The medicine is not currently marketed in New Zealand

DATA SHEET

IMIGRAN™ NASAL SPRAY
Sumatriptan Nasal Spray 20mg

Qualitative and quantitative composition

Unit dose spray device for intranasal administration. The device delivers either 10mg or 20mg of sumatriptan in 0.1mL of an aqueous buffered solution.

Pharmaceutical form

Solution for intranasal administration. The solution has a characteristic taste.

Clinical particulars

Therapeutic Indications

IMIGRAN Nasal Spray is indicated for the acute treatment of migraine attacks with or without aura. It is particularly suitable for patients who suffer with nausea and vomiting or who require a rapid onset of effect during an attack.

The onset of effect for the nasal spray is more rapid than the tablet formulation.

Posology and Method of Administration

IMIGRAN Nasal Spray 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.

The optimal dose of IMIGRAN Nasal Spray is 20mg for administration into one nostril. Although, due to inter/intra patient variability of both the migraine attacks and the absorption of sumatriptan, 10mg may be effective in some patients and attacks.

If the 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 there is a minimum interval of two hours between the two doses.

No more than two IMIGRAN 20mg Nasal Sprays should be used in any 24 hour period.

**Children (under 18 years of age):-**

The safety and effectiveness of IMIGRAN Nasal Spray in children has not yet been established.

**Elderly (over 65):-**

There is no experience of the use of IMIGRAN Nasal Spray in patients over 65.

**Contra-indications**

Hypersensitivity to any component of the preparation.

Sumatriptan should not be given to patients who have had 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 uncontrolled hypertension is contraindicated.

Sumatriptan should not be administered to patients with severe hepatic impairment.

The concomitant use of ergotamine or derivatives of ergotamine (including methysergide) is contraindicated (see Interaction with Other Medicaments and Other Forms of Interaction).

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.

**Special Warnings and Special Precautions for Use**

IMIGRAN Nasal Spray 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 Undesirable Effects). Where such symptoms are thought to indicate ischaemic heart disease 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 weakness, hyper-reflexia, and incoordination following the use of a selective serotonin reuptake inhibitor (SSRI) and sumatriptan. If concomitant treatment with sumatriptan and an SSRI is clinically warranted, appropriate observation of the patient is advised (see Interaction with Other Medicaments and Other Forms of Interaction).

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.

Interaction with Other Medicaments and Other Forms of Interaction

There is no evidence of interactions with propranolol, flunarizine, pizotifen or alcohol.
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.

An interaction may occur between sumatriptan and MAOIs and concomitant administration is contra-indicated (see Contra-indications). Rarely an interaction may occur between sumatriptan and SSRIs (see Special Warnings and Special Precautions for Use).

**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. In a rat fertility study oral doses of sumatriptan resulting in plasma levels approximately 750 times those seen in man after a 20mg intranasal dose were associated with a reduction in the success of insemination.

This effect did not occur during a subcutaneous study where maximum plasma levels in rats achieved approximately 500 times those seen in man by the intranasal route.

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 any possible risk to the foetus.

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.

**Effects on Ability to Drive and Operate Machinery**

Drowsiness may occur as a result of migraine or its treatment with sumatriptan.

Caution is recommended in patients performing skilled tasks, e.g. driving or operating machinery.

**Undesirable Effects**

General:
Following administration of IMIGRAN Nasal Spray mild, transient irritation or burning sensation in the nose or throat or epistaxis have been reported.

The following symptoms are usually transient and may be intense and can affect any part of the body including the chest and throat.

Pain, sensations of tingling, heat, heaviness, pressure or tightness, stinging and lightheadedness.

The following symptoms are mostly mild to moderate in intensity and transient: Flushing, dizziness and feelings of weakness.

Fatigue and drowsiness have been reported.

Cardiovascular:

- Hypotension.
- Bradycardia.
- Tachycardia.
- Palpitations.
- Hypertension.
- Constriction of coronary arteries.

Transient increases in blood pressure arising soon after treatment have been recorded.

Cardiac arrhythmias, transient ischaemic ECG changes, coronary artery vasospasm, and myocardial infarction have been reported rarely (see Contraindications and Warnings and Precautions).

There have been rare reports of Raynaud’s phenomenon and ischaemic colitis.

Gastrointestinal:

A bitter taste after a dose of IMIGRAN Nasal Spray is a frequent adverse event. The duration of the bitter taste lasts longer with higher doses of sumatriptan.

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

CNS:

There have been rare reports of seizures, following use of sumatriptan. 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.

Eye:

Patients treated with IMIGRAN rarely exhibit visual disorders like flickering and diplopia. Additionally cases of nystagmus, scotoma and reduced vision have been observed.

Very rarely a transient loss of vision has been reported.

However, visual disorders may also occur during a migraine attack itself.

Hypersensitivity/Skin:

Hypersensitivity reactions ranging from cutaneous hypersensitivity to rare cases of anaphylaxis.

Laboratory values:

Minor disturbances in liver function tests have occasionally been observed.

Overdose

Single doses of sumatriptan, up to 40mg intranasally, and in excess of 16mg subcutaneously and 400mg orally have not been associated with side effects other than those mentioned.

In clinical studies volunteers have received 20mg of sumatriptan by the intranasal route three times a day for a period of 4 days without significant adverse effects.

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.

Pharmacological properties

Pharmacodynamic Properties

Sumatriptan has been demonstrated to be a selective vascular 5-hydroxytryptamine-1-(5HT1D) receptor agonist with no effect at other 5HT receptor (5HT2-5HT7) subtypes. The vascular 5HT1D 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 10-15 minutes following a 6mg subcutaneous injection, 15 minutes following a 20mg dose given by intra-nasal administration and around 30 minutes following a 100mg oral dose.

**Pharmacokinetic Properties**

After intranasal administration, sumatriptan is rapidly absorbed, maximum plasma concentration occurring in 1-1.5 hours. After a 20mg dose, the mean maximum concentration is 12.9ng/mL. Mean intranasal bioavailability, relative to sub-cutaneous administration is 15.8%, partly due to pre-systemic metabolism. Following oral administration presystemic clearance is reduced in patients with hepatic impairment resulting in increased plasma levels, of sumatriptan a similar increase would be expected following intranasal administration.

Plasma protein binding is low (14-21%), the mean total volume of distribution is 170 litres. The elimination half-life is approximately 2 hours. The 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. 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 5HT₁ or 5HT₂ activity. Minor metabolites have not been identified. The pharmacokinetics of intra-nasal 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.

**Pharmaceutical particulars**

**List of Excipients**

- Potassium Dihydrogen Phosphate PhEur.
- Dibasic Sodium Phosphate anhydrous USP.
- Sulphuric Acid BP.
- Sodium Hydroxide PhEur.
- Purified Water PhEur.

**Incompatibilities**
The medicine is not currently marketed in New Zealand

None reported.

**Shelf Life**

2 years.

**Special Precautions for Storage**

IMIGRAN Nasal Spray should be stored between 2-30°C.

It should be kept in the sealed blister, preferably in the box, to protect from light.

**Nature and Contents of Container**

Unit dose disposable nasal spray device.

**Instructions for Use/Handling**

The nasal spray must only be removed from the blister packaging immediately before use.

The nasal spray consists of the following parts:-

**The Nozzle:**

This is the part that you put into your nostril. The spray comes out of a tiny hole in the top.

**The Finger-grip:**

This is the part that you hold when you use the Spray.

**The Blue Plunger:**

When you press the Plunger the whole dose sprays into your nostril in one go. The Plunger only works once so do not press it until you have put the Nozzle into your nostril or you will waste the dose.

**Instructions for Use:**

First, get into a comfortable position. You may like to sit down if there is a seat close-by.

Blow your nose if it feels blocked, or if you have a cold.

Peel open a blister pack and take out a nasal spray.

Hold the nasal spray gently with your fingers and thumb.

Do not press the blue plunger yet.
Block one nostril by pressing a finger firmly on the side of your nose - just before spray is inserted into one nostril.

Breathe out gently through your mouth.

Put the nozzle of the nasal spray into the other nostril, as far as feels comfortable (about 1cm or ½ inch).

Hold your head in an upright position and close your mouth.

Start to breathe in gently through your nose and at the same time press the blue plunger firmly with your thumb.

The plunger may feel a bit stiff and you may hear it click.

Keep your head upright and breathe gently in through your nose and out through your mouth for 10-20 seconds. DO NOT BREATHE DEEPLY.

You can remove the Spray and your finger from the other side of your nose whilst you do this.

Your nose may feel wet inside and you may notice a slight taste after using the spray - this is normal and will soon pass.

After being used once your nasal spray is empty. It should be disposed of safely and hygienically.

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**Medicines classification**

Prescription Only Medicine

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**Name and address**

Glaxo Wellcome New Zealand Limited
Quay Tower
Cnr Albert & Customs Streets
Private Bag 106600
Downtown
Auckland
NEW ZEALAND

**Telephone:** (09) 367 2900  
**Facsimile:** (09) 367 2506

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1 November 1999
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