New Drug Review

Generic Name: lomitapide
Trade Name: Juxtapid®
Formulation: 5 mg, 10 mg and 20 mg capsules
Manufacturer: Aegerion Pharmaceuticals
FDA Approval Date: December 24, 2012
Product Launch Date: January 2013

Overview/Summary

Juxtapid® (lomitapide) is a microsomal triglyceride transfer protein inhibitor that is Food and Drug Administration-approved as an adjunct to a low-fat diet and other lipid-lowering treatments, including low density lipoprotein apheresis where available, to reduce low density lipoprotein, total cholesterol, apolipoprotein B (ApoB), and non-high-density lipoprotein cholesterol in patients with homozygous familial hypercholesterolemia (HoFH).[1] This agent directly binds and inhibits microsomal triglyceride transfer protein, which resides in the lumen of the endoplasmic reticulum, thereby preventing the assembly of Apo B-containing lipoproteins in enterocytes and hepatocytes. This inhibits the synthesis of chylomicrons and very low density lipoprotein leading to reduced levels of plasma low density lipoprotein.[1]

Familial hypercholesterolemia is a genetically modulated clinical syndrome in which the phenotype is characterized by a high low density lipoprotein cholesterol level from birth and early onset coronary heart disease (including the absence of other risk factors). Established causes include: low density lipoprotein receptor mutations (most common), gain-of-function PCSK9 mutations (less than five percent of cases in most clinics) and familial defective ApoB (less than five percent of cases). The disorder is inherited with a gene dosing effect, in which homozygotes are more adversely affected than heterozygotes. The incidence of HoFH is rare (1 in 250,000 births) unless there is co-sanguineous union in a family with heterozygous familial hypercholesterolemia.[2] Treatment guidelines support the use of high-dose statins, low density lipoprotein apheresis and other cholesterol lowering agents (e.g., ezetimibe), often as part of combination regimens to reach cholesterol goals.[2-13] In refractory cases, liver transplant may be therapeutic options.

The safety and effectiveness of lomitapide has not been established in patients with hypercholesterolemia who do not have HoFH. In addition, the effect of this agent on cardiovascular morbidity and mortality has not been established.[1,14] Lomitapide is associated with significant drug-drug interactions and treatment is contraindicated in patients receiving moderate or strong inhibitors of the cytochrome P450 3A4 enzyme. The prescribing information for lomitapide includes a Black Box Warning regarding the risk of elevations in transaminases, increases in hepatic fat content and risk of hepatotoxicity. As a result, lomitapide is only available through a restricted distribution program under a risk evaluation and mitigation strategy.[1]

Pharmacokinetics

Table 1. Pharmacokinetics[1]

Generic Name	Bioavailability (%)	Absorption (%)	Renal Excretion (%)	Active Metabolites	Serum Half-Life (hours)
Lomitapide	7	Not reported	59	M1, M3	39.7 hours

Clinical Trials

The safety and efficacy of lomitapide in treating elevated cholesterol has been evaluated in fourteen Phase I and eight Phase II clinical trials, as well as a Phase III clinical trial in patients with homozygous familial hypercholesterolemia (HoFH).[15] To date, only one Phase III clinical trial has been published supporting lomitapide in the treatment of HoFH.

Lomitapide was evaluated in a Phase I trial of six patients with HoFH. At doses ranging from 0.03 and 1.00 mg/kg/day, lomitapide treatment significantly decreased low density lipoprotein cholesterol (LDL-C) by 51% and apolipoprotein B (ApoB) by 56% from baseline values (*P*<0.001 for both comparisons).[16]

A subsequent Phase II study was designed to evaluate adverse events associated with lomitapide. In this trial, 84 patients with moderate hypercholesterolemia were randomly assigned to receive ezetimibe, escalating doses of lomitapide (5, 7.5 and 10 mg per day), or both. After 12 weeks, LDL was significantly lowered by 20, 30 and 46% from baseline in the three groups, respectively (*P*<0.05 for all comparisons).[17]

In an open-label, Phase III, non-randomized, dose-escalating study, 29 patients with HoFH who were 18 years of age or older received lomitapide at a median dose of 40 mg daily. Most patients received a high-dose statin and 18 patients underwent regular LDL-apheresis. After 26 weeks, LDL was reduced by approximately 50% from baseline (from 336 to 166 mg/dL; *P*<0.0001). Percent changes from baseline for key secondary endpoints (total cholesterol [-46%; *P*<0.0001], ApoB [-49%; *P*<0.0001] and triglycerides [-45%; *P*<0.0001]) were consistent with those for LDL-C.[1,14]

Gastrointestinal adverse events occurred commonly in all trials evaluated. The most serious adverse events observed were elevation of liver aminotransferase levels and accumulation of hepatic fat.[1,14,16-17]

Table 2. Clinical Trials

Study and Drug Regimen	Study Design and Demographics	Sample Size and Study Duration	End Points	Results
Cuchel et al[14] Lomitapide 5 mg QD for two weeks then 10, 20, 40, and 60 mg QD at four-week intervals or until a maximum dose was reached based on tolerability All patients entered a minimum of a six-week run in period during which concomitant LDL lowering therapies (including apheresis, other lipid lowering agents, vitamin E, fatty acid supplementation and low fat diet) were stabilized.	MC, OL Patients with HoFH	N=29 26 week efficacy phase followed by a 52 week safety phase	Primary: Percent change from baseline in LDL-C (maximum tolerated dose) after 26 weeks of treatment Secondary: Percent changes in other lipid parameters, long-term safety and changes in hepatic fat content	Primary: The mean LDL-C level decreased by 50% from baseline to the end of the efficacy phase (*P*<0.0001). Overall, 19 of 23 patients (with data at week-26) had decreased concentrations of LDL-C >25%, with 12 patients having a reduction >50%. On the basis of LDL-C response, three patients permanently discontinued LDL apheresis and three patients permanently increased the time interval between apheresis treatments at some point during the safety phase. Secondary: The percent changes from baseline for key secondary endpoints (TC [-46%; *P*<0.0001], ApoB [-49%; *P*<0.0001] and triglycerides [-45%; *P*<0.0001]) were consistent with those for LDL-C at week-26. Concentrations of HDL-C were significantly reduced at week-26 (-12%; *P*<0.0001) and remained reduced at 78 weeks (-5%; *P*<0.0001). Most patients experienced at least one adverse event during both the efficacy (27 of 29 patients) and safety (21 of 23 patients) phases, most of which were mild to moderate in intensity and gastrointestinal in nature. Ten patients had elevated levels of ALT, AST, or both of ≥3x ULN at least once during the study. No patient discontinued treatment due to elevations in liver function test parameters and all elevations were managed either by dose reduction or temporary interruption of lomitapide. Mean hepatic fat in the 20 patients with evaluable NMRS scans was 1% (range 0 to 5%) at baseline, 8.6% (0 to 33.6%) at week-26, 5.8% (0 to 16.5%) at week-56 and 8.3% (0 to 19%) at week-78.

Drug regimen and study abbreviations: ALT=alanine aminotransferase, ApoB=apolipoprotein B, AST=aspartate aminotransferase, HDL-C=high density lipoprotein cholesterol, HoFH=homozygous familial hypercholesterolemia LDL-C=low density lipoprotein cholesterol, MC=multicenter, NMRS=nuclear magnetic resonance spectroscopy, OL=open-label, QD=once daily, TC=total cholesterol, ULN=upper limit of normal

Special Populations

Table 3. Special Populations[1]

Population	Precaution
Elderly	Reported clinical experience has not identified differences in responses between the elderly and younger patients. In general, dosing for an elderly patient should reflect the greater frequency of decreased hepatic, renal, or cardiac function and of concomitant disease or other drug therapy.
Renal Dysfunction	Patients with end-stage renal disease receiving dialysis should not exceed 40 mg daily. There are no data available to guide dosing in other patients with renal impairment.
Hepatic Dysfunction	Patients with mild hepatic impairment (Child-Pugh A) should not exceed 40 mg daily. Treatment is generally contraindicated in patients with moderate or severe hepatic impairment (based on Child-Pugh category B or C) and patients with active liver disease, including unexplained persistent elevations of serum transaminases.
Pregnancy/Nursing	Category: X Percent excretion through breast milk is not known.
Children	Safety and efficacy in children have not been established.
Age Restrictions	Food and Drug Administration-approved for use in patients ages ≥18 years.

Adverse Drug Events

One single-arm, open-label, 78-week trial has been conducted in 29 patients with homozygous familial hypercholesterolemia (HoFH), 23 of whom completed at least one year of treatment. The most common adverse events were gastrointestinal, reported by 27 (93%) of 29 patients. Adverse events reported by ≥5% of patients with HoFH include diarrhea, nausea, vomiting, dyspepsia, abdominal pain, weight loss, abdominal discomfort, abdominal distension, constipation, flatulence, increased alanine aminotransferase, chest pain, influenza, nasopharyngitis and fatigue. Adverse events reported in ≥10% of patients are summarized below in Table 4.

Table 4. Adverse Events[1]

Adverse Event	Reported Frequency; n (%), N=29
Cardiac Disorders	
Angina pectoris	3 (10)
Chest pain	7 (24)
Palpitations	3 (10)
Gastrointestinal Disorders	
Abdominal discomfort	6 (21)
Abdominal distension	6 (21)
Abdominal pain	10 (34)
Constipation	6 (21)
Defecation urgency	3 (10)
Diarrhea	23 (79)
Dyspepsia	11 (38)
Flatulence	6 (21)
Gastroesophageal reflux disease	3 (10)

Adverse Event	Reported Frequency; n (%), N=29
Increase in hepatic fat from baseline	18 (78)*
Nausea	19 (65)
Rectal tenesmus	3 (10)
Vomiting	10 (34)
Infections	
Gastroenteritis	4 (14)
Influenza	6 (21)
Nasopharyngitis	5 (17)
Investigations	
Decreased weight	7 (24)
Increased ALT/AST ≥3x ULN	10 (34)
Increased ALT	5 (17)
Musculoskeletal Disorders	
Back pain	4 (14)
Nervous System Disorder	
Dizziness	3 (10)
Fatigue	5 (17)
Fever	3 (10)
Headache	3 (10)
Respiratory Disorders	
Nasal congestion	3 (10)
Pharyngolaryngeal pain	4 (14)

*23 patients had evaluable data.
ALT= alanine aminotransferase, AST= aspartate aminotransferase, ULN=upper limit of normal

Contraindications/Precautions

Black Box Warning for Juxtapid® (lomitapide)[1]

WARNING

Juxtapid® (lomitapide) can cause elevations in transaminases. In the clinical trial, 10 (34%) of the 29 patients treated with lomitapide had at least one elevation in alanine aminotransferase (ALT) or aspartate aminotransferase (AST) ≥3x upper limit of normal (ULN). There were no concomitant clinically meaningful elevations of total bilirubin, international normalized ratio (INR), or alkaline phosphatase.

Lomitapide also increases hepatic fat, with or without concomitant increases in transaminases. The median absolute increase in hepatic fat was 6% after both 26 and 78 weeks of treatment, from 1% at baseline, measured by magnetic resonance spectroscopy. Hepatic steatosis associated with lomitapide treatment may be a risk factor for progressive liver disease, including steatohepatitis and cirrhosis.

Measure ALT, AST, alkaline phosphatase, and total bilirubin before initiating treatment and then ALT and AST regularly as recommended. During treatment, adjust the dose of lomitapide if the ALT or AST are ≥3x ULN. Discontinue lomitapide for clinically significant liver toxicity.

Because of the risk of hepatotoxicity, lomitapide is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the Juxtapid® REMS program.

Lomitapide is associated with significant drug-drug interactions. Treatment is contraindicated in patients receiving moderate or strong cytochrome P450 3A4 (CYP3A4) inhibitors. Dosage of this agent should not exceed 30 mg daily when used concomitantly with weak CYP3A4 inhibitors. In addition, grapefruit juice must be omitted from the diet while being treated. This agent can also cause elevations in transaminases and hepatic steatosis. Therefore, patients receiving treatment should not consume more than one

alcoholic drink a day and caution should be exercised if used with other agents known to have a potential for hepatotoxicity (e.g. isotretinoin, amiodarone). Furthermore, treatment is contraindicated in those patients with moderate or severe hepatic impairment (based on Child-Pugh category B or C) or active liver disease.[1]

This agent may cause fetal harm when administered to a pregnant woman based on findings of teratogenicity in rats and ferrets. Females of reproductive potential should have a negative pregnancy test before initiation and should use contraception during therapy. If oral contraceptives are used, the maximum recommended dosage of lomitapide is 30 mg daily.[1]

Lomitapide may reduce the absorption of fat-soluble nutrients. To reduce the risk of developing a fat-soluble nutrient deficiency, patients should take daily supplements that contain 400 international units vitamin E and ≥200 mg linoleic acid, ≥210 mg alpha-linolenic acid, ≥110 mg eicosapentaenoic acid, and ≥80 mg docosahexaenoic acid. Patients with chronic bowel or pancreatic diseases may be at increased risk for deficiencies in these nutrients. [1]

The risk of myopathy, including rhabdomyolysis, with simvastatin and lovastatin monotherapy is dose-related. Lomitapide approximately doubles the exposure to simvastatin. The interaction between lovastatin and lomitapide has not been studied; however, the metabolizing enzymes and transporters responsible for the disposition of lovastatin and simvastatin are similar, suggesting that lomitapide may increase the exposure of lovastatin. Dose adjustment of both simvastatin and lovastatin should be considered when initiating therapy.[1]

Treatment may contribute to increases in the plasma concentrations of warfarin leading to difficulty controlling international normalized ratio. Patients taking warfarin should undergo regular monitoring dose adjustment as indicated.[1]

Patients with hereditary problems of galactose intolerance, the Lapp lactase deficiency, or glucose-galactose malabsorption should avoid treatment as this may result in diarrhea and malabsorption.[1]

Drug Interactions

Table 5. Drug Interactions[1]

Interacting Medication or Disease	Potential Result
Bile Acid Sequestrants	Administration with bile acid sequestrants should be separated by at least four hours since bile acid sequestrants can interfere with the absorption of oral medications.
Cytochrome P-450 3A4 inhibitors	Use of this agent is contraindicated with concomitant use of moderate and strong cytochrome CYP3A4 inhibitors. The recommended maximum dosage is 30 mg daily with concomitant use of weak CYP3A4 inhibitors.
P-glycoprotein Substrates	Lomitapide is an inhibitor of P-glycoprotein (P-gp). Coadministration of lomitapide with P-gp substrates may increase the absorption of these substrates. Dose reduction of the P-gp substrate should be considered when used concomitantly with lomitapide.
Simvastatin/lovastatin	The risk of myopathy, including rhabdomyolysis, with simvastatin and lovastatin monotherapy is dose related. Lomitapide approximately doubles the exposure to simvastatin. The interaction between lovastatin and lomitapide has not been studied. However, the metabolizing enzymes and transporters responsible for the disposition of lovastatin and simvastatin are similar, suggesting that lomitapide may increase the exposure of lovastatin. Dose adjustment of both simvastatin and lovastatin should be considered when initiating therapy.

Interacting Medication or Disease	Potential Result
Warfarin	Lomitapide increases plasma concentrations of R(+) -warfarin and S(-) -warfarin by approximately 30% and increased the international normalized ratio (INR) 22%.Patients taking warfarin should undergo regular monitoring of INR, particularly after any changes in lomitapide dosage. The dose of warfarin should be adjusted as clinically indicated

Dosage and Administration

Lomitapide should be taken with a glass of water, without food, at least two hours after the evening meal because administration with food may increase the risk of adverse reaction. Capsules should not be opened, crushed, dissolved or chewed.

Table 6. Dosing and Administration[1]

Adult Dose	Pediatric Dose	Availability
Homozygous familial hypercholesterolemia: Capsule: initial, 5 mg QD; maintenance, titrate dose based on safety/tolerability. Increase to 10 mg QD after two weeks and then at four week intervals to 20 mg, 40 mg and the maximum dose of 60 mg QD; maximum, 60 mg QD*	Safety and efficacy in children have not been established.	Capsule: 5 mg 10 mg 20 mg

Drug regimen abbreviations: QD=once daily

*Liver transaminases should be monitored prior to any increase in dose. Dose adjustments may be required for patients taking concomitant CYP 3A4 inhibitors, renal impairment, baseline hepatic impairment or any increase in transaminase levels ≥3X the upper limit of normal.

Clinical Guidelines

Table 7. Clinical Guidelines[3-11]

Clinical Guideline	Recommendations
The Third Report of the National Cholesterol Education Program (NCEP): **Expert Panel on Detection, Evaluation and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III)** (2001)[3] **Implications of Recent Clinical Trials for the National Cholesterol Education Program Adult Treatment Panel III Guidelines** (2004)[4]	• Low-density lipoprotein cholesterol (LDL-C) is identified as the primary target of cholesterol-lowering therapy. • Therapeutic lifestyle changes remain an essential modality in clinical management. • In high-risk patients, the recommended LDL-C goal is <100 mg/dL; however, when risk is very high, an LDL-C goal of <70 mg/dL is a therapeutic option. • When a high-risk patient has high triglycerides (TG) or low high-density lipoprotein cholesterol (HDL-C), consideration can be given to combining a fibrate or nicotinic acid within an LDL-lowering drug. • For moderately high-risk patients, the recommended LDL-C goal is <130 mg/dL, but an LDL-C goal <100 mg/dL is a therapeutic option. • When LDL-lowering drug therapy is employed in high-risk or moderately high-risk persons, it is advised that intensity of therapy be sufficient to achieve at least a 30 to 40% reduction in LDL-C levels. • With lower-risk patients, the recommended LDL-C goal is <160 mg/dL. • Initial LDL-lowering treatment is typically with a moderate-dose statin but alternatives are a bile acid sequestrant or nicotinic acid. • If after six weeks the goal of therapy has not been achieved, LDL-lowering therapy can be intensified, either by increasing the dose of statin or by combining a statin with a bile acid sequestrant, nicotinic acid, or fibric acid derivative. • For patients with familial hypercholesterolemia, management with high-dose statins, nicotinic acid or LDL-apheresis should be considered to

Clinical Guideline	Recommendations
	reduce coronary heart disease risk.
American Heart Association (AHA)/American College of Cardiology (ACC) National Heart, Lung, and Blood Institute (NHLBI): **AHA/ACC Guidelines for Secondary Prevention for Patients With Coronary and Other Atherosclerotic Vascular Disease: 2006 Update** (2006)[5]	• For patients without atherosclerotic disease, including those with other risk factors, recommendations of the NCEP ATP III guidelines and their 2004 update should still be considered current. • Therapeutic options to reduce non-high-density lipoprotein cholesterol (HDL-C) include the following: more intense LDL-C lowering therapy, or niacin (after LDL-C lowering therapy) or fibrate therapy (after LDL-C lowering therapy). • If triglycerides are ≥500 mg/dL, therapeutic options to prevent pancreatitis are fibrate or niacin before LDL-lowering therapy. Treat LDL-C to goal after triglyceride-lowering therapy.
Institute for Clinical Systems Improvement (ICSI): Healthcare Guideline: **Lipid Management in Adults** (2011)[6]	• For monotherapy, statins are the drugs of choice for lowering LDL. These agents should be initiated in patients with coronary heart disease (CHD) or CHD equivalents. • If a patient is intolerant to a statin, other statins should be tried or the dose should be decreased before attempting alternate therapies. • If patients are unable to take statins, then bile acid sequestrants, niacin, ezetimibe, fibric acids and niacin can be used. • Although combination therapy is not supported by outcome-based studies, some high-risk patients will require it.
American Heart Association (AHA): **Drug Therapy of High-Risk Lipid Abnormalities in Children and Adolescents: a Scientific Statement From the American Heart Association** (2007)[7]	• For children meeting criteria for lipid-lowering drug therapy, a statin is recommended as first-line treatment. The choice of statin is dependent upon preference but should be initiated at the lowest dose once daily, usually at bedtime. • For patients with high-risk lipid abnormalities, the presence of additional risk factors or high-risk conditions may reduce the recommended LDL level for initiation of drug therapy and the desired target LDL levels. Therapy may also be considered for initiation in patients <10 years of age. • Additional research regarding drug therapy of high-risk lipid abnormalities in children is needed to evaluate the long-term efficacy and safety and impact on the atherosclerotic disease process.
Fourth Joint Task Force of the European Society of Cardiology (ESC) and Other Societies: **European Guidelines on Cardiovascular Disease Prevention in Clinical Practice** (2012)[8]	• Total plasma cholesterol should be <5 mmol/L (<190 mg/dL), and LDL-C should be <3 mmol/L (<115 mg/dL). • Statins are considered first-line drugs for lowering LDL-C. • Non-statin treatment o Selective cholesterol absorption inhibitors are not used as monotherapy to decrease LDL-C concentrations. o Bile acid sequestrants also decrease total and LDL-C but tend to increase triglyceride concentrations. o Fibrates and niacin are used primarily for triglyceride lowering and increasing HDL-C, while fish oils (omega-3 fatty acids) in doses of 2 to 4 g/day are used for triglyceride lowering. • Combination therapy may be used in patients needing additional therapy to reach goals and the selection of appropriate drugs should vary based upon lipid levels. • All patients with familial hypercholesterolemia must be recognized as

Clinical Guideline	Recommendations
	high-risk patients and be treated with lipid-lowering therapy. o Rare patients with severe hypercholesterolemia, especially homozygous familial hypercholesterolemia, require specialist evaluation of the need for LDL apheresis.
National Heart Lung and Blood Institute: **Expert Panel on Integrated Guidelines for Cardiovascular Health and Risk** (2011)[9]	Specific recommendations regarding the management of familial hypercholesterolemia include: • Children with homozygous familial hypercholesterolemia and extremely elevated LDL-C levels (>500 mg/dL) have undergone effective LDL-C lowering therapy with biweekly LDL apheresis under the care of lipid specialists in academic medical centers. • Statins have been shown to reduce LDL-C in children and adolescents with marked LDL-C elevation or familial hypercholesterolemia. • Plant sterol esters and/or plant stanol esters up to 2 g/day as replacement for usual fat sources can be used after two years of age in children with familial hypercholesterolemia
National Institute for Health and Clinical Excellence (NICE): **Identification and Management of Familial Hypercholesterolemia** (2008)[10]	• Healthcare professionals should consider prescribing a high-intensity statin to achieve a recommended reduction in LDL-C concentration of greater than 50% from baseline. • The dose of statin should be increased to the maximum licensed or tolerated dose to achieve a recommended reduction in LDL-C concentration of greater than 50% from baseline. • Healthcare professionals should offer treatment with a statin with a low acquisition cost for adults with familial hypercholesterolemia in whom the diagnosis is made after the 60 years of age and who do not have coronary heart disease. • Prescribing of drug therapy for adults with homozygous familial hypercholesterolemia should be undertaken within a specialist center. • Healthcare professionals should offer adults with familial hypercholesterolemia a referral to a specialist with expertise in familial hypercholesterolemia if treatment with the maximum tolerated dose of a high-intensity statin and ezetimibe does not achieve a recommended reduction in LDL-C concentration of greater than 50% from baseline. • Adults with familial hypercholesterolemia with intolerance or contraindications to statins or ezetimibe should be offered a referral to a specialist with expertise in familial hypercholesterolemia for consideration for treatment with either a bile acid sequestrant (resin), nicotinic acid, or a fibrate to reduce their LDL-C concentration. • Lipid-modifying drug therapy for a child or young person with familial hypercholesterolemia should usually be considered by 10 years of age. Statins should be considered as initial treatment.
National Lipid Association (NLA): Management of Familial Hypercholesterolemia in Adult Patients: **Recommendations from the National Lipid Association Expert Panel on Familial Hypercholesterolemia** (2011)[11]	• For adult familial hypercholesterolemia patients, initial treatment is the use of moderate to high doses of high-potency statins titrated to achieve an LDL-C reduction ≥50% from baseline. Low potency statins are generally inadequate for familial hypercholesterolemia patients. • If the initial statin is not tolerated, consider changing to an alternative statin, or every-other-day statin therapy. • If initial statin therapy is contraindicated or poorly tolerated, ezetimibe, a bile acid sequestrant (colesevelam) or niacin may be considered. • For patients who cannot use a statin, most will require combination drug therapy. • If the patient is not at LDL-C treatment goal with the maximum available and tolerable dose of statin, then combine with ezetimibe, niacin, or a

Clinical Guideline	Recommendations
	bile acid sequestrant (colesevelam preferred). • Decisions regarding selection of additional drug combinations should be based on concomitant risk factors for myopathy, concomitant medications, and the presence of other disease conditions and lipid abnormalities. • In patients who, after six months, do not have an adequate response to maximum tolerated drug therapy, LDL apheresis is indicated according to these guidelines: o Functional homozygous familial hypercholesterolemia patients with LDL-C ≥300 mg/dL (or non-HDL-C ≥330 mg/dL). o Functional heterozygous familial hypercholesterolemia patients with LDL-C ≥300 mg/dL (or non-HDL-C ≥330 mg/dL) and one or fewer risk factors. o Functional heterozygous familial hypercholesterolemia patients with LDL-C ≥200 mg/dL (or non-HDL-C ≥230 mg/dL) and high risk characteristics such as two or more risk factors or high lipoprotein (a) ≥50 mg/dL using an isoform insensitive assay. o Functional heterozygotes with LDL-C ≥160 mg/dL (or non-HDL-C ≥190 mg/dL) and very high-risk characteristics (established CHD, other cardiovascular disease, or diabetes).

Conclusions

Juxtapid® (lomitapide) is a microsomal triglyceride transfer protein inhibitor indicated as an adjunct to a low-fat diet and other lipid-lowering treatments in patients with homozygous familial hypercholesterolemia (HoFH), a genetically modulated clinical syndrome characterized by a high low-density lipoprotein cholesterol (LDL-C) level from birth and early onset coronary heart disease.[1] Available treatment guidelines for this condition support the use of high-dose statins, LDL apheresis and other cholesterol lowering agents (e.g., ezetimibe), often as part of combination regimens to reach cholesterol goals.[2-13]

Lomitapide has been evaluated as an adjunctive treatment and was associated with a significant decrease from baseline in LDL and other secondary measures of cholesterol. Lomitapide is associated with significant tolerability issues including liver toxicity, increased hepatic fat, teratogenicity, drug-drug interactions and common gastrointestinal side effects. Moreover, the effects of lomitapide on cardiovascular outcomes in patients with HoFH have not been established.[1,14]

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