of SLCO1B1 (OATP1B1) c.521CC and ABCG2 (BCRP) c.421AA have been shown to be associated with an increase in rosuvastatin exposure (AUC) compared to SLC 1B1 c.521TT and ABCG2 c.421CC. For patients known to have the c.521CC or c.421AA genotype, a maximum once daily dose of 20 mg of rosuvastatin is recommended.

PREGNANCY AND LACTATION

Use in pregnancy

● **Olmesartan medoxomil**
There is no experience with the use of olmesartan medoxomil in pregnant women. However, drugs that act directly on the renin-angiotensin system administered during the second and third trimesters of pregnancy have been reported to cause fetal and neonatal injury (hypotension, renal dysfunction, oliguria and/or anuria, oligohydramnios, skull hypoplasia, intrauterine growth retardation, lung hypoplasia, facial abnormalities, limb contracture) and even death. Thus, as for any drug in this class, olmesartan medoxomil is contraindicated during the second and third trimesters of pregnancy. In addition, olmesartan medoxomil must not be used during the first trimester. If pregnancy occurs during therapy, olmesartan medoxomil must be discontinued as soon as possible. Olmesartan is excreted in the milk of lactating rats but it is not known whether olmesartan is excreted in human milk. Mothers must not breast-feed if they are taking olmesartan medoxomil.

● **Rosuvastatin**
There are no adequate and well-controlled studies of rosuvastatin in pregnant women or in nursing mother therefore, it is contraindicated in pregnancy and lactation. Women of child bearing potential should use appropriate contraceptive measures. Since cholesterol and other products of cholesterol biosynthesis are essential for the development of the foetus, the potential risk from inhibition of HMG-CoA reductase outweighs the advantage of treatment during pregnancy. If a patient becomes pregnant during use of this product, treatment should be discontinued immediately. Rosuvastatin is excreted in the milk of rats. There are no data with respect to excretion in milk in human.

PAEDIATRIC

The safety and efficacy in paediatric population has not been established.

EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

It should be taken into account that dizziness may occur during treatment.

OVERDOSE

● **Olmesartan medoxomil**

Only limited information is available regarding overdosage in humans. The most likely effect of overdosage is hypotension. In the event of overdosage, the patient should be carefully monitored and treatment should be symptomatic and supportive. No information is available regarding the dialysability of olmesartan

●**Rosuvastatin**

There is no specific treatment in the event of overdose. In the event of overdose, the patient should be treated symptomatically and supportive measures instituted as required. Liver function and CK level should be monitored. Hemodialysis is unlikely to be of benefit.

STORAGE AND HANDLING

1) Keep out of reach of the children.
2) Do not change container to keep a quality and to prevent from misusing.

[STORAGE] Store below 30°C
[PACKAGE] Box, 3 Blisters @ 10 film coated tablets
[EXPIRY] 24 months from the date of manufacture

※ Do not use if the product is damaged or if there is any visible foreign substance.

※ This drug product has completed strict quality control. If the expiry date has been passed or product has been altered, deteriorated, contaminated or damaged at the time of purchase, it can be exchanged or refunded at the pharmacy or distributor of purchase, in accordance with Fair Trade Commission Notice (consumer dispute resolution criteria).

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EREG 100401118000006
EREG 100401118000007

Registration number: DKI.....

HARUS DENGAN RESEP DOKTER

Manufactured by : DAEWOONG PHARMACEUTICAL CO., LTD.
Hyangnam, Korea

Imported by : PT Daewoong Infion
Pandaan – Indonesia

※ Any change in this attached document since the last revision date can be found from the website (www.daewoong.com) and the consumer hotline (82-80-550-8308 ~ 9).

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Nama obat
Oloduo

Bentuk Sediaan
Tablet salut selaput

Pemerian Obat
Tablet salut selaput berwarna putih hingga kuning muda

Apa yang terkandung dalam obat?
Tiap tablet Oloduo 40/20 mg mengandung

Olmesartan medoxomil ..... 40,0 mg

Rosuvastatin calcium ..... 20,80 mg
(sebagai Rosuvastatin 20mg)

Tiap tablet Oloduo 20/10 mg mengandung

Olmesartan medoxomil ..... 20,0 mg

Rosuvastatin calcium ..... 10,40 mg
(sebagai Rosuvastatin 10mg)

Untuk apa obat digunakan?
Obat ini hanya diberikan pada pasien yang mengalami tekanan darah tinggi serta memiliki kadar kolesterol yang tinggi dan sebelumnya telah mendapatkan pengobatan dengan olmesartan medoxomil dan rosuvastatin

Berapa banyak dan seberapa sering obat ini boleh digunakan?

- Obat ini hanya boleh diberikan pada pasien dewasa dengan dosis satu tablet sekali sehari; dianjurkan untuk meminum obat ini pada waktu yang sama setiap hari, sebelum atau sesudah makan. Tablet harus ditelan dengan meminum air dalam jumlah yang cukup. Tablet tidak boleh dikunyah.

  Jika tekanan darah pasien tidak dapat diturunkan dengan Oloduo 20/10 sekali sehari maka dosis dapat ditingkatkan dengan pemberian Oloduo 40/20 sekali sehari.

- **Pasien Lanjut usia (65 tahun atau lebih)**
  Pasien lanjut usia hanya boleh diberikan Oloduo 20/10.

- **Pasien yang mengalami kerusakan ginjal**
  Pasien dengan kerusakan ginjal ringan sampai sedang (bersihan kreatinin 20 – 60 mL/menit) hanya boleh diberikan Oloduo 20/10 sekali sehari.

Apa yang perlu diperhatikan bila menggunakan obat ini?

1) Jika diketahui sedang hamil, hentikan penggunaan obat ini sesegera mungkin
2) Obat ini harus diberikan dengan hati-hati pada pasien berikut ini:

   - pasien yang sedang diobati dengan diuretik dosis tinggi (misalnya furosemide, hidroklorotiazid), karena risiko tekanan darah rendah dapat ditingkatkan.
   - penderita kerusakan ginjal; dianjurkan untuk melakukan pemantauan berkala terhadap kadar kalium dalam darah dan kreatinin. Tidak dianjurkan untuk pasien dengan bersihan kreatinin kurang dari 20 mL/menit.
   - penderita gagal jantung; dianjurkan untuk melakukan pemeriksaan berkala untuk memantau kadar kalium dalam darah
   - penderita hipotiroidisme (tiroid kurang aktif)
   - pasien yang memiliki riwayat pribadi atau keluarga adanya gangguan otot
   - pasien berusia di atas 70 tahun
   - pasien yang kecanduan alkohol
   - penderita kencing manis

Anda tidak diperbolehkan menggunakan obat ini pada keadaan berikut ini :

a. JIka Anda alergi terhadap obat ini atau bahan lain dari obat ini.
b. Wanita hamil, selama masa menyusui, dan wanita yang memiliki kemungkinan hamil yang tidak menggunakan kontrasepsi.
c. Jika Anda menjalani cuci darah
d. Jika Anda mengalami penyumbatan empedu, menderita penyakit hati, kelainan otot
e. Jika Anda menderita kencing manis dan sedang mendapat pengobatan dengan aliskiren.
f. Jika Anda sedang mendapatkan pengobatan dengan siklosporin, fibrat dan lithium
g. Karena obat mengandung laktosa, maka pasien yang mengalami masalah seperti intoleransi galaktosa atau ketidakmampuan tubuh untuk mengolah glukosa-galaktosa tidak boleh mengkonsumsi obat ini.

Apa efek yang tidak diinginkan yang mungkin terjadi?

- sakit kepala, pusing, tekanan darah rendah, mengantuk, rasa letih, gangguan tidur
- gangguan saluran cerna, nyeri perut, diare, mual sembelit
- kerusakan pada gigi
- Kaku otot, nyeri dada, nyeri tulang belakang
- kadar gula darah rendah
- batuk

Obat apa yang harus dihindari jika menggunakan obat ini?

- Golongan litium
- Obat anti inflamasi non steroid
- Diuretik, suplemen kalium
- Aliskiren
- Obat untuk asam empedu *colesevelam hydrochloride*
- Antasida
- Siklosporin
- Gemfibrozil, fenofibrat dan obat penurun kadar lemak lainnya.
- Ezetimibe

Apakah boleh digunakan pada wanita hamil dan menyusui?
Tidak

Apakah boleh digunakan pada anak-anak?
Tidak, karena keamanan dan khasiat obat ini pada anak-anak belum diteliti.

Apakah boleh mengendarai dan menjalankan mesin selama minum obat ini?
Karena adanya efek samping pusing, sebaiknya Jangan mengendarai, mengoperasikan mesin atau melakukan aktivitas apapun di tempat yang tinggi yang membutuhkan kewaspadaan.

Apa tanda dan gejala bila kelebihan dosis dan apa yang harus dilakukan jika menggunakan obat ini melebihi dosis yang dianjurkan?
Tanda dan gejala bila kelebihan dosis yang paling sering terjadi adalah tekanan darah rendah. Jika terjadi, hubungi dokter.

Bagaimana cara menyimpan obat ini?
Jauhkan dari jangkauan anak-anak; simpan pada suhu di bawah 30°C

[KEMASAN] Dus, 3 blister @ 10 Tablet Salut Selaput
[MASA DALUARSA] 24 bulan dari tanggal produksi

※ Jangan gunakan obat ini jika sudah rusak atau terlihat adanya benda asing.

Nomor Registrasi : DKI.....

HARUS DENGAN RESEP DOKTER

Diproduksi oleh : DAEWOONG PHARMACEUTICAL CO., LTD.
Hyangnam, Korea

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PT Daewoong Infion
Pandaan - Indonesia

DISETUJUI OLEH BADAN POM:09/09/19

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EREG 100401118000007