LOJUXTA CAPSULES
DRUG-DRUG INTERACTIONS

Lojuxta is metabolised through the liver and is a sensitive substrate for cytochrome p450 (CYP) 3A4 and therefore is subject to many significant drug-drug interactions. The table below shows the recommended adjustments of other commonly prescribed medications when used concomitantly with Lojuxta.
This list is not intended to be comprehensive, and prescribers should check the prescribing information of drugs to be co-administered with Lojuxta for potential interactions. Please see the Lojuxta SPC for further information for a list of drugs and Lojuxta/drug and dosage requirements.

CYTOCHROME P450 (CYP) 3A4 INHIBITORS	
CYP3A4 inhibitors increase the exposure of lomitapide. Concomitant use of moderate or strong CYP3A4 inhibitors with Lojuxta is contraindicated (see section 4.3 of Lojuxta SPC).	Examples of strong/moderate CYP3A4 inhibitors include: antifungal azoles; the antiarrhythmic dronedarone; macrolide antibiotics; ketolide antibiotics; HIV protease inhibitors; the calcium channel blockers diltiazem and verapamil. Grapefruit juice is a moderate inhibitor of CYP3A4 and patients taking Lojuxta should avoid consumption of grapefruit juice.
Weak CYP3A4 inhibitors are expected to increase the exposure of lomitapide when taken simultaneously. **See next page for dosing recommendations.**	Examples of weak CYP3A4 inhibitors include: alprazolam, amiodarone, amlodipine, atorvastatin, azithromycin, bicalutamide, cilostazol, cimetidine, ciclosporin, clotrimazole, fluoxetine, fluvoxamine, fosaprepitant, ginkgo, goldenseal, isoniazid, ivacaftor, lacidipine, lapatinib, linagliptin, nilotinib, oestrogen containing oral contraceptives, pazopanib, peppermint oil, propiverine, ranitidine, ranolazine, roxithromycin, Seville oranges, tacrolimus, ticagrelor and tolvaptan.

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For patients **already on a stable maintenance dose of Lojuxta** who receive **atorvastatin** either:

- **Separate the dose of the medication by 12 hours;**

OR

- **Decrease the dose of Lojuxta by half.**

Patients on 5 mg should remain on 5 mg.

Careful titration may then be considered according to LDL-C response and safety/tolerability.
Upon discontinuation of atorvastatin, the dose of Lojuxta should be up-titrated according to LDL-C response and safety/tolerability.

For patients already **on a stable dose of any other weak CYP3A4 inhibitor**, separate the dose of the medications (Lojuxta and the weak CYP3A4 inhibitor) by 12 hours.

Exercise additional caution if administering more than 1 weak CYP3A4 inhibitor with Lojuxta. Consider limiting the maximum dose of Lojuxta according to desired LDL-C response.

CYTOCHROME P450 (CYP) 3A4 INDUCERS	
Co-administration of a CYP3A4 inducer is expected to reduce the effect of Lojuxta. It is recommended to increase the frequency of LDL-C assessment and consider increasing the dose of Lojuxta to ensure maintenance of the desired level of efficacy.	Examples of CYP3A4 inducers include: aminoglutethimide, nafcillin, non-nucleoside reverse transcriptase inhibitors, phenobarbital, rifampicin, carbamazepine, pioglitazone, glucocorticoids, modafinil and phenytoin. Use of St John's Wort (a CYP3A4 inducer) should be avoided.
HMG-CoA REDUCTASE INHIBITORS ('STATINS')	
Lomitapide increases plasma concentrations of statins. **Patients receiving Lojuxta as adjunctive therapy to a statin should be monitored for adverse events that are associated with the use of high doses of statins.** **All patients receiving Lojuxta in addition to a statin should be advised of the potential increased risk of myopathy and told to report promptly any unexplained muscle pain, tenderness, or weakness.**	Simvastatin: The risk of myopathy with simvastatin is dose related. Doses of simvastatin > 40 mg are contraindicated with Lojuxta. Atorvastatin: Atorvastatin is a weak CYP3A4 inhibitor – see above for dosing recommendations. Rosuvastatin: No dosage adjustments are required.
FENOFIBRATE, NIACIN, EZETIMIBE	
The pharmacokinetics of these agents are not altered when prescribed with Lojuxta.	No dose adjustments are required when co administered with Lojuxta.

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BILE ACID SEQUESTRANTS	
Bile acid sequestrants can interfere with the absorption of oral medicines.	Administration of Lojuxta and bile acid sequestrants should be separated by at least 4 hours.
COUMARIN ANTICOAGULANTS	
Lojuxta increases the plasma concentrations of warfarin. Increases in the dose of Lojuxta may lead to supratherapeutic anticoagulation, and decreases in the dose may lead to subtherapeutic anticoagulation.	Patients taking coumarins (such as warfarin) should undergo regular monitoring of the INR, especially after any changes in the dose of Lojuxta. The dose of warfarin should be adjusted as clinically indicated.
P-GLYCOPROTEIN SUBSTRATES	
Lojuxta may increase the absorption of P-gp substrates and dose reduction of the P-gp substrate should be considered when taken with Lojuxta.	Examples of p-glycoprotein substrates include: aliskiren, ambrisentan, colchicine, dabigatran etexilate, digoxin, everolimus, fexofenadine, imatinib, lapatinib, maraviroc, nilotinib, posaconazole, ranolazine, saxagliptin, sirolimus, sitagliptin, talinolol, tolvaptan, topotecan.
ORAL CONTRACEPTIVES	
Lojuxta is not expected to directly influence the efficacy of oestrogen based oral contraceptives.	Patients taking oestrogen based oral contraceptives should be advised about possible loss of effectiveness due to diarrhoea and/or vomiting. In cases of protracted or severe diarrhoea and/or vomiting lasting more than two days, additional contraceptive measures should be used until seven days after resolution of symptoms.

Lojuxta® lomitapide

Reporting adverse events

Healthcare professionals are asked to report any suspected adverse reactions.

Adverse events can be reported to the Ministry of Health using the online form for adverse event reporting which can be found on the Ministry of Health website: www.health.gov.il or by using the following link: https://sideeffects.health.gov.il/.

Adverse events can be also reported to Medison Pharma Ltd. by email: PVIsrael@medisonpharma.com.

This guide was reviewed and approved by the Ministry of Health in Jan-2025.

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