הודעה על החמרה (מידע בטיחות) בעלון לרופא
(מעודכן 05.2013)

תאריך: 24/11/2016

שם תכשיר באנגלית ומספר הרישום:

JUXTAPID 5 MG 152-85-33996-00

JUXTAPID 10 MG 152-86-33998-00

JUXTAPID 20 MG 152-87-33999-00

שם בעל הרישום: מדיסון פארמה בע"מ

טופס זה מיועד לפרוט ההחמרות בלבד !

ההחמרות המבוקשות		
פרק בעלון	**טקסט נוכחי**	**טקסט חדש**
Header	**---------- INDICATIONS AND USAGE ----------** JUXTAPID is a microsomal triglyceride transfer protein inhibitor indicated as an adjunct to a low-fat diet and other lipid-lowering treatments, including LDL apheresis where available, to reduce low-density lipoprotein cholesterol (LDL-C), total	**---------- INDICATIONS AND USAGE ----------** JUXTAPID is a microsomal triglyceride transfer protein inhibitor indicated as an adjunct to a low-fat diet and other lipid-lowering treatments, including LDL apheresis where available, to reduce low-density lipoprotein cholesterol (LDL-

C), total cholesterol (TC), apolipoprotein B (apo B), and non-high-density lipoprotein cholesterol (non-HDL-C) in patients with homozygous familial hypercholesterolemia (HoFH) (1). Limitations of Use • The safety and effectiveness of JUXTAPID have not been established in patients with hypercholesterolemia who do not have HoFH established in patients with hypercholesterolemia who do not have HoFH, including those with heterozygous familial hypercholesterolemia (HeFH) (1). • The effect of JUXTAPID on cardiovascular morbidity and mortality has not been determined (1).	cholesterol (TC), apolipoprotein B (apo B), and non-high-density lipoprotein cholesterol (non-HDL-C) in patients with homozygous familial hypercholesterolemia (HoFH) (1). Limitations of Use • The safety and effectiveness of JUXTAPID have not been established in patients with hypercholesterolemia who do not have HoFH (1). • The effect of JUXTAPID on cardiovascular morbidity and mortality has not been determined (1).
---------- **DRUG INTERACTIONS** ---------- • CYP3A4 inhibitors increase exposure to lomitapide. Strong and moderate CYP3A4 inhibitors are contraindicated with JUXTAPID. Patients must avoid grapefruit juice. • When administered ~~Do not exceed 30 mg daily of JUXTAPID when used concomitantly~~ with weak CYP3A4 inhibitors, the dose of JUXTAPID should be decreased by half. The dosage of JUXTAPID may then be up-titrated to a maximum recommended dosage of 30 mg daily ~~including atorvastatin and oral contraceptives (2.3, 4, 5.5, 7.1, 7.2).~~ • Warfarin: Lomitapide increases plasma concentrations of warfarin. Monitor international normalized ratio (INR) regularly, especially with JUXTAPID dose adjustment (5.7, 7.3). • Simvastatin and lovastatin exposure increase with	---------- **DRUG INTERACTIONS** ---------- • CYP3A4 inhibitors increase exposure to lomitapide. Strong and moderate CYP3A4 inhibitors are contraindicated with JUXTAPID. Patients must avoid grapefruit juice. Do not exceed 30 mg daily of JUXTAPID when used concomitantly with weak CYP3A4 inhibitors, including atorvastatin and oral contraceptives (2.3, 4, 5.5, 7.1, 7.2). • Warfarin: Lomitapide increases plasma concentrations of warfarin. Monitor international normalized ratio (INR) regularly, especially with JUXTAPID dose adjustment (5.7, 7.3). • Simvastatin and lovastatin exposure increase with JUXTAPID. Limit dose when co-administered with JUXTAPID due to myopathy risk (5.6, 7.4).

JUXTAPID. Limit dose when co-administered with JUXTAPID due to myopathy risk (5.6, 7.4). • P-glycoprotein (P-gp) Substrates: Consider dose reduction of P-gp substrate because of possible increased absorption with JUXTAPID (7.5). • Bile Acid Sequestrants: Separate JUXTAPID dosing by at least 4 hours (7.6).	• P-glycoprotein (P-gp) Substrates: Consider dose reduction of P-gp substrate because of possible increased absorption with JUXTAPID (7.5). • Bile Acid Sequestrants: Separate JUXTAPID dosing by at least 4 hours (7.6).
FULL PRESCRIBING INFORMATION	**FULL PRESCRIBING INFORMATION**
JUXTAPID can cause elevations in transaminases. In the JUXTAPID clinical trial, 10 (34%) of the 29 patients treated with JUXTAPID 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 *[see Warnings and Precautions (5.1)]*. **JUXTAPID 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 JUXTAPID treatment may be a risk factor for progressive liver disease, including steatohepatitis and cirrhosis *[see Warnings and Precautions (5.1)]*.**	**JUXTAPID can cause elevations in transaminases. In the JUXTAPID clinical trial, 10 (34%) of the 29 patients treated with JUXTAPID 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 *[see Warnings and Precautions (5.1)]*.** **JUXTAPID 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 JUXTAPID treatment may be a risk factor for progressive liver disease, including steatohepatitis and cirrhosis *[see Warnings and Precautions (5.1)]*.**

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 JUXTAPID if the ALT or AST are ≥3x ULN. Discontinue JUXTAPID for clinically significant liver toxicity [*see Dosage and Administration (2.4) and Warnings and Precautions (5.1)]*. **Prescribe JUXTAPID only to patients with a clinical or laboratory diagnosis consistent with HoFH. The safety and effectiveness of JUXTAPID have not been established in patients with hypercholesterolemia who do not have HoFH *[see Indications and Usage (1)]*.**	**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 JUXTAPID if the ALT or AST are ≥3x ULN. Discontinue JUXTAPID for clinically significant liver toxicity [*see Dosage and Administration (2.4) and Warnings and Precautions (5.1)]*.**	
Homozygous Familial Hypercholesterolemia JUXTAPID is indicated as an adjunct to a low-fat diet and other lipid-lowering treatments, including LDL apheresis where available, to reduce low-density lipoprotein cholesterol (LDL-C), total cholesterol (TC), apolipoprotein B (apo B), and non-high-density lipoprotein cholesterol (non-HDL-C) in patients with homozygous familial hypercholesterolemia (HoFH). Limitations of Use • The safety and effectiveness of JUXTAPID have not been established in patients with hypercholesterolemia who do	***Homozygous Familial Hypercholesterolemia*** JUXTAPID is indicated as an adjunct to a low-fat diet and other lipid-lowering treatments, including LDL apheresis where available, to reduce low-density lipoprotein cholesterol (LDL-C), total cholesterol (TC), apolipoprotein B (apo B), and non-high-density lipoprotein cholesterol (non-HDL-C) in patients with homozygous familial hypercholesterolemia (HoFH). Limitations of Use • The safety and effectiveness of JUXTAPID have not been established in patients with hypercholesterolemia who do	**1.1.**

not have HoFH, including those with heterozygous familial hypercholesterolemia (HeFH). • The effect of JUXTAPID on cardiovascular morbidity and mortality has not been determined.	not have HoFH. • The effect of JUXTAPID on cardiovascular morbidity and mortality has not been determined.
Initiation and Maintenance of Therapy Before beginning treatment with JUXTAPID: • Measure transaminases (ALT, AST), alkaline phosphatase, and total bilirubin *[see Warnings and Precautions (5.1)]*; • Obtain a negative pregnancy test in females of reproductive potential *[see Warnings and Precautions (5.2)]*; and, • Initiate a low-fat diet supplying <20% of energy from fat *[see Warnings and Precautions (5.4)]*. The recommended starting dosage of JUXTAPID is 5 mg once daily, and the dose should be escalated gradually based on acceptable safety and tolerability. Transaminases should be measured prior to any increase in dose *[see Warnings*	***Initiation and Maintenance of Therapy*** Before beginning treatment with JUXTAPID: • Measure transaminases (ALT, AST), alkaline phosphatase, and total bilirubin *[see Warnings and Precautions (5.1)]*; • Obtain a negative pregnancy test in females of reproductive potential *[see Warnings and Precautions (5.2)]*; and, • Initiate a low-fat diet supplying <20% of energy from fat *[see Warnings and Precautions (5.4)]*. The recommended starting dosage of JUXTAPID is 5 mg once daily, and the dose should be escalated gradually based on acceptable safety and tolerability. Transaminases should be measured prior to any increase in dose *[see Warnings and*

and Precautions (5.1)]. The maintenance dosage of JUXTAPID should be individualized, taking into account patient characteristics such as goal of therapy and response to treatment, to a maximum of 60 mg daily as described in Table 2. Modify dosing for patients taking concomitant weak CYP3A4 inhibitors and for those with, renal impairment, or baseline hepatic impairment *[see Dosage and Administration (2.3), (2.5), and (2.6)]*.

Monitor transaminases during treatment with JUXTAPID as described in *Warnings and Precautions (5.1)*, and reduce or withhold dosing ~~Dose adjustments are also required~~ for patients who develop transaminase values ≥3x the upper limit of normal (ULN) ~~during treatment with JUXTAPID~~ *[see Dosage and Administration (2.4)]*.

Table 2: Recommended Regimen for Titrating Dosage

DOSAGE	DURATION OF ADMINISTRATION BEFORE CONSIDERING INCREASE TO NEXT DOSAGE
5 mg daily	At least 2 weeks
10 mg daily	At least 4 weeks
20 mg daily	At least 4 weeks
40 mg daily	At least 4 weeks
60 mg daily	Maximum recommended dosage

Precautions (5.1)]. The maintenance dosage of JUXTAPID should be individualized, taking into account patient characteristics such as goal of therapy and response to treatment, to a maximum of 60 mg daily as described in Table 2. Modify dosing for patients taking concomitant CYP3A4 inhibitors, renal impairment, or baseline hepatic impairment *[see Dosage and Administration (2.3), (2.5), and (2.6)]*.

Dose adjustments are also required for patients who develop transaminase values ≥3x the upper limit of normal (ULN) during treatment with JUXTAPID *[see Dosage and Administration (2.4)]*.

Table 1: Recommended Regimen for Titrating Dosage

DOSAGE	DURATION OF ADMINISTRATION BEFORE CONSIDERING INCREASE TO NEXT DOSAGE
5 mg daily	At least 2 weeks
10 mg daily	At least 4 weeks
20 mg daily	At least 4 weeks
40 mg daily	At least 4 weeks
60 mg daily	Maximum recommended dosage

To reduce the risk of developing a fat-soluble nutrient deficiency due to JUXTAPID's mechanism of action in the small intestine, patients treated with JUXTAPID should take daily supplements that contain 400 international units vitamin E and at least 200 mg linoleic acid, 210 mg alpha-linolenic acid (ALA), 110 mg eicosapentaenoic acid (EPA), and 80 mg docosahexaenoic acid (DHA) *[see Warnings and Precautions (5.3)*].	To reduce the risk of developing a fat-soluble nutrient deficiency due to JUXTAPID's mechanism of action in the small intestine, patients treated with JUXTAPID should take daily supplements that contain 400 international units vitamin E and at least 200 mg linoleic acid, 210 mg alpha-linolenic acid (ALA), 110 mg eicosapentaenoic acid (EPA), and 80 mg docosahexaenoic acid (DHA) *[see Warnings and Precautions (5.3)*].
Dosing with Cytochrome P450 3A4 Inhibitors JUXTAPID is contraindicated with concomitant use of moderate and strong cytochrome P450 3A4 (CYP3A4) inhibitors *[see Contraindications (4) and Drug Interactions (7.1)]*. The recommended maximum dosage of JUXTAPID is 30 mg daily with concomitant use of weak CYP3A4 inhibitors (such as alprazolam, amiodarone, amlodipine, atorvastatin, bicalutamide, cilostazol, cimetidine, cyclosporine, fluoxetine, fluvoxamine, ginkgo, goldenseal, isoniazid, lapatinib, nilotinib, ~~oral contraceptives~~, pazopanib, ranitidine, ranolazine, ticagrelor, zileuton) However, the recommended	***Dosing with Cytochrome P450 3A4 Inhibitors*** JUXTAPID is contraindicated with concomitant use of moderate and strong cytochrome P450 3A4 (CYP3A4) inhibitors *[see Contraindications (4) and Drug Interactions (7.1)]*. The recommended maximum dosage of JUXTAPID is 30 mg daily with concomitant use of weak CYP3A4 inhibitors (such as alprazolam, amiodarone, amlodipine, atorvastatin, bicalutamide, cilostazol, cimetidine, cyclosporine, fluoxetine, fluvoxamine, ginkgo, goldenseal, isoniazid, lapatinib, nilotinib, oral contraceptives, pazopanib, ranitidine, ranolazine, ticagrelor,

maximum dosage of JUXTAPID is 40 mg daily with concomitant use of oral contraceptives. When initiating a weak CYP3A4 inhibitor in a patient already taking JUXTAPID 10 mg daily or more, decrease the dose of JUXTAPID by half; patients taking JUXTAPID 5 mg daily may continue with the same dosage. Careful titration of JUXTAPID may then be considered according to LDL-C response and safety/tolerability to a maximum recommended dosage of 30 mg daily except when coadministered with oral contraceptives, in which case the maximum recommended lomitapide dosage is 40 mg daily. *[see Drug Interactions (7.2)]*.	zileuton) *[see Drug Interactions (7.2)]*.
Embryo-Fetal Toxicity JUXTAPID may cause fetal harm when administered to a pregnant woman based on findings of teratogenicity in rats and ferrets *[see Use in Specific Populations (8.1)]*. Females of reproductive potential should have a negative pregnancy test before starting JUXTAPID and should use effective contraception during therapy with JUXTAPID *[see Use in Specific Populations (8.6)]*.	***Embryo-Fetal Toxicity*** JUXTAPID may cause fetal harm when administered to a pregnant woman based on findings of teratogenicity in rats and ferrets *[see Use in Specific Populations (8.1)]*. Females of reproductive potential should have a negative pregnancy test before starting JUXTAPID and should use effective contraception during therapy with JUXTAPID *[see Use in Specific Populations (8.6)]*.

~~If~~ Oral contraceptives are ~~used, the maximum recommended dosage of JUXTAPID is 30 mg daily~~ *[see Dosage and Administration (2.3) and Drug Interactions (7.2)]*.	If oral contraceptives are used, the maximum recommended dosage of JUXTAPID is 30 mg daily *[see Dosage and Administration (2.3) and Drug Interactions (7.2)]*.	
Gastrointestinal Adverse Reactions Gastrointestinal adverse reactions were reported by 27 (93%) of 29 patients in the HoFH clinical trial. Diarrhea occurred in 79% of patients, nausea in 65%, dyspepsia in 38%, and vomiting in 34%. Other reactions reported by at least 20% of patients include abdominal pain, abdominal discomfort, abdominal distension, constipation, and flatulence *[see Adverse Reactions (6)]*. Gastrointestinal adverse reactions of severe intensity were reported by 6 (21%) of 29 patients in the HoFH clinical trial, with the most common being diarrhea (4 patients, 14%); vomiting (3 patients, 10%); and abdominal pain, distension, and/or discomfort (2 patients, 7%). Gastrointestinal reactions contributed to the reasons for early discontinuation from the trial for 4 (14%) patients. There have been postmarketing reports of severe diarrhea with the use of JUXTAPID, including patients being hospitalized	***Gastrointestinal Adverse Reactions*** Gastrointestinal adverse reactions were reported by 27 (93%) of 29 patients in the HoFH clinical trial. Diarrhea occurred in 79% of patients, nausea in 65%, dyspepsia in 38%, and vomiting in 34%. Other reactions reported by at least 20% of patients include abdominal pain, abdominal discomfort, abdominal distension, constipation, and flatulence *[see Adverse Reactions (6)]*. Gastrointestinal adverse reactions of severe intensity were reported by 6 (21%) of 29 patients in the HoFH clinical trial, with the most common being diarrhea (4 patients, 14%); vomiting (3 patients, 10%); and abdominal pain, distension, and/or discomfort (2 patients, 7%). Gastrointestinal reactions contributed to the reasons for early discontinuation from the trial for 4 (14%) patients.	5.4 **A**

because of diarrhea-related complications such as volume depletion. Monitor patients who are more susceptible to complications from diarrhea, such as older patients and patients taking drugs that can lead to volume depletion or hypotension. Instruct patients to stop JUXTAPID and contact their healthcare provider if severe diarrhea occurs or if they experience symptoms of volume depletion such as lightheadedness, decreased urine output, or tiredness. In such cases, consider reducing the dose or suspending use of JUXTAPID. Absorption of concomitant oral medications may be affected in patients who develop diarrhea or vomiting. To reduce the risk of gastrointestinal adverse events, patients should adhere to a low-fat diet supplying <20% of energy from fat and the dosage of JUXTAPID should be increased gradually *[see Dosage and Administration (2.1) and (2.2)]*.	Absorption of concomitant oral medications may be affected in patients who develop diarrhea or vomiting. To reduce the risk of gastrointestinal adverse events, patients should adhere to a low-fat diet supplying <20% of energy from fat and the dosage of JUXTAPID should be increased gradually *[see Dosage and Administration (2.1) and (2.2)]*.
Concomitant Use of CYP3A4 Inhibitors CYP3A4 inhibitors increase the exposure of lomitapide, with strong inhibitors increasing exposure approximately 27-fold. Concomitant use of moderate or strong CYP3A4 inhibitors	***Concomitant Use of CYP3A4 Inhibitors*** CYP3A4 inhibitors increase the exposure of lomitapide, with strong inhibitors increasing exposure approximately 27-fold. Concomitant use of moderate or strong CYP3A4 inhibitors with

with JUXTAPID is contraindicated *[see Drug Interactions (7.1)]*. In the JUXTAPID clinical trials, one patient with HoFH developed markedly elevated transaminases (ALT 24x ULN, AST 13x ULN) within days of initiating the strong CYP3A4 inhibitor clarithromycin. If treatment with moderate or strong CYP3A4 inhibitors is unavoidable, JUXTAPID should be stopped during the course of treatment. Grapefruit juice must be omitted from the diet while being treated with JUXTAPID. Weak CYP3A4 inhibitors can increase the exposure of lomitapide approximately 2-fold; therefore, when JUXTAPID is administered with weak CYP3A4 inhibitors, the dose of JUXTAPID should be decreased by half. Careful titration may then be considered based on LDL-C response and safety/tolerability to a maximum recommended dosage of 30 mg daily except when coadministered with oral contraceptives, in which case the maximum recommended lomitapide dosage is 40 mg daily ~~dosage should not exceed 30 mg daily when it is used concomitantly with these inhibitors, including atorvastatin and oral contraceptives~~ *[see Dosage and Administration (2.3)* and *Drug Interactions*	JUXTAPID is contraindicated *[see Drug Interactions (7.1)]*. In the JUXTAPID clinical trials, one patient with HoFH developed markedly elevated transaminases (ALT 24x ULN, AST 13x ULN) within days of initiating the strong CYP3A4 inhibitor clarithromycin. If treatment with moderate or strong CYP3A4 inhibitors is unavoidable, JUXTAPID should be stopped during the course of treatment. Grapefruit juice must be omitted from the diet while being treated with JUXTAPID. Weak CYP3A4 inhibitors increase the exposure of lomitapide approximately 2-fold; therefore, JUXTAPID dosage should not exceed 30 mg daily when it is used concomitantly with these inhibitors, including atorvastatin and oral contraceptives *[see Dosage and Administration (2.3)* and *Drug Interactions (7.2)]*.

(7.2)].		
Weak CYP3A4 Inhibitors Weak CYP3A4 inhibitors ~~increase lomitapide exposure approximately 2-fold *[see Clinical Pharmacology (12.3)]*. Lomitapide dosage should not exceed 30 mg daily when it is used concomitantly with weak CYP3A4 inhibitors~~ ~~(such~~ as alprazolam, amiodarone, amlodipine, atorvastatin, bicalutamide, cilostazol, cimetidine, cyclosporine, fluoxetine, fluvoxamine, ginkgo, goldenseal, isoniazid, lapatinib, nilotinib, ~~oral contraceptives~~, pazopanib, ranitidine, ranolazine, ticagrelor, zileuton) can increase lomitapide exposure approximately 2-fold *[see Clinical Pharmacology ()]*. When administered with weak CYP3A4 inhibitors, the dose of JUXTAPID should be decreased by half. Careful titration of JUXTAPID may then be considered based on LDL-C response and safety/tolerability to a maximum recommended dosage of 30 mg daily except when coadministered with oral contraceptives, in which case the maximum recommended lomitapide dosage is 40 mg daily *[see Dosage and Administration (2.3), Warnings and*	***Weak CYP3A4 Inhibitors*** Weak CYP3A4 inhibitors increase lomitapide exposure approximately 2-fold *[see Clinical Pharmacology (12.3)]*. Lomitapide dosage should not exceed 30 mg daily when it is used concomitantly with weak CYP3A4 inhibitors (such as alprazolam, amiodarone, amlodipine, atorvastatin, bicalutamide, cilostazol, cimetidine, cyclosporine, fluoxetine, fluvoxamine, ginkgo, goldenseal, isoniazid, lapatinib, nilotinib, oral contraceptives, pazopanib, ranitidine, ranolazine, ticagrelor, zileuton) *[see Dosage and Administration (2.3), Warnings and*	7.2

Precautions (5.5), and Clinical Pharmacology (12.3)].	*Precautions (5.5), and Clinical Pharmacology (12.3)]*.
Females of Reproductive Potential *Contraception* Females of reproductive potential should use effective contraception during JUXTAPID therapy. ~~The recommended maximum dosage of JUXTAPID is 30 mg daily with concomitant use of oral contraceptives, since~~ oral contraceptives are weak CYP3A4 inhibitors *[see Dosage and Administration(2.3) and Drug Interactions(7.2)]*. Hormone absorption from oral contraceptives may be incomplete if vomiting or diarrhea occurs while taking JUXTAPID, warranting the use of additional contraceptive methods *[see Warnings and Precautions (5.4)]*.	***Females of Reproductive Potential*** *Contraception* Females of reproductive potential should use effective contraception during JUXTAPID therapy. The recommended maximum dosage of JUXTAPID is 30 mg daily with concomitant use of oral contraceptives, since oral contraceptives are weak CYP3A4 inhibitors *[see Drug Interactions (7.2)]*. Hormone absorption from oral contraceptives may be incomplete if vomiting or diarrhea occurs while taking JUXTAPID, warranting the use of additional contraceptive methods *[see Warnings and Precautions (5.4)]*.
~~CYP3A4 Inhibitors~~ ~~Lomitapide exposure increased 27-fold in the presence of ketoconazole, a strong CYP3A4 inhibitor. Thus, concomitant use of strong CYP3A4 inhibitors and lomitapide is contraindicated. The effect of moderate CYP3A4 inhibitors on~~	CYP3A4 Inhibitors Lomitapide exposure increased 27-fold in the presence of ketoconazole, a strong CYP3A4 inhibitor. Thus, concomitant use of strong CYP3A4 inhibitors and lomitapide is contraindicated. The effect of moderate CYP3A4 inhibitors on

~~lomitapide exposure has not been studied. However, moderate CYP3A4 inhibitors will likely increase lomitapide exposure significantly based on the results of concomitant use of strong and weak CYP3A4 inhibitors *[see Drug Interactions (7.1) and (7.2)]*. Thus, concomitant use of moderate CYP3A4 inhibitors and lomitapide is contraindicated.~~ ~~Interaction between weak CYP3A4 inhibitors and lomitapide has not been studied. Based on cross-studies comparisons, the lomitapide exposure approximately doubles in the presence of oral contraceptives, which are weak CYP3A4 inhibitors. Do not exceed 30 mg daily of JUXTAPID when used concomitantly with weak CYP3A4 inhibitors. *[See Dosage and Administration (2.3) and Drug Interactions (7.2)]*.~~	lomitapide exposure has not been studied. However, moderate CYP3A4 inhibitors will likely increase lomitapide exposure significantly based on the results of concomitant use of strong and weak CYP3A4 inhibitors *[see Drug Interactions (7.1) and (7.2)]*. Thus, concomitant use of moderate CYP3A4 inhibitors and lomitapide is contraindicated. Interaction between weak CYP3A4 inhibitors and lomitapide has not been studied. Based on cross-studies comparisons, the lomitapide exposure approximately doubles in the presence of oral contraceptives, which are weak CYP3A4 inhibitors. Do not exceed 30 mg daily of JUXTAPID when used concomitantly with weak CYP3A4 inhibitors. *[See Dosage and Administration (2.3) and Drug Interactions (7.2)]*.

על החמרה (מידע בטיחות) בעלון לצרכן

תאריך: 24/11/2016

שם תכשיר באנגלית ומספר הרישום:

JUXTAPID 5 MG 152-85-33996-00

JUXTAPID 10 MG 152-86-33998-00

JUXTAPID 20 MG 152-87-33999-00

שם בעל הרישום: מדיסון פארמה בע"מ

טופס זה מיועד לפרוט ההחמרות בלבד !

ההחמרות המבוקשות		
פרק בעלון	**טקסט נוכחי**	**טקסט חדש**
2. לפני השימוש בתרופה **אזהרות מיוחדות הנוגעות לשימוש בתרופה**	לא ידוע אם ג'קסטפיד בטוחה לשימוש באנשים הסובלים מרמת כולסטרול גבוהה אך אינם סובלים מהיפרכולסטרולמיה משפחתית הומוזיגוטית (HoFH)	לא ידוע אם ג'קסטפיד בטוחה לשימוש באנשים הסובלים מרמת כולסטרול גבוהה אך אינם סובלים מהיפרכולסטרולמיה משפחתית הומוזיגוטית (HoFH), כולל באנשים בעלי היפרכולסטרולמיה משפחתית הומוזיגוטית (HeFH)

תסמינים במערכת העיכול- תסמינים שכיחים מאד שלשול, בחילות/הקאות, כאבים ובעיות בקיבה. הקפדה על דיאטה דלת שומן יכולה לעזור בהקטנת הסיכוי להופעת תסמינים אלה.	**תסמינים במערכת העיכול-** תסמינים שכיחים מאד : שלשול, בחילות/הקאות, כאבים ובעיות בקיבה. הקפדה על דיאטה דלת שומן יכולה לעזור בהקטנת הסיכוי להופעת תסמינים אלה. הפסק לקחת ג'קסטפיד ודווח לרופא מיידית אם יש לך שלשול חריף, במיוחד אם יש לך בנוסף סחרחורת , ירידה בתפוקת השתן או עייפות.	**אי**