Imigran™ tablets

sumatriptan succinate

Presentations
Not all presentations are registered in every country.
Tablets containing 50 mg and 100 mg of sumatriptan base as the succinate salt.

Indications
Imigran Tablets are indicated for the acute relief of migraine attacks with or without aura. Imigran should only be used where there is a clear diagnosis of migraine.

Dosage and Administration
Imigran is indicated for the acute intermittent treatment of migraine. Imigran Tablets should not be used prophylactically. It is advisable that Imigran be given as early as possible after the onset of a migraine headache. It is equally effective at whatever stage of the attack it is administered.
Dosage in adults:
The recommended adult dose of oral Imigran is a single 50 mg tablet. Some patients may require 100 mg.
If a patient does not respond to the first dose of Imigran, a second dose should not be taken for the same attack. Imigran may be taken for subsequent attacks.
If the patient has responded to the first dose, but the symptoms recur a second dose may be given in the next 24 hours, provided that not more than 300 mg is 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 to withhold products containing aspirin or non-steroidal anti-inflammatory drugs for further treatment of the attack.
The tablets should be swallowed whole with water.

Dosage in children (under 18 years of age):
The safety and effectiveness of sumatriptan in children has not yet been established.

Dosage in Elderly (over 65):
Experience of the use of sumatriptan 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 sumatriptan in patients aged over 65 years is not recommended.

Contra-indications
Hypersensitivity to any component of the preparation.
Sumatriptan should not be given to patients who have had a myocardial infarction or have ischaemic heart disease (IHD), Prinzmetal's angina/coronary vasospasm, peripheral vascular disease or patients who have symptoms or signs consistent with IHD.
Sumatriptan should not be administered to patients with a history of cerebrovascular accident (CVA) or transient ischaemic attack (TIA).
The use of sumatriptan in patients with moderate and severe hypertension and mild uncontrolled hypertension is contra-indicated.
Sumatriptan should not be administered to patients with severe hepatic impairment.
The concomitant use of ergotamine or derivatives of ergotamine (including methysergide) is contra-indicated (see Drug Interactions).
Concurrent administration of monoamine oxidase inhibitors (MAOIs) and sumatriptan is contraindicated. Sumatriptan must not be used within two weeks of discontinuation of therapy with monoamine oxidase inhibitors.

Precautions and Warnings
Imigran Tablets should only be used where there is a clear diagnosis of migraine.
Sumatriptan is not indicated for use in the management of hemiplegic, basilar or ophthalmoplegic migraine.
As with other acute migraine therapies, before treating headaches 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 conditions. It should be noted that migraineurs may be at increased risk of certain cerebrovascular events (eg. cerebrovascular accident, transient ischaemic attack).
Following administration, sumatriptan can be associated with transient symptoms including chest pain and tightness which may be intense and involve the throat (see Adverse Reactions). Where such symptoms are thought to indicate ischaemic heart disease no further doses of sumatriptan should be given and appropriate evaluation should be carried out.
Sumatriptan should not be given to patients in whom unrecognised cardiac disease is likely without a prior evaluation for underlying cardiovascular disease. Such patients include postmenopausal women, males over 40 and patients with risk factors for coronary artery disease. However, these evaluations may not identify every patient who has cardiac disease and, in very rare cases, serious cardiac events have occurred in patients without underlying cardiovascular disease.
Sumatriptan should be administered with caution to patients with controlled hypertension as transient increases in blood pressure and peripheral vascular resistance have been observed in a small proportion of patients.
There have been rare postmarketing reports describing patients with serotonin syndrome (including altered mental status, autonomic instability and neuromuscular abnormalities) following the use of a selective serotonin reuptake inhibitor (SSRI) and sumatriptan. Serotonin syndrome has been reported following concomitant treatment with triptans and serotonin noradrenaline reuptake inhibitors (SNRIs). If concomitant treatment with sumatriptan and an SSRI is clinically warranted, appropriate observation of the patient is advised (see Drug Interactions).
The concomitant administration of any triptan/5-HT1 agonist with sumatriptan is not recommended.
Sumatriptan should be administered with caution to patients with conditions which may affect significantly the absorption, metabolism or excretion of the drug, eg. impaired hepatic or renal function.
Sumatriptan should be used with caution in patients with a history of epilepsy or structural brain lesions which lower their convulsion threshold.
Patients with known hypersensitivity to sulphonamides may exhibit an allergic reaction following administration of sumatriptan. Reactions may range from cutaneous hypersensitivity to anaphylaxis. Evidence of cross sensitivity is limited, however, caution should be exercised before using sumatriptan in these patients.
The recommended dose of Imigran should not be exceeded.
Overuse of acute migraine treatments has been associated with the exacerbation of headache (medication overuse headache, MOH) in susceptible patients. Withdrawal of the treatment may be necessary.
Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine as it contains lactose.

Drug Interactions
There is no evidence of interactions with propranolol, flunarizine, pizotifen or alcohol.
There are limited data on an interaction with preparations containing ergotamine or another triptan/5-HT1 receptor agonist. The increased risk of coronary vasospasm is a theoretical possibility and concomitant administration is contraindicated.
The period of time that should elapse between the use of sumatriptan and ergotamine-containing preparations or another triptan/5-HT1 receptor agonist is not known. This will also depend on the doses and types of products used. As these effects may be additive, 24 hours should elapse before sumatriptan can be taken following any ergotamine containing preparation or another triptan/5-HT1 receptor agonist.
Conversely, ergotamine containing preparations should not be taken until 6 hours have elapsed following sumatriptan administration and at least 24 hours before administering another triptan/5-HT1 receptor agonist.
An interaction may occur between sumatriptan and MAOIs and concomitant administration is contra-indicated (see Contra-indications). There have been rare post-marketing reports describing patients with serotonin syndrome (including altered mental status, autonomic instability and neuromuscular abnormalities) following the use of SSRIs and sumatriptan. Serotonin syndrome has also been reported following concomitant treatment with triptans and SNRIs. (see Precautions and Warnings).

Pregnancy and Lactation
No teratogenic effects have been seen in rats or rabbits and sumatriptan had no effect on the post-natal development of rats.
When administered to pregnant rabbits throughout the period of organogenesis sumatriptan has occasionally caused embryolethality at doses which were sufficiently high to produce maternal toxicity.
Caution should be exercised by considering the expected benefit to the mother against possible risk to the foetus.
Post-marketing data from multiple prospective pregnancy registries have documented the pregnancy outcomes in over 1,000 women exposed to sumatriptan. Although there is insufficient information to draw definitive conclusions, the findings have not detected an increase in the frequency of birth defects nor a consistent pattern of birth defects, amongst women exposed to sumatriptan compared with the general population.
It has been demonstrated that following subcutaneous administration sumatriptan is excreted into breast milk. Infant exposure can be minimised by avoiding breast feeding for 12 hours after treatment, during which time any breast milk expressed should be discarded.

Effects on Ability to Drive and Use Machines
Drowsiness may occur as a result of migraine or its treatment with sumatriptan.
Caution is recommended in patients performing skilled tasks, eg. driving or operating machinery.

Adverse Reactions:
Frequencies are defined as: very common (>1/10), common (>1/100, <1/10), uncommon (>1/1000, <1/100), rare (>1/10,000, <1/1000) and very rare (<1/10,000) including isolated reports.
Clinical Trial Data

Nervous System Disorders
Common: Dizziness, drowsiness, sensory disturbance including paraesthesia and hypoaesthesia.
Vascular Disorders
Common: Transient increases in blood pressure arising soon after treatment. Flushing.
Respiratory, Thoracic and Mediastinal Disorders
Common: Dyspnoea
Gastrointestinal
Common: Nausea and vomiting occurred in some patients but the relationship to sumatriptan is not clear.
Musculoskeletal and Connective Tissue Disorders
The following symptom is usually transient and may be intense and can affect any part of the body including the chest and throat:
Common: Sensations of heaviness.
General Disorders
The following symptoms are usually transient and may be intense and can affect any part of the body including the chest and throat:
Common: Pain, sensations of heat, or cold, pressure or tightness.
The following symptoms are mostly mild to moderate in intensity and transient:
Common: Feelings of weakness, fatigue.
Investigations
Very rare: Minor disturbances in liver function tests have occasionally been observed.
Post-Marketing Data
Immune System Disorders
Very rare: Hypersensitivity reactions ranging from cutaneous hypersensitivity to anaphylaxis.
Nervous System Disorders
Very rare: Seizures, although some have occurred in patients with either a history of seizures or concurrent conditions predisposing to seizures there are also reports in patients where no such predisposing factors are apparent.
Tremor, dystonia, nystagmus, scotoma.
Eye Disorders
Very rare: Flickering, diplopia, reduced vision. Loss of vision including reports of permanent defects. However, visual disorders may also occur during a migraine attack itself.
Cardiac Disorders
Very rare: Bradycardia, tachycardia, palpitations, cardiac arrhythmias, transient ischaemic ECG changes, coronary artery vasospasm, angina, myocardial infarction (see Contraindications, Warnings and Precautions).
Vascular Disorders
Very rare: Hypotension, Raynaud's phenomenon.
Gastrointestinal
Very rare: Ischaemic colitis.
Musculoskeletal, connective tissue and bone disorders
Very rare: Neck stiffness

Overdosage
Doses in excess of 400 mg orally were not associated with side effects other than those mentioned.
If overdosage 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 sumatriptan.

Pharmacodynamic Properties
Mode of action:
Pharmacotherapeutic group:- Selective 5-HT_1 receptor agonists.
Sumatriptan has been demonstrated to be a selective vascular 5-hydroxytryptamine-1-(5-HT_1D) receptor agonist with no effect at other 5-HT receptor (5-HT_2-7) subtypes. The vascular 5-HT_1D receptor is found predominantly in cranial blood vessels and mediates vasoconstriction.
In animals sumatriptan selectively constricts the carotid arterial circulation, but does not alter cerebral blood flow. The carotid arterial circulation supplies blood to the extracranial and intracranial tissues such as the meninges and dilatation and/or oedema formation in these vessels is thought to be the underlying mechanism of migraine in man. In addition, experimental evidence suggests that sumatriptan inhibits trigeminal nerve activity. Both these actions may contribute to the anti-migraine action of sumatriptan in humans.
Clinical response begins around 30 minutes following a 100 mg oral dose.
Although the recommended dose of oral Imigran is 50 mg, migraine attacks vary in severity both within and between patients. Doses of 25-100 mg have shown greater efficacy than placebo in clinical trials, but 25 mg is statistically significantly less effective than 50 and 100 mg.
Sumatriptan remains effective in treating menstrual migraine i.e. migraine without aura that occurs between 3 days prior and up to 5 days post onset of menstruation. Sumatriptan should be taken as soon as possible in an attack.

Pharmacokinetic Properties
The elimination half life is approximately 2 hours. After oral administration, sumatriptan is rapidly absorbed, 70% of maximum concentration occurring at 45 minutes. After 100 mg dose the mean maximum plasma concentration is 54 ng/ml. Mean absolute oral bioavailability is 14% partly due to presystemic metabolism and partly due to incomplete absorption. Plasma protein binding is low (14-21%), the mean total volume of distribution is 170 litres. Mean total plasma clearance is approximately 1160 ml/min and the mean renal plasma clearance is approximately 260 ml/min. Non-renal clearance accounts for about 80% of the total clearance. Sumatriptan is eliminated primarily by oxidative metabolism mediated by monoamine oxidase A. The major metabolite, the indole acetic acid analogue of sumatriptan is mainly excreted in 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.

Further Information
Preclinical Safety Data
Sumatriptan was devoid of genotoxic and carcinogenic activity in in-vitro systems and animal studies.
In a rat fertility study oral doses of sumatriptan resulting in plasma levels approximately 200 times those seen in man after a 100 mg oral dose were associated with a reduction in the success of insemination.
This effect did not occur during a subcutaneous study where maximum plasma levels achieved approximately 150 times those in man by the oral route.

Pharmaceutical Precautions and Recommendations
Do not store above 30°C

List of Excipients
Imigran 50 mg tablets: Lactose, microcrystalline cellulose, croscarmellose sodium, magnesium stearate, methylhydroxypropylcellulose, titanium dioxide, triacetin and iron oxide.
Imigran 100 mg tablets: Lactose, microcrystalline cellulose, croscarmellose sodium, magnesium stearate, methylhydroxypropylcellulose and opaspray white.

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Manufactured by:
Glaxo Operations UK Limited*, Ware, UK

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GlaxoSmithKline

THIS IS A MEDICAMENT

Medicament is a product which affects your health and its consumption contrary to instructions is dangerous for you.

Follow strictly the doctor's prescription, the method of use and the instructions of the pharmacist who sold the medicament.

- The doctor and the pharmacist are the experts in medicines, their benefits and risks.
- Do not by yourself interrupt the period of treatment prescribed.
- Do not repeat the same prescription without consulting your doctor.
- Keep all medicaments out of reach of children.

Council of Arab Health Ministers,
Union of Arab Pharmacists.