DRUG INTERACTIONS

Effects of other drugs on eletriptan

CYP3A4 inhibitors: *In vitro* studies have shown that eletriptan is metabolized by the CYP3A4 enzyme.

Ketoconazole: A clinical study demonstrated about a 3-fold increase in C_{max} and about a 6-fold increase in the AUC of eletriptan when co-administered with ketoconazole. The half-life of eletriptan increased from 5 h to 8 h and the T_{max} increased from 2.8 h to 5.4 h.

Erythromycin: A clinical study demonstrated about a 2-fold increase in eletriptan C_{max} and about a 4-fold increase in AUC when erythromycin was co-administered with eletriptan. This increased exposure was associated with an increase in eletriptan half-life from 4.6 h to 7.1 h.

Fluconazole: Co-administration of fluconazole and eletriptan yields about a 1.4-fold increase in C_{max} and about a 2-fold increase in AUC of eletriptan.

Verapamil: It has also been shown that co-administration of verapamil and eletriptan yields about a 2-fold increase in C_{max} and about a 3-fold increase in AUC of eletriptan.

Propranolol: The C_{max} and AUC of eletriptan were increased by 10% and 33%, respectively, following an 80 mg BID dose of propranolol administered for 7 days. No interactive increases in blood pressure were observed. No dose adjustment is necessary for patients also taking propranolol.

MAO inhibitors: Eletriptan is not a substrate for monoamine oxidase (MAO) enzymes. Therefore there is no expectation of an interaction between **RELPAX** and MAO inhibitors.

The effect of eletriptan on other drugs

The effect of eletriptan on enzymes other than cytochrome P450 has not been investigated. *In vitro* human liver microsome studies suggest that eletriptan has little potential to inhibit CYP1A2, 2C9, 2E1 and 3A4 at concentrations up to 100 μM. While eletriptan has an effect on CYP2D6 at high concentration (IC_{50} of about 41 μM), this effect should not interfere with metabolism of other drugs when eletriptan is used at recommended doses. There is no *in vitro* or *in vivo* evidence that clinical doses of eletriptan will induce drug metabolizing enzymes. Therefore, eletriptan is unlikely to cause clinically important drug interactions mediated by these enzymes.

Drug-herb interactions

Interactions with herbal products have not been established.

Drug-laboratory interactions

Interactions with laboratory tests have not been established.

SYMPTOMS AND TREATMENT OF OVERDOSE

Symptoms: No significant overdoses in clinical trials have been reported. Twenty-one (21) subjects have received single doses of 120 mg in Phase 1 trials and 427 in Phase 2/3 trials without significant adverse effects. Based on the pharmacology of 5-HT_1 agonists, hypertension or other more serious cardiovascular symptoms could occur on overdose.

Treatment: In case of overdose, standard supportive measures should be adopted. The elimination half-life of eletriptan is about 4 h, and therefore monitoring of patients after overdose with eletriptan should continue for at least 20 h, or longer should symptoms or signs persist. There is no specific antidote to eletriptan. In cases of severe intoxication, intensive care procedures are recommended, including establishing and maintaining a patent airway, ensuring adequate oxygenation and ventilation, and monitoring and support of the cardiovascular system. It is unknown what effect hemodialysis or peritoneal dialysis has on the serum concentration of eletriptan.

For complete prescribing information, please refer to the Product Monograph. The full Product Monograph can be found at: **www.pfizer.ca** or by contacting the Pfizer Canada Inc. Medical Information Services at: **1-800-463-6001**.

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