For patients with primary or mixed hypercholesterolemia

Choose ATOZET® for the power to help take LDL-C lower

V Powerful **dual action** to **help lower LDL-C** in patients with hypercholesterolemia and reduce CV events in patients with CHD and a history of acute coronary syndrome¹¹ **ATOZET**[®] provided **53% mean LDL-C reduction** at the lowest dose (10/10mg) - similar to the highest dose of atorvastatin (80mg, 54%)⁷ **ATOZET®** provided **significantly greater mean additional LDL-C reduction** vs. doubling dose of atorvastatin or switching to *rosuvastatin*^{8,9} **V** ATOZET[®] was generally well tolerated in multiple clinical trials¹²



Before prescribing ATOZET®, please read the prescribing information .



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WPRAVF-II

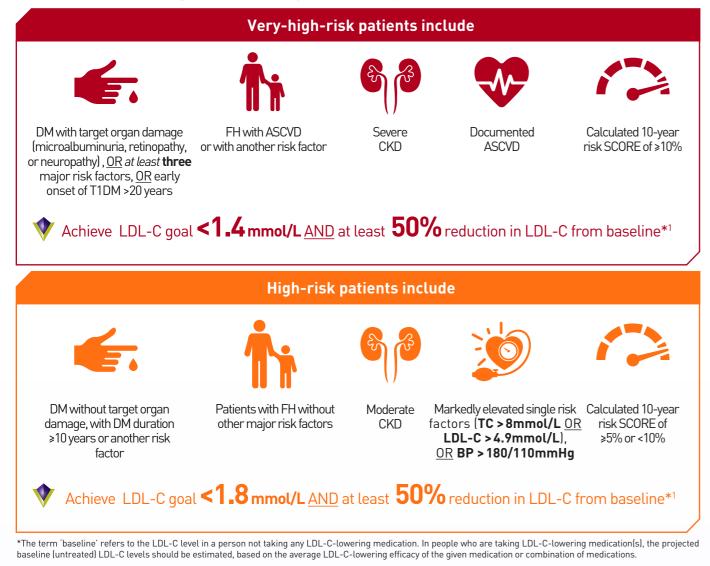
WITH POWERFUL DUAL ACTION OF

ACHIEVE TARGET LDL-C LEVELS



2019 ESC/EAS Guidelines for the Management of Dyslipidaemia¹

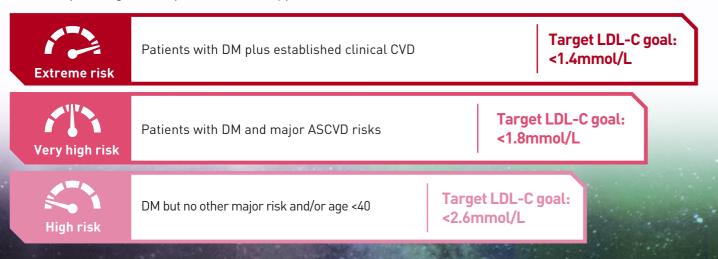
Recommended LDL-C goals for very-high-risk and high-risk patients¹



Combination therapy may be needed to reach LDL-C goal

2019 AACE/ACE Consensus Statement²

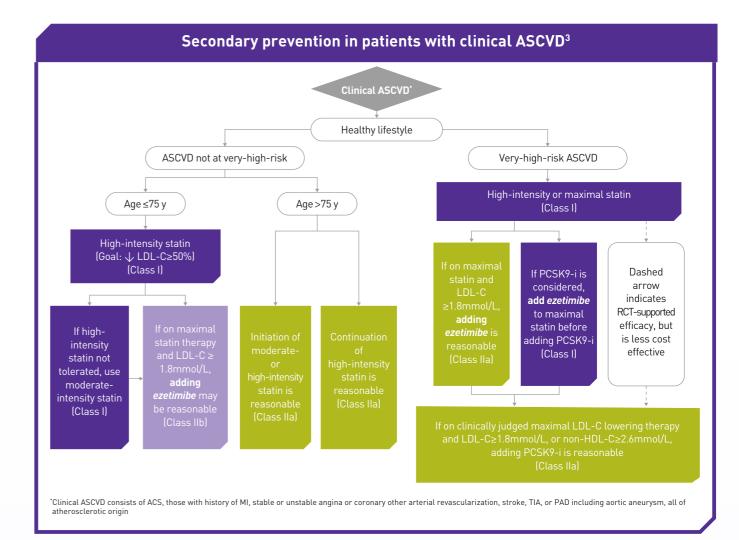
AACE Lipid targets for patients with Type II Diabetes²



Abbreviations: AACE=American Association of Clinical Endocrinologists; ACE=American College of Endocrinology; ASCVD=atherosclerotic cardiovascular disease; BP=blood pressure; CKD=chronic kidney disease; CVD=cardiovascular disease; DM=diabetes mellitus; EAS=European Atherosclerosis Society; ESC=European Society of Cardiology; FH=familial hypercholesterolemia; LDL-C=low-density lipoprotein cholesterol; SCORE=Systematic Coronary Risk Estimation; TC=total cholesterol; T1DM=Type 1 diabetes mellitus

2018 AHA/ACC Guideline on the Management of Blood Cholesterol³

AHA/ACC guideline recommends to use *ezetimibe* as second-line therapy in association with statins if LDL-C levels continue to exceed ≥1.8mmol/L.³



Very-high-risk includes a history of multiple major ASCVD events or 1 major ASCVD event and multiple high-risk conditions.³

| Major ASCVD events | High |
|---|--------------|
| Recent ACS (within the past 12 months) | Age ≥6 |
| History of MI (other than recent ACS event listed a | bove) Hetero |
| History of ischemic stroke | History |
| Symptomatic PAD | corona |
| | DM |
| | Hypert |
| | CKD (e |
| | Currer |
| | Persist |
| | statin t |
| | History |
| | |

Abbreviations: ACC=American College of Cardiology; ACS=acute coronary syndrome; AHA=American Heart Association; ASCVD=atherosclerotic cardiovascular disease; CKD=chronic kidney disease; DM=diabetes mellitus; eGFR=estimated glomerular filtration rate; FH=familial hypercholesterolemia; HDL-C=high-density lipoprotein cholesterol; HF=heart failure; LDL-C=low-density lipoprotein cholesterol; MI=myocardial infarction; PAD=peripheral artery disease; PCSK9-i=proprotein convertase subtilisin/kexin type 9 inhibitor; RCT=randomized controlled trial; TIA=transient ischemic attack

n-risk conditions

| ≥65 years old |
|--|
| rozygous FH |
| ory of prior coronary artery bypass surgery or percutaneous nary intervention outside of the major ASCVD event(s) |
| rtension |
| (eGFR 15-59mL/min/1.73m²) ent smoking |
| istently elevated LDL-C (>2.6mmol/L) despite maximally tolerated n therapy and <i>ezetimibe</i> |
| bry of congestive HF |
| |

DYSIS II: a multinational, multicenter, observational study of lipid profiles, lipid target value attainment, and LLT of 10,661 patients with stable CHD or being hospitalized for an ACS event in 18 countries⁴

About 2 in 3 patients did not reach their recommended LDL-C levels of <1.8mmol/L⁴

In CHD patients⁴

(n=6,794), mean baseline LDL-C was 2.27mmol/L

About 70.6% of patients did not reach their LDL-C goal, with a median distance of 0.62mmol/L from LDL-C goal



93.8% (n=6,370) were on LLT, of which 82.3% were on statin monotherapy

Mean LLT-treated LDL-C baseline was 2.22mmol/L

🐐 In ACS patients4

(n=3,867), mean baseline LDL-C was 2.80mmol/L

About 81.1% of patients did not reach their LDL-C goal, with a median distance of **1.11mmol/L** from LDL-C goal

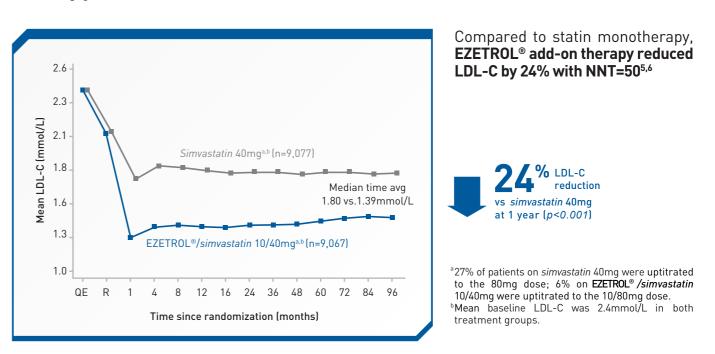


65.2% (n=2.521) were on LLT. of which **90.4%** were on statin monotherapy

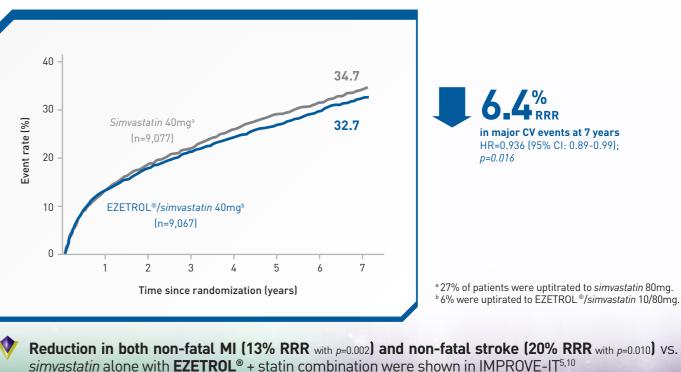
Mean LLT-treated LDL-C baseline was 2.51mmol/L

EZETROL[®] (ezetimibe)

IMPROVE-IT: A trial of 18,144 patients with high-risk ACS Powerful LDL-C reductions with EZETROL® + statin combination therapy^{5,6}



Primary endpoint: Significant reductions in major CV events with EZETROL® + statin combination therapy compared with *simvastatin* alone at 7 years^{5,6}



Study design: The DYSIS II study aimed to determine LDL-C target value attainment, use of LLT, and car ular outcomes in patients with stable CHD and those suffering from ACS. The study included 10,661 patients from 18 countries. Patients with either stable CHD or an ACS were enrolled if they were >18 years old and had a full lipid profile available. Data were collected at a physician visit (CHD cohort) or at hospital admission and 120 days later (ACS cohort).

Abbreviations: ACS=acute coronary syndrome; CHD=coronary heart disease; DYSIS=Dyslipidemia International Study; LDL-C=low-density lipoprotein cholesterol; LLT=lipid lowering therapy

non-fatal stroke. The median follow-up was 6 years.

Trial; LDL-C=low-density lipoprotein cholesterol; LLT=lipid-lowering therapy; MI=myocardial infarction; NNT=number needed to treat; RRR=relative risk reduction

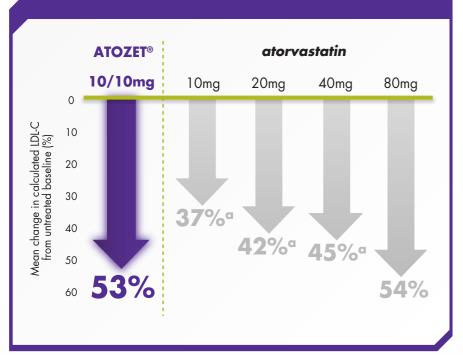
Study design: The IMPROVE-IT was a double-blind, randomized study involving 18,144 patients who had been hospitalized for an ACS within the preceding 10 days and had LDL-C levels of 1.3-2.6mmol/L if they were receiving LLT or 1.3-3.2mmol/L if they were not receiving LLT. The combination of *simvastatin* (40mg) and *ezetimibe* (10mg) was compared with *simvastatin* (40mg) alone and placebo. The primary end point was a composite of CV death, non-fatal MI, unstable angina requiring rehospitalization, coronary revascularization (>30 days after randomization), or

Abbreviations: ACS=acute coronary syndrome; CI=confidence interval; CV=cardiovascular; HR=hazard ratio; IMPROVE-IT=Improved Reduction of Outcomes: Vytorin Efficacy International

In a clinical study of patients with hyperlipidemia and not on lipid-lowering therapy,

ATOZET® 10/10mg powerfully lowered mean LDL-C by 53%7

Efficacy of the lowest dose of ATOZET® (10/10mg) was similar to that the highest dose of atorvastatin (80mg)⁷



Mean pooled untreated baseline calculated LDL-C was 4.70mmol/L for the group receiving ATOZET® and 4.69mmol/L for the group receiving atorvastatin. Mean change in calculated LDL-C from untreated baseline was 54% for ATOZET® 10/20mg; 56% for ATOZET® 10/40mg* and 61% for ATOZET® 10/80mg*.7

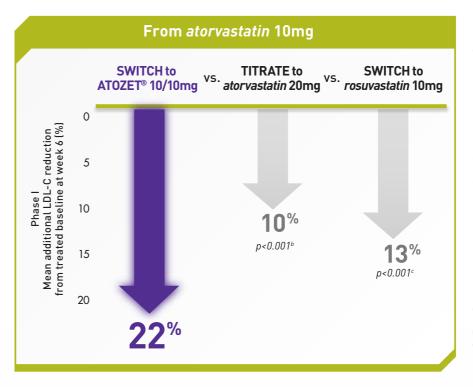
*Strengths not available in Hong Kong ^a*p*<0.01 for combination therapy vs. corresponding dose of atorvastatin alone

e 10mg plus atorvastatin 20mg, atorvastatin 40mg, ezetimibe 10mg

For every 1mmol/L reduction in LDL-C, 22% relative reduction in the incidence of any major vascular event over 5 years¹

In a study of high-risk patients with hypercholesterolemia^a not at LDL-C<2.6mmol/L on atorvastatin 10mg,

Switching to ATOZET® 10/10mg provided greater LDL-C reduction versus doubling atorvastatin to 20mg or switching to rosuvastatin 10mg⁸



10mg (7%) (p<0.001 for both comparison)8

Study design: A rando with atorvastatin would result in a significantly greater reduction in LDL-C than atorvastatin alone. 628 patients were randomly assigned to 1 of 10 treatments: placebo ezetimibe 10mg, atorvastatin 10mg, ezetimibe 10mg plus atorvastatin 10mg, atorvastatin 20mg, ezetimibe 10mg plus atorvastatin 20mg, atorvastatin 40mg, ezetimibe 10mg plus atorvastatin 40mg, or ezetimibe 10mg plus atorvastatin 80mg. The primary efficacy endpoint was the percentage reduction in direct LDL-C from baseline to final assessment for the intent-to-treat population

nized double-blind placebo-co

Abbreviation: LDL-C=low-density lipoprotein cholesterol

ATOZET® has been shown to be bioequivalent to coadministration of corresponding doses of ezetimibe and atorvastatin tablets.1

Study design: The PACE study was a random LDL-C>2.6mmol/L and <4.14mmol/L while on atorvastatin 10mg. The study *statin* to 20mg or switching to *ros* or doubled the atorvastatin dose from 20mg to 40mg, or switched from from treated baseline LDL-C levels at the end of phase I. Secondary efficacy comparisons included the percentages of patients achieving LDL-C<2.6mmol/L or <1.8mmol/L among the same groups? Abbreviations: CV=cardiovascular; LDL-C=low-density lipoprotein cholestero

ATOZET® has been shown to be bioequivalent to coadministration of corresponding doses of ezetimibe and atorvastatin tablets.

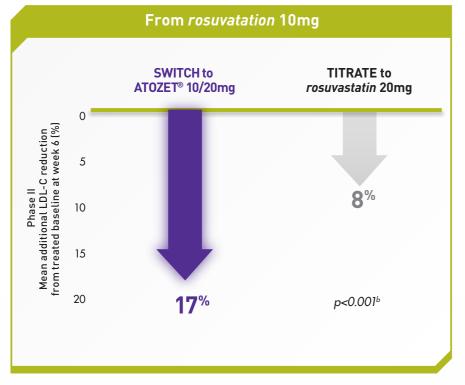
The mean statin-treated baseline LDL-C was 3.13mmol/L for the group receiving **ATOZET**[®] **10/10mg** (n=120), 3.10mmol/L for the group titrated to atorvastatin 20mg (n=483), and 3.13mmol/L for the group that switched to rosuvastatin 10mg (n=944).8

^aBased on National Cholesterol Education Program Adult Treatment Panel III guidelines ^bATOZET[®] 10/10mg vs *atorvastatin* 20mg ^cATOZET[®] 10/10mg vs *rosuvastatin* 10mg

Significantly more patients reached LDL-C<1.8mmol/L after 6 weeks by switching to ATOZET® 10/10mg (19%) vs. titrating to atorvastatin 20mg (3%) and switching to rosuvastatin

lit into 2 phases, each 6 weeks. Patients in phase I received *ezetimibe* 10mg add-on to *atorvastatin* 10mg vs. doubling astatin 10mg. Phase II patients did not achieve an LDL-C target of <2.6mmol/L after phase I, and received either the addition ofezetimibe 10mg to atomas in 10mg to ezetimibe 10mg plus atorvastatin 20mg or doubled rosuvastatin to 20mg. Primary efficacy was the percent change In the same study of high-risk patients with hypercholesterolemia^a, among those patients still not at LDL-C<2.6mmol/L, after 6 weeks of treatment at the end of phase I

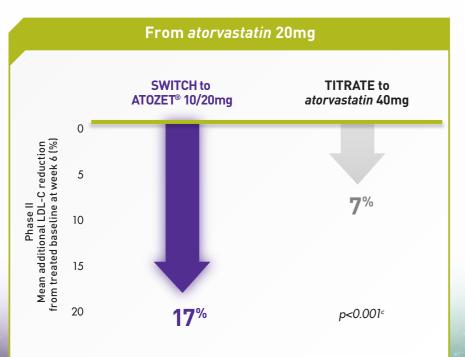
Switching to ATOZET[®] 10/20mg provided greater LDL-C reduction versus doubling to rosuvastatin 20mg or atorvastatin 40mg8



Mean baseline LDL-C for receiving ATOZET® 10/20mg (n=234) was 3.08mmol/L, and 3.10mmol/L for those titrated to rosuvastatin 20mg (n=206)8

Significantly more patients reached LDL-C<1.8mmol/L at week 6 after phase II by switching to ATOZET® 10/20mg (15%) or titrating to rosuvastatin 20mg (3%) (p<0.001)8

^aBased on National Cholesterol Education Program Adult Treatment Panel III guidelines ^bATOZET[®] 10/20mg vs. *rosuvastatin* 20mg



Mean baseline LDL-C for receiving ATOZET® 10/20mg (n=124) was 3.08mmol/L, and 3.13mmol/L for those titrated to atorvastatin 40mg (n=126)8

Significantly more patients reached LDL-C<1.8mmol/L at 6 weeks after phase II by switching to ATOZET® 10/20mg (18%) or titrating to atorvastatin 40mg (1%) (p<0.01)8

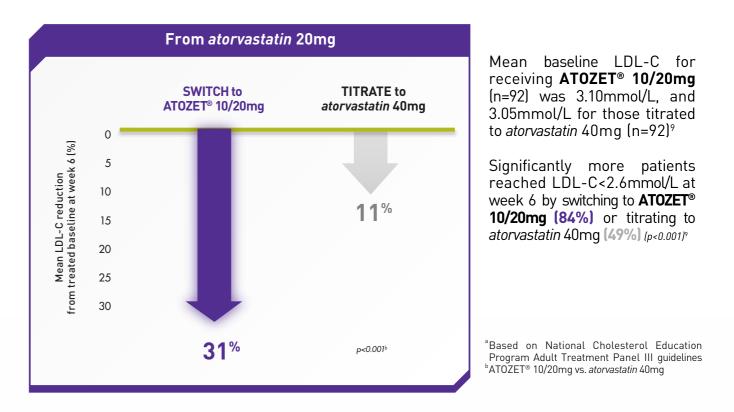
^aBased on National Cholesterol Education Program Adult Treatment Panel III guidelines °ATOZET® 10/20mg vs. atorvastatin 40mg

ed 18 to <80 years with primary hypercholesterolemia and high CV risk who had

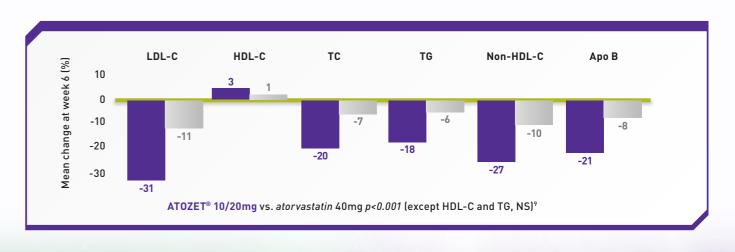
LDL-C>2.6mmol/L and <4.14mmol/L while on atonastatin 10mg. The study was split into 2 phases, each 6 weeks. Patients in phase I received ezetimibe 10mg add-on to atonastatin 10mg vs. doubling atonastatin to 20mg or switching to roswastatin 10mg. Phase II patients did not achieve an LDL-C target of <2.6mmol/L after phase I, and received either the addition of ezetimibe 10mg to atonastatin 20mg or doubled the atonastatin dose from 20mg to 40mg, or switched from roswastatin 10mg to ezetimibe 10mg plus atonastatin 20mg or doubled roswastatin to 20mg. Primary efficacy was the percent change from treated baseline LDL-C levels at the end of phase I. Secondary efficacy comparisons included the percentages of patients achieving LDL-C <2.6mmol/L or <1.8mmol/L among the same groups.

In a study of patients with hypercholesterolemia at moderately high-risk^a for coronary heart disease not at LDL-C<2.6mmol/L on atorvastatin 40mg

Switching to ATOZET[®] 10/20mg provided superior LDL-C lowering efficacy versus doubling the dose of atorvastatin⁹



ATOZET® 10/20mg showed comparable changes in lipid levels to atorvastatin 40mg⁹



Study design: The TEMPO study was an international, multicenter, double-blind, randomized, parallel-group, titration 6-week study, including 196 patients. The study was designed to evaluate the efficacy and safety profile of ATOZET® 10/20mg compared with doubling atorvastatin to 40mg/day in patients with hypercholesterolemia at moderate Abbreviations: ApoB=apolipoprotein B; CHD=coronary heart disease; HDL-C=high-density lipoprotein cholesterol; LDL-C=low-density lipoprotein cholesterol; NS=not significant; TC=total cholesterol; TG=triglycerides

ATOZET® has been shown to be bioequivalent to coadministration of corresponding doses of ezetimibe and atorvastatin tablets.11

Study design: The PACE study was a randomized, double-blind, active-controlled, multicenter study of 1,547

Abbreviations: CV=cardiovascular; LDL-C=low-density lipoprotein cholesterol

risk of CHD who did not reach LDL-C goal<2.6mmol/L with atorvastatin 20mg. Patients receiving atorvastatin 20mg with LDL-C>2.6mmol/L and <4.13mmol/L were randomized to receive ATOZET® 10/20mg or atorvastatin 40mg. The primary end point was the mean percentage change from baseline LDL-C. Secondary end points included percentage of patients achieving LDL-C<2.6mmol/L and the percentage change from baseline to 6 weeks in TC, TG, HDL-C, non-HDL-C, apo B and high-sensitivity C-reactive protein.⁹

ATOZET[®] was generally well-tolerated in multiple clinical trials¹²

ATOZET[®] has been evaluated for safety in more than 2,400 patients in 7 clinical trials^{11,12}

The following common (≥1/100, <1/10) or uncommon (≥1/1,000, <1/100) drug-related adverse experiences were reported in patients taking ATOZET®:

| System organ class | Frequency and adverse reactions | |
|--|---------------------------------|--|
| | | |
| Infections and infestations | Uncommon: | influenza |
| Psychiatric disorders | Uncommon: | depression; insomnia; sleep disorder |
| Nervous system disorders | Uncommon: | dizziness; dysgeusia; headache; paresthesia |
| Cardiac disorders | Uncommon: | sinus bradycardia |
| Vascular disorders | Uncommon: | hot flush |
| Respiratory, thoracic, and mediastinal disorders | Uncommon: | dyspnea |
| Gastrointestinal disorders | Common: | diarrhea |
| | Uncommon: | abdominal discomfort; abdominal distension; abdominal pain; abdominal pain lower; abdominal pain upper; constipation; dyspepsia; flatulence; frequent bowel movements; gastritis; nausea; stomach discomfort |
| Skin and subcutaneous tissue disorders | Uncommon: | acne; urticaria |
| Musculoskeletal | Common: | myalgia |
| and connective tissue disorders | Uncommon: | arthralgia; back pain; muscle fatigue; muscle |
| | | spasms; muscular weakness; pain in extremity |
| General disorders and administration site conditions | Uncommon: | asthenia; fatigue; malaise; edema |
| Investigations | Uncommon: | ALT and/or AST increased; alkaline phosphatase increased; blood CPK increased; gamma- glutamyltransferase increased; hepatic enzyme increased; liver function test abnormal; weight increased |
| | | In controlled clinical trials, the incidence of clinically important elevations in serum transaminases (ALT and/or AST≥3 × ULN, consecutive) was 0.6% for |

patients treated with ATOZET[®]. These elevations in transaminases were generally asymptomatic, not associated with cholestasis, and returned to baseline spontaneously or after discontinuation of therapy.

References: 1. Mach, F. et al. 2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk The Task Force for the management of dyslipidaemias of the European Society of Cardiology (ESC) and European Atherosclerosis Society (EAS). Eur Heart J. doi:10.1093/eurheartj/ehz455 2. Garber, A. J. et al. Consensus Statement by the American Association of Clinical Endocrinologists and American Collage of Endocrinology on the Comprehensive Type 2 Diabetes Management Algorithm - 2019 Executive Summary. *Endocrine Practice*. 25, 69-100 (2019). **3.** Grundy, S. M. *et al.* 2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/ NLA/PCNA Guideline on the Management of Blood Cholesterol: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. J Am Coll Cardiol. 73, e285–e350 (2019). 4. Gitt, A. K. et al. Cholesterol target value attainment and lipid-lowering therapy in patients with stable or acute coronary heart disease: Results from the Dyslipidemia International Study II. Atherosclerosis. 266,158-166 (2017). 5. Cannon, C. P. et al. Ezetimibe Added to Statin Therapy after Acute Coronary Syndromes. N Engl J Med. 372(25), 2387-2397 (2015). 6. TIMI Study Group. IMPROVE_IT Main Study *Circulation*. 107,2409–2415 (2003). 8. Bays, H. E. *et al.* Efficacy and Safety of Ezetimibe Added to Atorvastatin Versus Atorvastatin Uptitration or Switching to Rosuvastatin in Patients With Primary Hypercholesterolemia. Am J Cardiol. 112,1885–1895 (2013). 9. Conard, S. E. et al. Efficacy and Safety of Ezetimibe Added on to Atorvastatin (20 mg) Versus Uptitration of Atorvastatin (to 40 mg) in Hypercholesterolemic Patients at Moderately High Risk for Coronary Heart Disease. Am J Cardiol. 102(11), 1489-1494 (2008). 10. Worldwide Product Circular (ezetimibe). 11. Hong Kong Product Circular (Atozet, MSD). 12. Data on file, MSD.

ATOZET Selected Safety Informatio

INDICATIONS: Prevention of Cardiovascular Events: ATOZET is indicated to reduce the risk of cardiovascular events in patients with coronary heart disease (CHD) and a history of acute coronary syndrome (ACS), either previously treated with a statin or not. <u>Hypercholesterolaemia</u>: ATOZET is indicated as adjunctive therapy to diet for use in adults with primary (heterozygous familial and non-familial) hypercholesterolaemia or mixed hyperlipidaemia where use of a combination product is appropriate. Patients not appropriately controlled with a statin alone. Patients already treated with a statin and ezetimibe; <u>Homozygous Familial Hypercholesterolaemia</u> Hyperpilodemin and exemption and product is appropriate. Fallens not appropriate, continuer owner a standard and exemption and e The dose of ATOZET should be individualised based on the known emicacy of the various dose strengtms of ATOZET and the response to the current cholesterohowering merapy. Adjustment of acids should be made at intervals of 4 weeks or more. Homozygous Familial Hypercholesterolaemia - The dose of ATOZET in patients with homozygous FH is 10/10 to 10/80 mg daily. ATOZET may be used as an adjunct to other lipid lowering treatments (e.g., IDL apheresis) in these patients or if such treatments are unavailable. Coadministration with other medicines - Dosing of ATOZET should occur either ≥2 hours before or ≥4 hours differ administration of a bile acid sequestrant. In patients taking hepatitis C antiviral agents containing elbasvir or grazoprevir concomitantly with ATOZET, the dose of ATOZET should occur either ≥2 hours before or ≥4 hours differ administration of the excipients (including loctose). Therapy with ATOZET is contraindicated during pregnancy and breast-feeding, and in women of child-bearing potential not using a treatments are unavailable in excipients (including loctose). Therapy with ATOZET is contraindicated during pregnancy and breast-feeding. And in women of child-bearing potential not using riate contraceptive measures. ATOZET is contraindicated in patients with active liver disease or unexplained persistent elevations in serum transaminases exceeding 3 times the upper limit of normal (ULN) percontrols of section and the section of the secti areact the skeletal muscle and cause myolapit, myositis, and myopamy mait may progress to macdomyonysis. - A CFK level should be measured before starting treatment. If CFK levels are significantly elevated (> 5 times 0.04) at baseline, treatment should not be started. - Patients must be asked to promptly report muscle pain, cramps, or weakness especially if accompanied by malaise or fever or if muscle signs and symptoms persist after discontinuing ATOZET. Liver Enzymes - Liver function tests should be performed before the initiation of treatment and periodically thereafter. Should an increase in transminases of greater than 3 times the ULN persist, reduction of dase or withdrawal of ATOZET is recommended. Hepatic Insufficiency - Due to the unknown effects of the increased exposure to ezetimibe in patients with moderate or severe hepatic insufficiency. ATOZET is not recommended. Interstitial lung disease, statin therapy should be discontinued. Diabetes mellitus - Patients at risk ficating gluccase - 5.6 to 6.9 mmol/L, BMH 2016 - Recommended - Diabetes mellitus - Patients at risk ficating gluccase - 5.6 to 6.9 mmol/L. BMbs30kg/m², raised trighcerides, hypertension) should be monitored both clinically and biochemically according to national guidelines. Excipients - ATOZET contains lackes. Patients with rare bereditary problems of galactose intolerance, the Lapp lactose deficiency, or glucose-galactose malabsorption should not take this medicine. **ADVERSE EVENTS:** Common adverse reactions [21/100, <1/10] include diarrhoea and myalgia. In controlled clinical trials, the incidence of clinically important elevations in serum transaminases (ALT and/or AST \geq 3 X ULN, consecutive) was 0.6% for patients treated with ATOZET. These elevations were generally asymptomatic, not associated with cholestasis, and returned to baseline spontaneously or other discontinuation of therapy. The following additional adverse reactions have been reported in post-marketing use with ATOZET. or in clinical studies or post-marketing use with ezetimibe or atorvastatin: nasopharyngitis, thrombocytopaenia, hypersensitivity, decreased appetite, anorexia, hyperglycaemia, hypoglycaemia, nightmares, hypoesthesia, amnesia, peripheral neuropathy, vision blurred, visual disturbance, tinnitus, hearing loss, hypertension, cough, pharyngolaryngeal pain, epistaxis, pancreatitis, gastro-oesophageal reflux disease, eructation, vomiting, dry mouth, hepatitis, choleclithiasis, cholecystitis, cholestasis, fatal and nonfatal hepatic failure, alopecia, skin rash, pruritus, erythema multiforme, angioneurotic oedema, dermatitis bullous including erythema multiforme, Stevens-Johanna, summers, and taxic epidermal necrolysis, may pathy/habdomyolysis, neck pain, joint swelling, myosis, immune-mediated necrolizing myopathy, gynecomastic, chest pain, point swelling, myosis, immune-mediated necrolizing myopathy, gynecomastic, chest pain, point swelling, myosis, and taxic epidermal necrolysis, myopathy/habdomyolysis, neck pain, joint swelling, myosis, syname and taxic epidermal necrolysis, myopathy/habdomyolysis, neck pain, joint swelling, myosis, syname and taxic epidermal necrolysis, myopathy/habdomyolysis, neck pain, joint swelling, myosis, syname and taxic epidermal necrolysis, myopathy/habdomyolysis, neck pain, joint swelling, myosis, syname and taxic epidermal necrolysis, myopathy/habdomyolysis, neck pain, joint swelling, myosis, syname and taxic epidermal necrolysis, myopathy/habdomyolysis, neck pain, joint swelling, myosis, syname and taxic epidermal necrolysis, myopathy/habdomyolysis, neck pain, joint swelling, myosis, syname and taxic epidermal necrolysis, myopathy/habdomyolysis, neck pain, joint swelling, myosis, syname and taxic epidermal necrolysis, myopathy/habdomyolysis, neck pain, joint swelling, myosis, syname and taxic epidermal necrolysis, myopathy/habdomyolysis, neck pain, joint swelling, myosis, syname and taxic epidermal necrolysis, myopathy/habdomyolysis, neck pain, joint swelling, myosis, syname and taxic epidermal necrolysis, myopathy/habdomyolysis, neck pain, joint swelling, myosis, syname and taxic epidermal necrolysis, myopathy/habdomyolysis, neck pain, joint swelling, myosis, syname and taxic epidermal necrolysis, myopathy/habdomyolysis, neck pain, joint swelling, myosis, syname and taxic epidermal necrolysis, myopathy/habdomyolysis, neck pain, joint swelling, myosis, syname and taxic epidermal necrolysis, myopathy/habdomyolysis, neck pain, joint swelling, myosis, syname and taxic epidermal necrolysis, syname and taxic epidermal necrolysis, neck pain, joint swelling, myosis, syname and taxic epidermal necrolysis, syname and taxic epidermal necrolysis, DRUG INTERACTIONS: Multiple mechanisms may control potential interactions with HMG CoA reductase inhibitors. Drugs or herbal products that inhibit certain enzymes (e.g., CYP3A) and/or transporter (e.g., OATP1B) pathways may increase atorvastatin plasma concentrations and may lead to an increased risk of myopathy/habdomyolysis. Consult the prescribing information of all concomitantly used drugs to obtain further information about their potential interactions with atorvastatin and/or the potential for enzyme or transporter alterations and possible adjustments to dose and regimens. Ezetimibe - Concomitant cholestyramine administration may lessen reduction of low-density lipoprotein cholesterol (LDLC). - Caution should be exercised when initiating ATOZET in the setting of ciclosporin. Ciclosporin concentrations should be monitored in patients receiving ATOZET and ciclosporin. - Coadministration of ATOZET with fibrates is not recommended. Atorocatin - Coadministration of potent CYP3A4 inhibitors [e.g. ciclosporin, letlihromycin, clarithromycin, delavirdine, stripentol, ketoconazole, voriconazole, itraconazole, posaconazole and HIV protease inhibitors including ritonavir, lopinavir, atazanavir, indinavir, darunavir, etc.] should be avoided if possible. - When concomitantly used with A secondable, volcondable, indicating the posterior of ezetimibe or fusidic acid are associated with higher risk of muscle-related events, including rhabdomyolysis. Coadministration of ATOZET with fibrates is not recommended. Appropriate clinical monitoring of patients taking ATOZET and ezetimibe is recommended. Atorvastatin must not be co-administered with systemic formulations of fusidic acid or within 7 days of stopping fusidic acid treatment. In patients where the use of systemic fusidic acid is considered essential, statin treatment should be discontinued throughout the duration of fusidic acid treatment. - Cases of myopathy have been reported with atorvastatin co-administered with colchicine, and caution should be exercised when prescribing atorvastatin with colchicine. - Lipid effects were greater when atorvastatin and colestipol were coadministered than when either medicinal product was given alone. - In patients taking alload be calculated many performance and the second many methods and the second many of atorvastatin and an increased risk of myopathy. Effects of ATOZET on other medicinal products - If ATOZET is added to warfarin, another cournarin anticoagulant, or fluindione, INR should be appropriately monitored. - Patients taking digaxin should be monitored appropriately. Please consult the full prescribing information for detailed drug interaction. USE IN SPECIAL POPULATIONS: Pregnancy - ATOZET is contraindicated during pregnancy. Lactation - ATOZET is contraindicated during breast-feeding. Elderly - No dose adjustment is required for older patients. Children - The safety and efficacy of ATOZET in children has not been established. No data are available. Patients with hepatic impairment - ATOZET should be used with caution in patients with hepatic impairment. - ATOZET is contraindicated in patients with active liver disease. Patients with renal impairment dose adjustment is required for renally impaired patie Before prescribing, please consult the full prescribing information.

EZETROL Selected Safety Inform

INDICATION: Entropy Hypercholesterolemia: EZETROL, administered with an HWG-CoA reductase inhibitor (statin) or alone, is indicated as adjunctive therapy to diet for the reduction of elevated total-C, IDI-C, Apo B and TG and to increase HDI-C in patients with primary (heterozygous familial and non-familial) hypercholesterolemia. EZETROL, administered in combination with fendibitate, is indicated as adjunctive therapy to diet for the reduction of elevated total-C, IDI-C, Apo B, and non-HDI-C in patients with mixed hyperlipidemia. <u>Prevention of Cardiovascular Events</u>: Ezetrol is indicated to reduce the risk of cardiovascular events in patients with coronary heart disease (CHD) and history of acute coronary syndrome (ACS) when added to anging statin therapy or initiate concentiantly with a statin. <u>Homozygous Sinsterolemia (Phytosterolemia)</u> also indicated for the reduction of elevated staterol and campesterol levels in patients with homozygous familial alsosterolemia. **CONTRAINDICATIONS:** Hyperensitivity to any component of this medication. When EZETROL is concentitioned with a chatin, is or with family a chatin, expression of the total coronary for the the Reduction. **CONTRAINDICATIONS:** Hyperensitivity to any component of this medication. When EZETROL is concentitioned with a chatin, is a used in the acute and the acute in the reduction. The reduction of elevated situates of the the Reduction for the total-C in the reduction of the total coronary heart at the Reduction may also receive adjunctive treatments (e.g., IDL apheresis). <u>Homozygous Situaterolemia</u> also indicated for the reduction of elevated situates or for the the Reduction may also receive adjunctive treatments (e.g., IDL apheresis). <u>Homozygous Situaterolemia</u> also indicated for the reduction of elevated situates or for the total coronary participate patients with homozygous familial isotaterolemia. <u>CONTRAINDICATIONS</u>: <u>Hyperensitiaterol with a corrective treatment for the total corrective treatment and eventions to a state is a total correctione</u> with a statin or with fenofibrate, please refer to the Package Insert for that particular medication. **PRECAUTIONS:** When EZETROL is co-administered with a statin, consecutive transaminase elevations (>3 X the upper limit of normal [UIN]) have been observed. Liver function tests should be performed at initiation of therapy and according to the recommendations of the statin. EZETROL and any statin that the patient is taking concomitantly should be immediately discontinued if myopathy is diagnosed or suspected. Treatment with ezetimibe is not recommended in patients with moderate or severe liver dysfunction. Co-administration of EZETROL and fibrates (other than fenofibrate) is not recommended. If cholelithiasis is suspected in a patient receiving EZETROL and fenofibrate, gallbladder studies are indicated and alternative lipid-lowering therapy should be considered. Caution should be exercised when initiating ezetimibe in the setting of cyclosporine. If Ezetrol is added to warfarin or another coumarin anticoagulant, the International Normalized Ratio (INR) should be appropriately monitored. For detailed precautions, please consult the full prescribing information. SIDE EFFECTS: The following common (≥1/100, <1/10) drug-related adverse experiences were reported in patients taking EZETROL administered alone: abdominal pain: diarrhea: flatulence: fatiaue: EZETROL co-adm red with a statin: headache, increased ALT, increased AST; myalgia; EZETROL co-administered with fenofibrate: abdominal pain. For detailed side consult the full pres

Before prescribing, please consult the full prescribing information