IMIGRAN NASAL SPRAY
Professional Information

SCHEDULING STATUS:

S4

1. NAME OF THE MEDICINE:

IMIGRAN 20 mg Nasal Spray

2. QUALITATIVE AND QUANTITATIVE COMPOSITION:

A unit dose device for intranasal administration. The device contains 20 mg of sumatriptan in an aqueous buffered solution.

For full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM:

Nasal Spray.

A clear, pale yellow to dark yellow liquid.

4. CLINICAL PARTICULARS:

4.1 Therapeutic indications:

IMIGRAN nasal spray is indicated for the acute treatment of migraine attacks with or without aura.

4.2 Posology and method of administration:

IMIGRAN is recommended as monotherapy.

The recommended doses of IMIGRAN should not be exceeded.

IMIGRAN should not be used prophylactically.

It is advisable that IMIGRAN be given as early as possible after the onset of an attack of migraine.

Adults (18 years and over):

The optimal dose of IMIGRAN nasal spray is 20 mg.

If symptoms recur a second dose may be given in the next 24 hours provided that there is a minimum interval of 2 hours between the two doses.

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

No more than two IMIGRAN Nasal Sprays to be used in any 24-hour period

Special populations:

Elderly (over 65 years of age):

There is no experience of the use of IMIGRAN Nasal Spray in patients over 65. Therefore, the use of IMIGRAN Nasal Spray is not recommended until further data are available.

Hepatic impairment:

IMIGRAN should be administered with caution to patients with mild to moderate hepatic impairment (Child Pugh grade A or B; see section 5.2). IMIGRAN is contraindicated in patients with severe hepatic impairment (Child Pugh Grade C) (see section 4.3).

Renal impairment:

IMIGRAN should be administered with caution to patients with renal impairment (see section 5.2).

Paediatric population:

IMIGRAN 20 mg Nasal Spray is not recommended in children aged 17 years and below.

4.3 Contraindications:

Hypersensitivity to sumatriptan or to any of the excipients listed in section 6.1.

IMIGRAN should not be given to patients who have had previous 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 ischaemic heart disease.

IMIGRAN should not be administered to patients with a history of cerebrovascular accident (CVA) or transient ischaemic attack (TIA).

IMIGRAN should not be administered to patients with severe hepatic impairment (Child Pugh Grade C).

The concomitant use of ergotamine or derivatives of ergotamine (including methysergide) and IMIGRAN is contraindicated.

Concurrent administration of monoamine oxidase inhibitors or use within two weeks of discontinuation of MAOI therapy is contraindicated.

4.4 Special warnings and precautions for use:

IMIGRAN should only be used where there is a clear diagnosis of migraine.

IMIGRAN is not indicated for use in the management of hemiplegic, basilar or ophthalmoplegic migraine.

Before treating with IMIGRAN, care should be taken to exclude potentially serious neurological conditions (e.g. CVA, TIA), if the patient presents with atypical symptoms or if they have received an appropriate diagnosis for IMIGRAN use.

Administration of IMIGRAN can be associated with transient symptoms, including chest pain and tightness, which may be intense and involve the throat. Where such symptoms are thought to indicate ischaemic heart disease appropriate evaluation should be carried out.

IMIGRAN 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, serious cardiac events have occurred in patients without underlying cardiovascular disease.

IMIGRAN should be administered with caution in patients with controlled hypertension since transient increases in blood pressure and peripheral vascular resistance have been observed in a small proportion of patients.

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 IMIGRAN. Serotonin syndrome has been reported following concomitant treatment with triptans and serotonin noradrenaline reuptake inhibitors (SNRIs). If concomitant treatment with IMIGRAN and an SSRI/SNRI is clinically warranted, appropriate observation of the patient is advised (see section 4.5).

The concomitant administration of any triptan/5-HT1 agonist with IMIGRAN is not recommended.

IMIGRAN should also be administered with caution to patients with conditions which may alter the absorption, metabolism, or excretion of medicines, such as impaired hepatic (Child Pugh grade A or B; see section 5.2) or renal function.

IMIGRAN should be used with caution in patients with a history of seizures or other risk factors which lower the seizure threshold.

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 known hypersensitivity to sulphonamides may exhibit an allergic reaction following administration of IMIGRAN. Reactions may range from cutaneous hypersensitivity to anaphylaxis. Evidence of cross sensitivity is limited; however, caution should be exercised before using IMIGRAN in these patients.

Children (under 18 years of age):

The safety and effectiveness of IMIGRAN 20 mg Nasal Spray in children has not yet been established.

Elderly (over 65 years of age):

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

4.5 Interactions with other medicines and other forms of interactions:

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

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

An interaction may occur between IMIGRAN and MAOIs and concomitant administration is contraindicated.

There may be a risk of serotonergic syndrome also if sumatriptan is used concomitantly with lithium.

An interaction may occur between IMIGRAN and SSRIs.

There have been post-marketing reports describing patients with serotonin syndrome (including altered mental status, autonomic instability and neuromuscular abnormalities) following the use of SSRIs and IMIGRAN. Serotonin syndrome has also been reported following concomitant treatment with triptans and SNRIs (see section 4.4). IMIGRAN should be used with caution in patients on SSRIs or SNRIs.

Co-administration of IMIGRAN with other medicines that enhance the effect of serotonergic neurotransmission such as amphetamines, fentanyl and its analogues, pethidine, and tramadol should be undertaken with caution and avoided whenever possible due to the potential for pharmacodynamic interaction.

4.6 Fertility, pregnancy and lactation:

Safety in pregnancy and lactation has not been established.

It has been demonstrated that following subcutaneous administration IMIGRAN is excreted into breastmilk. Infant exposure can be minimised by avoiding breastfeeding for 12 hours after treatment.

4.7 Effects on ability to drive and use machines:

Drowsiness may occur as a result of migraine or its treatment with IMIGRAN. Caution is recommended in patients performing skilled tasks, e.g. driving or operating machinery. Patients experiencing drowsiness should avoid driving and use of machines.

4.8 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 (> 1/1 000, < 1/100), rare (> 1/10 000, < 1/1 000) and very rare (< 1/10 000), including isolated reports. It should be noted that the background rate in comparator groups was not taken into account. Post-marketing data refer to reporting rate rather than true frequency.

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.

Gastrointestinal disorders:

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

Respiratory, thoracic and mediastinal disorders:

Common: dyspnoea

Following administration of IMIGRAN nasal spray mild, transient irritation or burning sensation in the nose or throat or epistaxis have been reported

A characteristic taste has been reported. IMIGRAN nasal spray should not be used in upper airway obstruction

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.

Post-Marketing Data:

Immune System Disorders: hypersensitivity reactions ranging from cutaneous hypersensitivity to rare cases of anaphylaxis

Nervous System Disorders: 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: flickering, diplopia, reduced vision. Loss of vision (usually transient). However, visual disorders may also occur during a migraine attack itself

Cardiac disorders: bradycardia, tachycardia, palpitations, cardiac dysrhythmias, transient ischaemic ECG changes, coronary artery vasospasm, angina, myocardial infarction (see sections 4.3 and 4.4)

Vascular disorders: hypotension, Raynaud's phenomenon.

Gastrointestinal disorders: ischaemic colitis.

Reporting of side effects:

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare providers are asked to report any suspected adverse reactions to SAHPRA via the "6.04 Adverse Drug Reactions Reporting Form", found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8.

4.9 Overdose:

Single doses up to 40 mg intranasally, were not associated with side effects other than those mentioned. There is no experience of doses greater than these.

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

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 concentration of sumatriptan.

5. PHARMACOLOGICAL PROPERTIES:

A 7.3 Vascular medicines, migraine preparations

5.1 Pharmacodynamic properties:

Sumatriptan is demonstrated to be a selective 5-hydroxytryptamine$_1$-like (5HT$_1$-like) receptor agonist, with no effect at other 5HT receptor (5HT$_2$ - 5HT$_7$) subtypes. The 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 dilation 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.

5.2 Pharmacokinetic properties:

After intra-nasal administration of sumatriptan, the maximum plasma concentration occurs in about 1,5 hours. After a 20 mg dose, the mean maximum concentration is 12,9 ng/ml. Mean intranasal bioavailability, relative to sub-cutaneous administration is 15,8 %. 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 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. 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 intra-nasal sumatriptan does not appear to be significantly affected by migraine attacks.

Special Patient Populations:

Elderly (over 65):

The pharmacokinetics of sumatriptan in the elderly has not been established.

Hepatic impairment: Following oral administration, pre-systemic clearance is reduced in patients with hepatic impairment resulting *in* increased plasma levels of sumatriptan. A similar increase would be expected following intranasal administration.

6. PHARMACEUTICAL PARTICULARS:

6.1 List of Excipients:

Potassium dihydrogen phosphate, dibasic sodium phosphate anhydrous, sulphuric acid, sodium hydroxide and purified water.

6.2 Incompatibilities:

Not applicable

6.3 Shelf life:

36 months

6.4 Special precautions for storage:

Store at or below 30 °C**.**

Protect from light.

6.5 Nature of contents and container:

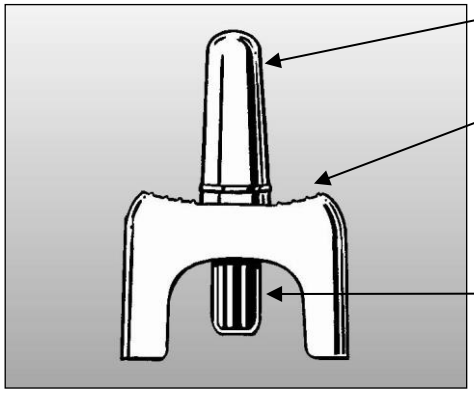
The nasal spray comprises a vial made of Ph.Eur. Type I glass sealed with a rubber stopper, fitted into a cup held with the actuation device. IMIGRAN 20 mg nasal spray are individually blister packed (a clear polymer laminate and paper lidding) and then cartoned in packs of one or two.

6.6 Special precautions for disposal and other handling:

Use and handling:

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

IMIGRAN nasal spray has the following parts:



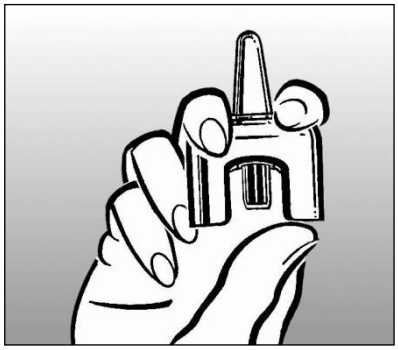
The nozzle
The part that you put into your nostril.
The spray comes out of a tiny hole in the top.

The finger-grip
Hold this when you use the spray

The blue plunger
Press this to spray the whole dose into your nostril in one go.
This only works once - **don't press the plunger until you have put the nozzle into your nostril** or you will lose the dose.

How to use the nasal spray:

1. Remove the nasal spray from the blister packaging just before you want to use it.
2. Get into a comfortable position. You may prefer to sit down.
3. Blow your nose if it feels blocked, or if you have a cold.
4. Hold the nasal spray gently with your fingers and thumb as shown in picture A. Don't press the blue plunger yet.



Picture A

5. Block one nostril by pressing a finger firmly on the side of your nose. It doesn't matter which nostril you choose.


Picture B

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

   Breathe out gently through your mouth.

   Hold your head upright and close your mouth.


Picture C

7. Start to breathe in gently through your nose.

   As you breathe in:

   Press the blue plunger firmly with your thumb.

   The plunger may feel a bit stiff and you may feel it click. Keep breathing in while spraying (picture C).

8. Remove the spray and remove your finger from the side of your nose.

   Keep your head upright for 10-20 seconds, breathing gently in through your nose and out through your mouth. This helps the medicine stay in your nose.

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

9. Your nasal spray is now empty. Throw it away safely and hygienically.

7. HOLDER OF CERTIFICATE OF REGISTRATION:

GlaxoSmithKline South Africa (Pty) Ltd

39 Hawkins Avenue

Epping Industria 1, 7460

8. REGISTRATION NUMBER:

31/7.3/0197

9. DATE OF FIRST AUTHORISATION/RENEWAL OF AUTHORISATION:

31 March 2006

10. DATE OF REVISION OF TEXT:

05 August 2022