

Data Sheet

Imigran Recovery

Sumatriptan (as the succinate salt) 50 mg, film-coated tablets.

QUALITATIVE AND QUANTITATIVE COMPOSITION

50 mg sumatriptan base (as the succinate salt).

For excipients, see Pharmaceutical Particulars.

PHARMACEUTICAL FORM

Film-coated tablet.

Pink, film-coated, capsule shaped, biconvex tablets debossed with 'GX ES3' on one side.

CLINICAL PARTICULARS

Therapeutic indications

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

Posology and method of administration

Adults (18-65 years of age)

The recommended dose is a single 50 mg tablet that should be swallowed whole with water. It is advisable that Imigran Recovery be taken as soon as possible after the onset of a migraine headache although it is effective at whatever stage of the headache it is taken.

If there is a response to the first tablet but the symptoms recur, a second tablet may be taken. However, this must be at least 2 hours after the first tablet. No more than two 50 mg tablets (total dose 100 mg) may be taken in any 24 hour period or to treat the same attack.

If there is no response to the first tablet, a second tablet should not be taken for the same attack.

Children and Adolescents (under 18 years of age)

Not to be used in children or adolescents under 18 years of age.

The safety and effectiveness of Imigran Recovery in children have not been established.

Elderly (over 65 years of age)

Not to be used in those over 65 years of age.

Experience of the use of Imigran Recovery in patients over 65 years is limited.

Contra-indications

Imigran Recovery must not be used prophylactically.

Hypersensitivity to any component of the preparation or to sulphonamides.

Previous myocardial infarction, or those who have ischaemic heart disease, coronary vasospasm (Prinzmetal's angina), cardiac arrhythmias, peripheral vascular disease or symptoms or signs consistent with ischaemic heart disease.

History of cerebrovascular accident (stroke) or transient ischaemic attack (TIA / mini-stroke).

Known hypertension.

Hepatic or renal impairment.

History of seizures or other risk factors which lower the seizure threshold.

Concurrent treatment with the following medications is contra-indicated:

- Ergotamine or derivatives of ergotamine (including methysergide) (see Interactions).
- Monoamine oxidase inhibitors (MAOIs). Imigran Recovery must not be used within 2 weeks of discontinuation of therapy with MAOIs.
- Any 5-HT₁ receptor agonist (triptan).

Imigran Recovery is not to be used to treat the following rare variants of migraine:

- Hemiplegic migraine - migraine with aura including unilateral motor weakness.
- Basilar migraine - migraine with aura symptoms originating from the brain stem and/or both hemispheres such as double vision, difficulty in articulating words, clumsy and unco-ordinated movements, tinnitus, reduced level of consciousness.
- Ophthalmoplegic migraine - migraine headache with involvement of one or more ocular cranial nerves resulting in weakness of the muscles controlling eye movement.

Special warnings and special precautions for use

Imigran Recovery should only be used where a clear diagnosis of migraine has been made by a doctor or a pharmacist. For pharmacy supply, patients should have an established pattern of migraine (a history of five or more migraine attacks occurring over a period of at least 1 year).

Imigran Recovery should not be taken concomitantly with other migraine therapies containing any triptan, ergotamine or derivative of ergotamine.

If a migraineur fails to respond to the first tablet of Imigran Recovery, the attack may be treated with simple analgesics. Further, the diagnosis of migraine should be reconsidered with a doctor.

The recommended dose of Imigran Recovery should not be exceeded.

Migraineurs whose typical headaches persist for longer than 24 hours should seek advice from their doctor.

Migraineurs in whom the pattern of symptoms has changed, or whose attacks have become more frequent, more persistent, or more severe, or who do not recover completely between attacks, should seek advice from their doctor.

Anyone with atypical symptoms which include, but are not limited to, unilateral motor weakness, double vision, clumsy and unco-ordinated movements, tinnitus, reduced level of consciousness, seizure-like movements, or recent onset of rash with headache should seek advice from their doctor.

Patients whose migraine symptoms appear for the first time after age 50 should seek advice from their doctor as there may be a more serious underlying cause.

Migraineurs who experience four or more migraine attacks per month should be referred to a doctor for ongoing management.

It should be noted that migraineurs may be at risk of certain cerebrovascular events (e.g. cerebrovascular accident, transient ischaemic attack).

Following administration, sumatriptan can be associated with transient symptoms including chest pain and tightness that may be intense and involve the throat (see Undesirable effects). Typically, such symptoms develop within 30 minutes of treatment and last for less than 2 hours. Where such symptoms are thought to indicate ischaemic heart disease, medical evaluation should be obtained immediately and no further doses of Imigran Recovery should be taken until considered appropriate by a doctor.

Imigran Recovery should not be used by migraineurs in whom unrecognised cardiac disease is likely without a prior risk assessment by a doctor or pharmacist (see Contra-indications). Special consideration should be given to post-menopausal women and men over 40. Risk factors for heart disease include hypercholesterolaemia, regular smoking, marked obesity, diabetes or a family history of early heart disease (father/brother developed heart disease before the age of 55, mother/sister developed heart disease before the age of 65). Anyone who has three or more of these risk factors is not suitable for pharmacy supply of sumatriptan. These evaluations may not identify everyone who has cardiac disease and, in very

rare cases, serious cardiac events have occurred without underlying cardiovascular disease.

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 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 use of sumatriptan and an SSRI/SNRI is considered to be appropriate, migraineurs should be warned to see their doctor if they develop symptoms of serotonin syndrome.

Undesirable effects may be more common during concomitant use of triptans and herbal preparations containing St John's wort (*Hypericum perforatum*).

Patients with known hypersensitivity to sulphonamides may exhibit an allergic reaction following administration of sumatriptan. Reactions may range from cutaneous hypersensitivity to anaphylaxis. Although evidence of cross-sensitivity is limited, treatment with Imigran Recovery is contraindicated in these patients (see Contra-indications).

Women with migraine who are taking the combined oral contraceptive have an increased risk of stroke and should seek advice from their doctor if migraine attacks started recently (within the last 3 months), migraine symptoms have worsened or they have migraine with aura.

Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

Interaction with other medicinal products and other forms of interaction

Studies in healthy subjects show that sumatriptan does not interact with propranolol, flunarizine, pizotifen or alcohol.

Sumatriptan has the potential to interact with MAOIs, ergotamine and derivatives of ergotamine. The increased risk of coronary vasospasm is a theoretical possibility and therefore concomitant administration with MAOIs and ergotamines is contraindicated (see Contra-indications).

Prolonged vasospastic reactions have been reported with ergotamine. As these effects may be additive, 24 hours should elapse before sumatriptan can be taken following any ergotamine-containing preparation. Conversely, ergotamine-containing preparations should not be taken until 6 hours have elapsed following sumatriptan administration.

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

Special warnings and special precautions for use). There is a risk of pharmacodynamic interaction between sumatriptan and tricyclic antidepressants.

Undesirable effects may be more common during concomitant use of triptans and herbal preparations containing St John's wort (*Hypericum perforatum*).

Pregnancy and lactation

Imigran Recovery is not to be used in pregnancy or when breastfeeding unless on the advice of a doctor.

Post-marketing data from the use of sumatriptan during the first trimester in over 1,000 women are available. Although these data contain insufficient information to draw definitive conclusions, they do not suggest an increased risk of congenital defects. Experience with the use of sumatriptan in the second and third trimester is limited.

Evaluation of experimental animal studies does not indicate direct teratogenic effects or harmful effects on peri- and postnatal development. However, embryofoetal viability might be affected in the rabbit (see Preclinical safety data).

It has been demonstrated that following subcutaneous administration, sumatriptan is excreted into breast milk. Infant exposure can be minimised by avoiding breast feeding for 24 hours after treatment.

Effect on ability to drive and use machines

Drowsiness may occur as a result of migraine or its treatment with sumatriptan. Caution is recommended when skilled tasks are to be performed e.g. driving or operating machinery.

Undesirable effects

Adverse events are listed below by system organ class and frequency. 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.

Immune System Disorders

Very rare: Hypersensitivity reactions ranging from cutaneous hypersensitivity to anaphylaxis.

Nervous System Disorders

Common: Dizziness, drowsiness, sensory disturbance including paraesthesia and hypoaesthesia.

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 (usually transient). 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 Contra-indications, Special Warnings and special precautions for use).

Vascular Disorders

Common: Transient increases in blood pressure arising soon after treatment. Flushing.

Very rare: Hypotension, Raynaud's phenomenon.

Respiratory, Thoracic and Mediastinal Disorders

Common: Dyspnoea.

Gastrointestinal Disorders

Common: Nausea and vomiting occurred in some patients but the relationship to sumatriptan is not clear.

Very rare: Ischaemic colitis.

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 and Administration Site Conditions

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.

Overdose

In the event of an overdose, medical advice should be sought immediately.

There have been some reports of overdosage with Imigran Recovery. Doses in excess of 400 mg orally were not associated with side effects other than those mentioned in Undesirable effects.

If overdosage occurs, the patient should be monitored for at least 10 hours and standard supportive treatment applied as required.

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

PHARMACOLOGICAL PROPERTIES

Pharmacodynamic properties

Pharmacotherapeutic group: Analgesics: Selective 5-HT₁ receptor agonists.

ATC code: N02CC01

Sumatriptan has been demonstrated to be a specific and selective 5-hydroxytryptamine-1 (5-HT_{1B/D}) receptor agonist with no effect on other 5-HT receptor (5-HT₂-5-HT₇) subtypes. The vascular 5-HT_{1B} 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 of and/or oedema formation in these vessels is thought to be the underlying mechanism of migraine in man.

In addition, evidence from animal studies suggests that sumatriptan inhibits trigeminal nerve activity. Both these actions (cranial vasoconstriction and inhibition of trigeminal nerve activity) may contribute to the anti-migraine action of sumatriptan in humans.

Sumatriptan relieves headache and other symptoms of migraine including nausea, and sensitivity to light and sound. Clinical response for relief of migraine headache begins around 30 minutes following a 50 mg oral dose.

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 after the onset of a migraine headache.

Pharmacokinetic properties

Following oral administration, sumatriptan is rapidly absorbed, 70% of maximum concentration occurring at 45 minutes. After a 50 mg dose, the mean maximum

plasma concentration is 32 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%), mean volume of distribution is 170 litres.

The major metabolite, the indole acetic acid 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 5-HT₁ or 5-HT₂ activity. Minor metabolites have not been identified.

The elimination phase half-life is approximately 2 hours, although there is an indication of a longer terminal phase. 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 pharmacokinetics of oral sumatriptan do not appear to be significantly affected by migraine attacks.

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.

In rabbits, embryoletality, without marked teratogenic defects, was seen. The relevance for humans of these findings is unknown.

PHARMACEUTICAL PARTICULARS

List of excipients

Lactose, microcrystalline cellulose, croscarmellose sodium, magnesium stearate, hypromellose (E464), titanium dioxide (E171), triacetin and iron oxide (E172).

Incompatibilities

Not applicable.

Shelf life

36 months.

Special precautions for storage

Do not store above 30°C.

Nature and contents of container

Aluminium double foil blister packs in a cardboard carton, containing 2 tablets.

Cardboard carton containing 2 tablets in an aluminium double foil blister pack and a plastic carry case.

Instructions for use/handling

None.

Medicine Classification

Restricted Medicine

Name and Address

GlaxoSmithKline Consumer Healthcare
Level 8 AMP Centre
Cnr Customs and Albert Streets
Auckland, New Zealand

Date of Preparation

3 April 2008