United Pharmaceuticals

MONTEER®
Amlodipine Besylate and Atorvastatin Calcium

Description:
MONTEER® (Amlodipine Besylate and Atorvastatin Calcium) is a combination of two drugs, a dihydropyridine Calcium antagonist (Calcium ion antagonist slow-channel blocker) Amlodipine (Antihypertensive/antianginal agent) and a HMG-CoA reductase inhibitor Atorvastatin (cholesterol lowering agent). The Amlodipine component of **MONTEER®** inhibits the transmembrane influx of Calcium ions into vascular smooth muscle and cardiac muscle. The Atorvastatin component of **MONTEER®** is a selective, competitive inhibitor of HMG-CoA reducnase, the rate-limiting enzyme that converts 3-hydroxy-3-methytgtutaryl-coenzyme A to mevalonate, a precursor of sterols including cholesterol.

Properties:
Absorption:
Following oral administration of **MONTEER®**, peak plasma concentrations of Amlodipine and Atorvastatin are seen at 6 to 12 hours and 1 to 2 hours post dosing, respectively. The rate and extent of absorption (bioavailability) of Amlodipine and Atorvastatin from **MONTEER®** are not significantly different from the bioavailability of Amlodipine and Atorvastatin administered separately.
The bioavailability of Amlodipine from **MONTEER®** was not affected by food, although food decreases the rate and extent of absorption of Atorvastatin from **MONTEER®** by approximately 32% and 11%, respectively, as it does with Atorvastatin when given alone. LDL-C reduction is similar whether Atorvastatin is given with or without food.

Distribution:
Amlodipine drug is bound to plasma proteins in hypertensive patients. Steady-state plasma levels of Amlodipine are reached after 7 to 8 days of consecutive daily dosing.
Atorvastatin is 98% bound to plasma proteins. A blood/plasma ratio of approximately 0.25 indicates poor drug penetration into red blood cells.
Metabolism:
Amlodipine is extensively (about 90%) converted to inactive metabolites via hepatic metabolism.
Atorvastatin is extensively metabolized to ortho- and para-hdroxylated derivatives and various beta oxidation products in vitro inhibition of HMG-COA reductase by ortho- and para-hydroxylated metabolites are equivalent to that of Atorvastatin.
Excretion:
Elimination of Amlodipine from the plasma is biphasic with a terminal elimination half-life of about 30 - 50 hours. 10% of the parent Amlodipine compound and 60% of the metabolites of Amlodipine are excreted in the urine.
Atorvastatin and its metabolites are eliminated primarily in bile following hepatic and/or extra-hepatic metabolites. Less than 2% of a dose of Atorvastatin is recovered in urine following oral administration.

Indications:
MONTEER® is indicated in patients for whom treatment with Amlodipine and Atorvastatin is appropriate.
Amlodipine:
I. Hypertension: Amlodipine is indicated for the treatment of hypertension. It may be used alone or with combination with other antihypertensive agents
2. Coronary Artery Disease (CAD):
- Chronic Stable Angina: Amlodipine is indicated for the treatment of chronic stable angina. Amlodipine may be used alone or in combination with other antianginal or antihypertensive agents.
- Vasospastic Angina (Prinzmetal's or Variant Angina): Amlodipine is indicated for the treatment of confirmed or suspected Vasospastic angina. Amlodipine may be used as monotherapy or in combination with other antianginal drugs.
- Angiographically Documented CAD: In patients with recently documented CAD by angiography and without heart failure or an ejection fraction <40%, Amlodipine is indicated to reduce the risk of hospitalization due to angina and to reduce the risk of a coronary revascularization procedure.
Atorvastatin:
1. Prevention of Cardiovascular Disease:
In adult patients without clinically evident of coronary heart disease, but with multiple risk factors such as age, smoking, hypertension, low HDL-C level or a family history of early coronary heart disease, Atorvastatin is indicated to:
- Reduce the risk of myocardial infarction.
- Reduce the risk of stroke.
- Reduce the risk for revascularization procedures and angina.
In patients with type 2 diabetes, and without clinically evident of coronary heart disease, but with multiple risk factors such as retinopathy, albuminuria, smoking or hypertension, Atorvastatin is indicated to:
- Reduce the risk of myocardial infarction.
- Reduce the risk of stroke.
In patients with clinically evident of coronary heart disease, Atorvastatin is indicated to:
- Reduce the risk of non-fatal myocardial infarction.
- Reduce the risk of fatal and non-fatal stroke.
- Reduce the risk for revascularization procedures.
- Reduce the risk of hospitalization for CHF.
- Reduce the risk of angina.
2. Heterozygous Familial and Nonfamilial Hypercholesterolemia: Atorvastatin is indicated as an adjunct to diet to reduce elevated total-C, LDL-C, apo B and TG levels and to increase HDL-C in patients with primary Hypercholesterolemia (heterozygous familial and nonfamilial) and mixed dyslipidemia (Fredrickson Types IIa and IIb).
3. Elevated Serum TG Levels: Atorvastatin is indicated as an adjunct to diet for the treatment of patients with elevated serum TG levels (Fredrickson type IV).
4. Primary Dysbetalipoproteinemia: Atorvastatin is indicated for the treatment of patients with primary dysbetalipoproteinemia (Fredrickson Type III) who do not respond adequately to diet.
5. Homozygous Familial Hypercholesterolemia: Atorvastatin is indicated to reduce total C and LDL-C in patients with homozygous familial hypercholesterolemia as an adjunct to other lipid-lowering treatments (e.g. LD apheresis) or if such treatments are unavailable
6. Pediatric patients: Atorvastatin is indicated as an adjunct to diet to reduce total C, LDL-C and apo B levels in boys and postmenarachal girls, 10 to 17 years of age, with heterozygous familial hypercholesterolemia if after in adequate trial of diet therapy the following findings are present:
a. LDL- C remains ≥190 mg/dL or LDL-C remains ≥160 mg/dL.
b. There is a positive family history of premature cardiovascular disease or two or more other CVD risk factors are present in the pediatric patients.
Therapy with lipid altering agents should be a component of multiple -risk- factor intervention in individuals at increased risk for atherosclerotic vascular disease due to hypercholesterolemia. Lipid-altering agents should be used in addition to diet restricted in saturated fat and cholesterol, only when the response to diet and other nonpharmacological measures has been inadequate.

Dosage and administration:
Dosage of **MONTEER®** must be individualized on the basis of both effectiveness and tolerance for each individual component in the treatment of hypertension/angina and hyperlipidemia.
Amlodipine (Hypertension or angina):
- Adult: The usual initial antihypertensive oral dose of Amlodipine is 5 mg once daily with a maximum dose of 10 mg once daily. Small, fragile, or elderly individuals or patients with hepatic insufficiency may be started on 2.5 mg once day and this dose may be used when adding Amlodipine to other antihypertensive therapy. Dosage should be adjusted according to each patient's need. In general, titration should proceed over 7 to 14 days so that the physician can fully assess the patient's response to each dose level. Titration may proceed more rapidly, however, if clinically warranted, provided the patient is assessed frequently.
The recommended dose of Amlodipine for chronic stable or vasospastic angina is 5-l0 mg, with the lower dose suggested in the elderly and in patients with hepatic insufficiency. Most patients will require 10 mg for adequate effect.
The recommended dose range of Amlodipine for patients with coronary artery disease is 5-10 mg once daily. In clinical studies the majority of patients required 10 mg.
- Children: The effective antihypertensive oral dose of Amlodipine in pediatric patients ages 6-17 years is 2.5 mg to 5 mg once daily. Doses in excess of 5 mg daily have not been studied in pediatric patients.
Atorvastatin (Hyperlipidemia):
The patient should be placed on a standard cholesterol-lowering diet before receiving Atorvastatin and should continue on this diet during treatment with Atorvastatin.
Hypercholesterolemia (Heterozygous Familial and Nonfamilial) and Mixed Dyslipidemia (Fredrickson Types IIa and IIb):
The recommended starting dose of Atorvastatin is 10 or 20mg once daily. Patients who require a large reduction in LDL-C (more than 45%) may be started at 40 mg once daily. The dosage range of Atorvastatin is l0 to 80 mg once daily. Atorvastatin can be administered as a single dose at any time of the day, with or without food.
The starting dose and maintenance doses of Atorvastatin should be individualized according to patient characteristics such as goal of therapy and response. After initiation and/or upon titration of Atorvastatin, lipid levels should be analyzed within 2 to 4 weeks and dosage adjusted accordingly.
Since the goal of treatments is to lower LDL-C, the NCEP recommends that LDL-C levels be used to initiate and assess treatment response. Only if LDL-C levels are not available, should total-C be used to monitor therapy.
Heterozygous Familial Hypercholesterolemia in Pediatric Patients (10-17 years of age):
The recommended starting dose of Atorvastatin is 10mg/day; the maximum recommended dose is 20 mg/day (doses greater than 20mg have not been studied in this patient population). Doses should be individualized according to the recommended goal of therapy. Adjustments should be made at intervals of 4 weeks or more.
Homozygous Familial Hypercholesterolemia:
The dosage of Atorvastatin in patients with homozygous familial hypercholesterolemia is 10 to 80mg daily. Atorvastatin should be used as an adjunct to other lipid-lowering treatments (e.g. LDL apheresis) in these patients or if such treatments are unavailable.
Concomitant Lipid Lowering Therapy:
Atorvastatin may be used in combination with a bile acid binding resin for additive effect. The combination of HMG-CoA reductase inhibitors and fibrates should generally be avoided.
Dosage in Patients with Renal insufficiency: Renal disease does not affect the plasma concentrations nor LDL-C reduction of Atorvastatin; thus, dosage adjustment in patients with renal dysfunction is not necessary.
Dosage in Patients Taking Cyclosporine, Clarithromycin or a Combination of Ritonavir plus Saquinavir or Lipinavir plus Ritonavir:
In patients taking cyclosporine, therapy should be limited to Atorvastatin 10mg once daily. In patients taking Clarithromycin or in patients with HIV taking a combination of ritonavir plus saquinavir or lopinavir plus ritonavir, for doses of Atorvastatin exceeding 20 mg appropriate clinical assessment is recommended to ensure that the lowest dose necessary of Atorvastatin is employed.
MONTEER® may be substituted for its individually titrated components. Patients may be given the equivalent dose of **MONTEER®** or a dose of **MONTEER®** with increased amounts of Amlodipine, Atorvastatin or both for additional antianginal effects, blood pressure lowering, or lipid lowering effect.
MONTEER® may be used to provide additional therapy for patients already on one of its components. As initial therapy for one indication and continuation of treatment of the other, the recommended starting dose of **MONTEER®** should be selected based on the continuation of the component being used and the recommended starting dose for the added monotherapy.
MONTEER® may be used to initiate treatment in patients with hyperlipidemia and either hypertension or angina. The recommended starting dose of **MONTEER®** should be based on the appropriate combination of recommendations for the monotherapies.
Pediatric Use: There have been no studies conducted to determine the safety or effectiveness of **MONTEER®** in pediatric populations.
Geriatric Use: There have been no studies conducted to determine the safety or effectiveness of **MONTEER®** in geriatric populations.
Use in Patients with Recent Stroke or TIA: The studies show a higher incidence of hemorrhagic stroke while taking Atorvastatin.

Contraindications:
- **MONTEER®** contains Atorvastatin and is therefore contraindicated in patients with active liver disease or unexplained persistent elevations of serum transaminases.
- **MONTEER®** is contraindicated in patients with known hypersensitivity to any component of this medication.

Precautions:
General:
- Since the vasodilation induced by the Amlodipine component of **MONTEER®** is gradual in onset, acute hypotension has rarely been reported after oral administration of Amlodipine. Nonetheless, caution should be exercised when administering **MONTEER®** as with any other peripheral vasodilator particularly in patients with severe aortic stenosis.
- Before instituting therapy with **MONTEER®**, an attempt should be made to control hypercholesterolemia with appropriate diet, exercise, and weight reduction in obese patients, and to treat other underlying medical problems.
Use in Patients with Congestive Heart Failure: In general, Calcium channel blockers should be used with caution in patients with heart failure.
Beta-Blocker Withdrawal: The Amlodipine component of **MONTEER®** is not a beta-blocker and therefore gives no protection against the dangers of abrupt beta-blocker withdrawal; any such withdrawal should be by gradual reduction of the dose of beta-blocker.
Endocrine Function: HMG-CoA reductase inhibitors, such as the Atorvastatin component of **MONTEER®** interfere with cholesterol synthesis and theoretically might blunt adrenal and/or gonadal steroid production. Clinical studies have shown that Atorvastatin does not reduce basal plasma cortisol concentration or impair adrenal reserve. The effects of HMG-CoA reductase inhibitors on male fertility have not been studied in adequate numbers of patients. The effects, if any, on the pituitary-gonadal axis in premenopausal women are unknown. Caution should be exercised if an HMG-CoA reductase inhibitor is administered concomitantly with drugs that may decrease the levels or activity or endogenous steroid hormones, such as ketoconazole, spironolactone and cimetidine.
CNS Toxicity: No CNS lesions have been observed in mice after chronic treatment for up to 2 years at doses of Atorvastatin Calcium equivalent to up to 400 mg Atorvastatin/kg/day or in rats at doses equivalent to up to 100 mg Atorvastatin/kg/day. These doses were 6 to 11 times (mouse) and 8 to 16 times (rat) the human AUG (0-24) based on the maximum recommended human dose of 80mg

Atorvastatin/day.
Patients Notes:
Patients should be aware of the following information:
• Patients should notify their doctor if they have the following symptoms: unusual fatigue or weakness; loss of appetite; upper belly pain; dark-colored urine; or yellowing of the skin or the whites of the eyes.
• Memory loss and confusion have been reported with statin use. These events were generally not serious and went away once the drug was no longer being taken.
• Increases in blood sugar levels with statin use.
Due to the risk of myopathy with drugs of the HMG-CoA reductase class, to which the Atorvastatin component of **MONTEER®** belongs, patients should be advised to report promptly unexplained muscle pain, tenderness, or weakness, particularly if accompanied by malaise or fever.
Increased Angina and/or Myocardial Infarction: Rarely, patients, particularly those with severe obstructive coronary artery disease, have developed documented increased frequency, duration and/or severity of angina or acute myocardial infarction on starting Calcium channel blocker therapy or at the time of dosage increase. The mechanism of this effect has not been elucidated.
Liver Dysfunction: HMG-CoA reductase inhibitors, like some other lipid-lowering therapies, have been associated with biochemical abnormalities of liver function. Persistent elevations (>3 times the upper limit of normal (ULN) occurring on 2 or more occasions) in serum transaminases occurred in 0.7% ai patients who received Atorvastatin in clinical trials.
Monitoring Liver Enzymes: Liver enzyme tests should be performed before starting statin therapy and as clinically indicated thereafter.
Liver enzyme changes generally occur in the first 3 months of treatment with Atorvastatin. Patients who develop increased transaminase levels should be monitored until the abnormalities resolve.
Should an increase in ALT or AST of >3 times ULN persist, reduction of dose or withdrawal of **MONTEER®** is recommended.
MONTEER® should be used with caution in patients who consume substantial quantities of alcohol and/or have a history of liver disease. Active liver disease or unexplained persistent transaminase elevations are contraindications to the use of **MONTEER®**.
Skeletal Muscle: Rare cases of rhabdomyolysis with acute renal failure secondary to myoglobinuria have been reported with the Atorvastatin component of **MONTEER®** and with other drugs in the HMG-CoA reductase inhibitor class.
Uncomplicated myalgia has been reported in Atorvastatin-treated patients.
Myopathy, defined as muscle aches or muscle weakness in conjunction with increases in creatine phosphokinase (CPK) values >10 times ULN, should be considered in any patient with diffuse myalgias, muscle tenderness or weakness, and/or marked elevation of CPK. Patients should be advised to report promptly unexplained muscle pain, tenderness or weakness, particularly it accompanied by malaise or fever. **MONTEER®** therapy should be discontinued if markedly elevated CPK levels occur or myopathy is diagnosed suspected.
The risk of myopathy during treatment with drugs in the HMG-CoA reductase inhibitor class is increased with concurrent administration of cyclosporine, fibric acid derivatives. Erythromycin, Clarithromycin, combination of ritonavir plus saguinavir or lopinavir plus ritonavir, niacin or azol antifungals. Physicians considering combined therapy with **MONTEER®** and fibric acid derivatives, erythromycin, clanthromycin, combination of ritonavir plus saguinavir or lopinavir plus ritonavir, immunosupportive drugs, azol antifungals or lipid-modifying doses of niacin should carefully weigh the potential benefits and risks and should carefully monitor patients for any signs or symptoms of muscle pain, tenderness or weakness, particularly during the initial months of therapy and during any periods of upward dosage titration of either drug. Lower starting and maintenance doses of Atorvastatin should be considered when taken concomitantly with the aforementioned drugs.
Periodic creatine phosphokinase (CPK) determinations may be considered in such situations, but there is no assurance that such monitoring will prevent the occurrence of severe myopathy.
In patients taking **MONTEER®**, therapy should be temporarily withheld or discontinued in any patient with an acute, serious condition suggestive of a myopathy or having a risk factor predisposing to the development of renal failure secondary to rhabdomyolysis (e.g. severe acute infection, hypotension, major surgery, trauma, severe metabolic, endocrine and electrolyte disorders, and uncontrolled seizures).
Use during pregnancy and lactation:
Pregnancy: HMG-CoA reductase inhibitors are contraindicated during pregnancy and in nursing mothers. **MONTEER®** which includes Atorvastatin should be administrated to women of childbearing age only when such patients are highly unlikely to conceive and have been informed of the potential hazards. If the patient becomes pregnant while taking this drug, therapy should be discontinued and the patients apprised of the potential hazard to the fetus.
Labor and Delivery: No studies have been conducted in pregnant women on the effect of **MONTEER®** Amlodipine or Atorvastatin on the mother or the fetus during labor or delivery, or on the duration of labor or delivery. Amlodipine has been shown to prolong the duration of labor in rats.
Lactation: It is not known whether the Amlodipine is excreted in human milk. Because of the potential for adverse reactions in nursing infants, women taking **MONTEER®** should not breast-feed.
Drug Interactions:
No drug interaction studies have been conducted with **MONTEER®** and other drugs, although studies have been conducted in the individual Amlodipine and Atorvastatin components, as described below
Studies with Amlodipine:
In vitro data in human plasma indicate that Amlodipine has no effect on the protein binding of drugs tested (digoxin, phenytoin, Warfarin and indomethacin).
Cimetidine: Co-administration of Amlodipine with Cimetidine did not alter the pharmacokinetics of Amlodipine.
Antacid: Co-administration of the antacid with a single dose of Amlodipine had no significant effect on the pharmacokinetics of Amlodipine.
Sildenafil: A single 100 mg dose of Sildenafil in subjects with essential hypertension had no effect on the pharmacokinetic parameters of Amlodipine. When Amlodipine and Sildenafil were used in combination each agent independently exerted its own blood pressure lowering effect.
Digoxin: Co-administration of Amlodipine with digoxin did not change serum digoxin levels or digoxin renal clearance in normal volunteers.
Ethanol (alcohol): Single and multiple 10 mg doses of Amlodipine had no significant effect on the pharmacokinetics of ethanol.
Warfarin: Co-administration of Amlodipine with warfarin did not change the warfarin prothrombin response time
In clinical trials, Amlodipine has been safely administered with thiazide diuretics, beta-blockers, angiotensin-converting enzyme inhibitors, long-acting nitrates, sublingual nitroglycerin, digoxin, warfarin, non-steroidal anti-inflammatory drugs, antibiotics and oral hypoglycemic drugs.
Studies with Atorvastatin:
The risk of myopathy during treatment with HMG-CoA reductase inhibitors is increased with concurrent administration of fibric acid derivatives, lipid-modifying doses of niacin or cytochrome P450 3A4 inhibitors (e.g. cyclosporine, erythromycin, Clarithromycin and azole antifungals).
Inhibitors of Cytochrome P450 3A4: Atorvastatin is metabolized by cytochrome P450 3A4. Concomitant administration of Atorvastatin with inhibitors of cytochrome P450 3A4 can lead to increases in plasma concentrations of Atorvastatin. The extent of interaction and potentiation of effects depends on the variability of effect on cytochrome P450 3A4.
- Clarithromycin: Concomitant administration of Atorvastatin 80mg with Clarithromycin (500mg twice daily) resulted in a 4.4-fold increase in Atorvastatin AUC.
- Erythromycin: In healthy individuals, plasma concentrations of Atorvastatin increased approximately 40% with co-administration of Atorvastatin and erythromycin, a known inhibitor of cytochrome P450 3A4.
- Combination of Protease Inhibitors: Concomitant administration of Atorvastatin 40 mg with ritonavir plus saquinavir (400 mg twice daily) resulted in a 3-fold increase in Atorvastatin AUC. Concomitant administration of Atorvastatin 20mg with lopinavir plus ritonavir (400 mg+100 mg twice daily) resulted in a 5.9-fold increase in Atorvastatin AUC.
- Itraconazole: Concomitant administration of Atorvastatin (20 to 40 mg) and Itraconazole (200 mg) was associated with a 2.5-3.3-fold increase in Atorvastatin AUC.
- Diltiazem hydrochloride: Co-administration of Atorvastatin (40 mg) with Diltiazem (240 mg) was associated with higher plasma concentrations of Atorvastatin.
- Cimetidine: Atorvastatin plasma concentrations and LDL-C reduction were not altered by co-administration of Cimetidine,
- Grapefruit Juice: Contains one or more components that inhibit CYP 3A4 and can increase plasma concentrations of Atorvastatin, especially with excessive grapefruit juice consumption (> 1 ,2 liters per day).
- Cyclosporine: Atorvastatin and Atorvastatin-metabolites are substrates of the OATP1B1 transporter. Inhibitors of the OATP1B1 (e.g. cyclosporine) can increase the bioavailability of Atorvastatin. Concomitant administration of Atorvastatin 10mg and cyclosporine 5.2 mg/kg/day resulted in an 8.7-fold increase in Atorvastatin AUC. In cases where co-administration of Atorvastatin with cyclosporine is necessary, the dose at Atorvastatin should not exceed 10 mg.
Inducers of cytochrome P450 3A4: Concomitant administration of Atorvastatin with inducers of cytochrome P450 3A4 (e.g. efavirenz, rifampin) can lead to variable reductions in plasma concentrations of Atorvastatin. Due to the dual interaction mechanism of rifampin, simultaneous co-administration of Atorvastatin with rifampin is recommended, as delayed administration of Atorvastatin after administration of rifampin has been associated with a significant reduction in Atorvastatin plasma concentrations.
- Antacid: When Atorvastatin and Antacid suspension were co-administered, plasma concentrations of Atorvastatin decreased approximately 35%. However, LDL-C reduction was not altered.
- Antipyrine: Because Atorvastatin does not affect the pharmacokinetics of antipyrine, interactions with other drugs metabolized via the same cytochrome isozymes are not expected.
- Colestipol: Plasma concentrations of Atorvastatin decreased approximately 25% when colestipol and Atorvastatin were co-administered. However, LDL-C reduction was greater when Atorvastatin and colestipol were co-administered than when either drug was given alone.
- Digoxin: When multiple doses of Atorvastatin and digoxin were co-administered steady-state plasma digoxin concentrations increased by approximately 20%. Patients taking digoxin should be monitored appropriately.
- Oral Contraceptive: Co-administration of Atorvastatin and an oral contraceptive increased AUC values for norethindrone and ethinyl estradiol by approximately 30% and 20%. These increases should be considered when selecting an oral contraceptive for a woman faking **MONTEER®**.
- Warfarin: Atorvastatin had no clinically significant effect on prothrombin time when administered to patients receiving chronic warfarin treatment.
- Amlodipine: In a drug-drug interaction study in healthy subjects, co-administration of Atorvastatin 80 mg and Amlodipine 10 mg resulted in an 18% increase in exposure to Atorvastatin which was not clinically meaningful.
Drug/Laboratory Test Infractions: Not known.
Side Effects:
In general, treatment with **MONTEER®** was well tolerated. For the most part, adverse experiences have been mild or moderate in severity. In clinical trials with **MONTEER®**, no adverse experiences peculiar to this combination have been observed. Adverse experiences are similar in terms of nature, severity, and frequency to those reported previously with Amlodipine and Atorvastatin,
The following information is based on the clinical experience with Amlodipine and Atorvastatin.
The Amlodipine Component of **MONTEER®**:
In general, treatment with Amlodipine was well tolerated at doses up to 10mg daily. Most adverse reactions reported during therapy with Amlodipine were of mild or moderate severity. The most common side effects are headache and edema. The side effects which occurred in a dose related manner are as follows: edema, dizziness, flushing and palpitations.
Other adverse experiences which were not clearly dose related but which were reported with an incidence greater than 1.0% in placebo-controlled clinical trials include the following: headache, fatigue, nausea, abdominal pain and somnolence. For several adverse experiences that appear to be drug and dose related there was a greater incidence in women than men associated with Amlodipine treatment include the following: edema, flushing, palpitations and somnolence.
Side Effects:
The following events occurred in ≤1% but >0.1% of patients treated with Amlodipine in controlled clinical trials or under conditions of open trials or marketing experience where a causal relationship is uncertain; they are listed to alert the physician to a possible relationship:
Cardiovascular: Arrhythmia (including ventricular tachycardia and atrial fibrillation), bradycardia, chest pain, hypotension, peripheral ischemia, syncope, tachycardia, postural dizziness, postural hypotension, vasculitis.
Central and Peripheral Nervous System: Hypoesthesia, neuropathy peripheral, paresthesia, tremor, vertigo.
Gastrointestinal: Anorexia, constipation, dyspepsia, dysphagia, diarrhea, flatulence, pancreatitis, vomiting, gingival hyperplasia.
General: Allergic reaction, asthenia, back pain, hot flushes, malaise, pain, rigors, weight gain, weight decrease.
Musculoskeletal System: Arthralgia, arthrosis, muscle cramps, myalgia.
Psychiatric: sexual dysfunction (male and female), insomnia, nervousness, depression, abnormal dreams, anxiety, depersonalization.
Respiratory System: Dyspnea, epistaxis.
Skin and Appendages: Angioedema, erythema multiforme, pruritus, rash, rash erythematous, rash maculopapular.
Special Senses: Abnormal vision, conjunctivitis, diplopia, eye pain, tinnitus,
Urinary System: Micturition frequency, micturition disorder, nocturia.
Autonomic Nervous System: Dry mouth, sweating increased.
Metabolic and Nutritional: Hyperglycemia, thirst.
Hemopoietic: Leukopenia, purpura, thrombocytopenia.
The following events occurred in ≤ 0.1 % of patients treated with Amlodipine in controlled clinical trials or under conditions of open trials or marketing experience cardiac failure, pulse irregularity, extrasystoles, skin discoloration, urticaria, skin dryness, alopecia, dermatitis, muscle weakness, twitching, ataxia, hypertonia, migraine, cold and clammy skin, apathy, agitation, amnesia, gastritis, increased appetite, loose stools, coughing, rhinitis, dysuria, polyuria, parosmia, taste perversion, abnormal visual accommodation, and xerophthalmia.
Other reactions occurred sporadically and cannot be distinguished from medications or concurrent disease states such as myocardial infarction and angina.
Amlodipine therapy has not been associated with clinically significant changes in routine laboratory tests. No clinically relevant changes were noted in serum potassium, serum glucose, total triglycerides, total cholesterol, HDL cholesterol, uric acid, blood urea nitrogen, or creatinine.
The following post marketing event has been reported infrequently with Amlodipine treatment where a causal relationship is uncertain: gynecomastia. In post marketing experience, jaundice and hepatic enzyme elevations (mostly consistent with cholestasis or hepatitis) in some cases severe enough to require hospitalization have been reported in association with use of Amlodipine.
Amlodipine has been used safely in patients with chronic obstructive pulmonary disease, well- compensated congestive heart failure, peripheral vascular disease, diabetes mellitus and abnormal lipid profiles.
The Atorvastatin Component of **MONTEER®**:
Atorvastatin is generally well-tolerated. Adverse reactions have usually been mild and transient. The most frequent adverse events thought to be related to Atorvastatin Calcium were constipation, flatulence, dyspepsia, and abdominal pain.
Clinical Adverse Experiences:
Adverse experiences reported in ≥2% of patients in placebo-controlled clinical studies of Atorvastatin.
The following adverse events were reported regardless of causality assessment. In patients treated with Atorvastatin in clinical trials. The events in italics occurred in ≥2% of patients and the events in plain type occurred in <2% of patients.
Body as a Whole: Chest pain, face edema, fever, neck rigidity, malaise, photosensitivity reaction, generalized edema.
Digestive System: Nausea, gastroenteritis, liver function tests abnormal, colitis, vomiting, gastritis, dry mouth, rectal hemorrhage, esophagitis, eructation, glossitis, mouth ulceration, anorexia, increased appetite, stomatitis, biliary pain, cheilitis, duodenal ulcer, dysphagia, enteritis, melena, gum hemorrhage, stomach ulcer, tenesmia, ulcerative stomatitis, hepatitis, pancreatitis. cholestatic jaundice.
Respiratory System: Bronchitis. rhinitis, pneumonia. dyspnea, asthma, epistaxis.
Nervous System: Insomnia, dizziness. paresthesia, somnolence, amnesia, abnormal dreams, libido decreased, emotional lability, incoordination, peripheral neuropathy, torticollis, facial paralysis. hyperkinesia, depression, hypesthesin, hypertonia.
Musculoskeletal System: Arthritis, leg cramps, bursitis. tenosynovitis, myasthenia, tendinous contracture, myositis.
Skin and Appendages: Pruritus, contact dermatitis, alopecia, dry skin, sweating, acne. urticaria, eczema, seborrhea, skin ulcer.
Urogenital System: Urinary tract infection, hematuria, albuminuria, urinary frequency, cystitis, impotence, dysuria, kidney calculus, nocturia, epididymitis. fibrocystic breast, vaginal hemorrhage, east enlargement, metrorrhagia, nephritis, urinary incontinence, urinary retention, urinary urgency, abnormal ejaculation, uterine hemorrage.
Special Senses: Amblyopia, tinnitus, dry eyes, refraction disorder, eye hemorrhage, deafness, glaucoma, parosmia, taste loss, taste perversion.
Cardiovascular System: Palpitation, vasodilatation, syncope, migraine, postural hypotension, phlebitis, arrhythmia, angina pectoris, hypertension.
Metabolic and Nutritional Disorders: Peripheral edema, hyperglycemia, creatine phosphokinase increased, gout, weight gain and hypoglycemia.
Hemic and Lymphatic System: Ecchymosis, anemia, lymphadenopathy, thrombocytopenia, petechia.
Post-introduction Reports with Atorvastatin: Adverse events associated with Atorvastatin therapy reported since market introduction, that are not listed above, regardless of causality assessment, include the following: anaphylaxis, angioneurotic edema, bullous rashes (including erythema multiforme, Stevens-Johnson syndrome, and toxic epidermal necrolysis), rhabdomyolysis, fatigue and tendon rupture.
Pediatric Patients (ages 10-17 years): The safety and tolerability profile of Atorvastatin 10 to 20mg daily was generally similar to that of placebo.
Information about the potential for generally non serious and reversible cognitive side effects (memory loss, confusion, etc.).
Increased blood sugar and glycosylated hemoglobin (HbAlc) levels has been have been reported with statin use.
Overdosage:
There is no information on overdosage with **MONTEER®** in humans.
Information on Amlodipine:
Overdosage might be expected cause excessive peripheral vasodilation with marked hypotension possibly a reflex tachycardia. In humans, experience with intentional overdosage of Amlodipine is limited.
If massive overdose should occur, active cardiac and respiratory monitoring should be instituted. Frequent blood pressure measurements are essential. Should hypotension occur, cardiovascular support including elevation of the extremities and the judicious administration of fluids should be initiated. If hypotension remains unresponsive to these conservative measures, administration of vasopressors (such as phenylephrine) should be considered with attention to circulating volume and urine output. Intravenous Calcium gluconate may help to reverse the effects of Calcium entry blockade. As Amlodipine is highly protein bound, hemodialysis is not likely to be of benefit.
Information on Atorvastatin:
There is no specific treatment for Atorvastatin overdosage. In the event of an overdose, the patient should be treated symptomatically, and supportive measures instituted as required. Due to extensive drug binding to plasma proteins, hemodialysis is not expected to significantly enhance Atorvastatin clearance.
Storage Conditions:
Store up to 30°C.
Presentation:
MONTEER® 5/10mg: Each film coated tablet contains Amlodipine Besylate equivalent to Amlodipine 5 mg and Atorvastatin Calcium equivalent to Atorvastatin 10 mg in packs of 30 tablets.
MONTEER® 10/10mg: Each film coated tablet contains Amlodipine Besylate equivalent to Amlodipine 10 mg and Atorvastatin Calcium equivalent to Atorvastatin 10 mg in packs of 30 tablets.
Hospital packs are also available.
Excipients:
- **MONTEER® 5/10mg**: Calcium Carbonate, Croscarmellose sodium, Hydroxypropyl Cellulose, Microcrystalline Cellulose, Pregelatinized starch, Polysorbate, Colloidal silicon dioxide, Magnesium Stearate & Opadry white.
- **MONTEER® 10/10mg**: Calcium Carbonate, Croscarmellose sodium, Hydroxypropyl Cellulose, Microcrystalline Cellulose, Pregelatinized starch, Polysorbate, Colloidal silicon dioxide, Magnesium Stearate, Opadry white & Blue 2 Indigo carmine lake blue.

This is a medicament
• 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
• Keep medicament out of the reach of children.

COUNCIL OF ARAB HEALTH MINISTERS
UNION OF ARAB PHARMACISTS

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Feb., 2013
M3-14-0562