Imigran Tablets

Trade Mark

Presentation

Imigran tablets: White, capsule-shaped, biconvex film-coated tablets, each tablet containing 100mg sumatriptan base (as the succinate salt) or pink, capsule-shaped, biconvex film-coated tablets, each tablet containing 50mg sumatriptan base (as the succinate salt).

Uses

Indications: Imigran tablets are indicated for the acute relief of migraine attacks, with or without aura.

Mode of Action/Pharmacology

Sumatriptan has been demonstrated to be a specific and selective 5-hydroxytryptamine-1- like ($5HT_1$ -like) receptor agonist with no effect on other 5HT receptor subtypes. This receptor is found predominantly in cranial blood vessels, and in animals sumatriptan selectively constricts the carotid arterial circulation which supplies blood to the extracranial and intracranial tissues such as the meninges. Dilatation of these vessels is thought to be the underlying mechanism of migraine in man. Clinical response begins around 30 minutes following oral administration.

Dosage and administration

Adults: Imigran is indicated for the acute intermittent treatment of migraine.

It should not be used prophylactically.

It is advisable that Imigran be given as early as possible after the onset of an attack of migraine but it is equally effective at whatever stage of the attack it is administered.

The recommended dose of oral Imigran is a single 50mg, or 100mg tablet. Patients who do not respond to this dose should not take a second dose of Imigran for the same attack. Imigran may be taken for subsequent attacks. Patients who respond initially but whose migraine returns may take a further dose provided that not more than three tablets are taken in any 24 hour period.

Imigran is recommended as monotherapy for the acute treatment of migraine and should not be given concomitantly with other acute migraine therapies. If a patient fails to respond to a single dose of Imigran there are no reasons, either on theoretical grounds or from limited clinical experience, to withhold products containing aspirin or non-steroidal anti-inflammatory drugs for further treatment of that attack. The tablets should be swallowed whole with water.

Children: The safety and effectiveness of Imigran in children has not yet been established.

Use in Patients aged more than 65 years: Experience of the use of Imigran in patients aged over 65 years is limited. The pharmacokinetics do not differ significantly from a younger population but until further clinical data are available, the use of Imigran in patients aged over 65 years is not recommended.

Contra-indications, warnings etc

Contra-indications: Hypersensitivity to any components of the preparation.

Ischaemic heart disease, previous myocardial infarction or prinzmetal angina.

Uncontrolled hypertension.

Until further data are available the use of Imigran is contraindicated in: patients receiving concurrent treatment with monoamine oxidase inhibitors, selective 5HT reuptake inhibitors and lithium.

Imigran should only be used where there is a clear diagnosis of migraine or cluster headache.

As with other acute migraine therapies, before treating headache in patients not previously diagnosed as migraineurs and in migraineurs who present with atypical symptoms care should be taken to exclude other potentially serious neurological symptoms.

Warnings: Following administration sumatriptan can be associated with transient chest pain. In extremely rare cases chest pain can be the result of coronary vasospasm.

The recommended dose of Imigran should not be exceeded.

Drowsiness may occur as a result of migraine or its treatment with Imigran. Caution is recommended in patients performing skilled tasks, eg. driving or operating machinery.

Precautions: Sumatriptan may cause short-lived elevation of blood pressure and peripheral resistance. Prolonged vasospastic reactions have been reported with ergotamine. As these effects may be additive, concomitant use of ergotamine and sumatriptan should be avoided.

Imigran should be used with caution in patients with conditions which may predispose to ischaemic heart disease or coronary vasospasm.

Imigran should be administered with caution to patients with conditions which may affect significantly the absorption, metabolism or excretion of drugs eg. impaired hepatic or renal function.

Pregnancy: No teratogenic effects have been seen in rats or rabbits.

Reproduction studies performed in rats have revealed no evidence of impaired fertility or post-natal development due to sumatriptan. As yet, experience of the use of Imigran during human pregnancy is limited. Because animal reproduction studies are not always predictive of human response, administration of this drug should only be considered if the expected benefit to the mother is greater than the possible risk to the foetus.

Lactation: Sumatriptan is excreted in breast milk in animals. No data exist in humans. Caution should therefore be exercised when considering the administration of Imigran to a nursing woman.

Side-effects: The most common side-effects associated with treatment with Imigran administered orally are malaise/fatigue, dizziness/vertigo, drowsiness/sedation, a feeling of heaviness and weakness, throat symptoms and pain or stiffness in the neck.

Tightness and pressure can occur in any part of the body, including the chest.

Minor disturbances in liver function tests have occasionally been observed.

Interactions: Studies in healthy subjects show that Imigran does not interact with propranolol, flunarizine, dihydroergotamine, pizotifen or alcohol.

Overdosage: There have been no reports of overdosage with Imigran tablets. Doses up to 400mg orally were not associated with side-effects other than those mentioned. There is no experience of doses greater than these.

If overdosage with Imigran occurs, the patient should be monitored for at least ten hours and standard supportive treatment applied as required.

It is unknown what effect haemodialysis or peritoneal dialysis has on the plasma concentrations of Imigran.

Pharmaceutical precautions

Imigran tablets should be stored below 30°C.

Further information

Pharmacokinetics: Following oral administration, Imigran is rapidly absorbed, 70% maximum concentration occurring at 45 minutes. After 100mg dose the mean maximum plasma concentration is 54ng/ml. Mean absolute oral bioavailability is 14% partly due to presystemic metabolism and partly due to incomplete absorption. The elimination phase half-life is approximately 2 hours, although there is an indication of a longer terminal phase. Plasma protein binding is low (14-21%), mean volume of distribution is 170 litres. Mean total plasma clearance is approximately 1160ml/min and the mean renal plasma clearance is approximately 260ml/min. Non-renal clearance accounts for about 80% of the total clearance suggesting that sumatriptan is eliminated primarily by metabolism. The major metabolite, the indole acetic analogue of sumatriptan is mainly excreted in the urine, where it is present as a free acid and the glucuronide conjugate. It has no known $5HT_1$ or $5HT_2$ activity. Minor metabolites have not been identified.

The pharmacokinetics of oral sumatriptan do not appear to be significantly affected by migraine attacks. In a pilot study no significant differences were found in the pharmacokinetic parameters between the elderly and young healthy volunteers.

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