NEW ZEALAND DATA SHEET

SUMAGRAN ACTIVE

1. Product Name

SUMAGRAN ACTIVE, 50 mg, film-coated tablet.

2. Qualitative and Quantitative Composition

Each film-coated tablet contains 50 mg of sumatriptan (as succinate)

Excipient(s) with known effect:

SUMAGRAN ACTIVE tablets contain lactose.

For the full list of excipients, see section 6.1.

3. Pharmaceutical Form

A pink, round, film-coated tablet debossed ‘SU50’ on one side and a ‘G’ on the other.

4. Clinical Particulars

4.1 Therapeutic indications

SUMAGRAN ACTIVE tablets are indicated for the acute treatment of migraine attacks, with or without aura.

SUMAGRAN ACTIVE tablets relieve migraine headache and the associated symptoms of nausea and sensitivity to light and sound.

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

4.2 Dose 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 SUMAGRAN ACTIVE be given as early as possible after the onset of a migraine headache although it is also effective if taken at a later stage of the migraine headache.

If there is no response to the first tablet, a second dose should not be taken for the same attack. SUMAGRAN ACTIVE may be taken for subsequent attacks.

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.

Special populations

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 sumatriptan in children has not yet been established.

Elderly (over 65 years of age)

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

Experience of the use of sumatriptan in patients aged over 65 years is limited.

4.3 Contraindications

SUMAGRAN ACTIVE tablets must not be used prophylactically.

Hypersensitivity to any component of the preparation listed in section 6.1 or to sulphonamides.

Sumatriptan should not be given to patients who have had a myocardial infarction, or have ischaemic heart disease (IHD), Prinzmetal's angina / coronary vasospasm, cardiac arrhythmias, peripheral vascular disease or patients who have symptoms or signs consistent with IHD.

Sumatriptan should not be administered to patients with a history of previous cerebrovascular accident (CVA / stroke) or transient ischaemic attack (TIA / mini-stroke).

The use of sumatriptan in patients with uncontrolled hypertension is contraindicated.

Sumatriptan should not be administered to patients with hepatic or renal impairment.

Sumatriptan should not be used in patients with a history of seizures or other risk factors that lower the seizure threshold.

The concurrent treatment with the following medications is contraindicated:

- Ergotamine or derivatives of ergotamine (including methysergide) (see section 4.5). SUMAGRAN ACTIVE treatment should not be used within 24 hours of treatment with an ergotamine containing or ergot-type medication.
- Monoamine oxidase inhibitors (MAOIs). SUMAGRAN ACTIVE must not be used within 2 weeks of discontinuation of therapy with monoamine oxidase inhibitors.
- Any 5-HT_1 receptor agonist (triptan).

SUMAGRAN ACTIVE 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 uncoordinated movements, tinnitus, reduced level of consciousness.
- Opthalmoplegic migraine – migraine headache with involvement of one or more ocular cranial nerves resulting in weakness of the muscles controlling eye movement.

4.4 Special warnings and precautions for use

SUMAGRAN ACTIVE tablets 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).

SUMAGRAN ACTIVE should not be taken concomitantly with other migraine therapies containing any triptan, ergotamine or derivatives of ergotamine.

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

The recommended dose of SUMAGRAN ACTIVE 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 uncoordinated 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 increased 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 section 4.8). 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 SUMAGRAN ACTIVE should be taken until considered appropriate by a doctor.

Sumatriptan should not be used by migraineurs in whom unrecognised cardiac disease is likely without a prior risk assessment by a doctor or pharmacist (see section 4.3). 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 every patient who has cardiac disease and, in very rare cases, serious cardiac events have occurred in patients 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) with 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.

Reversible cerebral vasoconstriction syndrome (thunderclap headache) has been associated with serotonergic agents such as SSRIs or triptans.

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 sulfonamides 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 SUMAGRAN ACTIVE is contraindicated in these patients (see section 4.3).

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

Prolonged use of any type of painkillers for headaches can make it worse. If this situation is experienced or suspected, medical advice should be obtained and treatment should be discontinued. The diagnosis of Medication Overuse Headache (MOH) should be suspected in patients who have frequent or daily headaches despite (or because of) regular use of headache medications.

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

4.5 Interaction with other medicines and other forms of interaction

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

An interaction may occur between sumatriptan and MAOIs and concomitant administration is contraindicated (see section 4.3).

There are limited data on an interaction with preparations containing ergotamine or another triptan/5-HT_1 receptor agonist. The increased risk of coronary vasospasm is a theoretical possibility and concomitant administration is contraindicated (see section 4.3).

The period of time that should elapse between the use of sumatriptan and ergotamine-containing preparations or another triptan/5-HT_1 receptor agonist is not known. This will also depend on the doses and types of products used. The effects may be additive. It is advised to wait at least 24 hours following the use of ergotamine-containing preparations or another triptan/5-HT_1 receptor agonist before administering sumatriptan. Conversely, it is advised to wait at least 6 hours following use of sumatriptan before administering an ergotamine-containing product and at least 24 hours before administering another triptan/5-HT_1 receptor agonist.

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 section 4.4). There is a risk of pharmacodynamic interaction between sumatriptan and tricyclic antidepressants.

4.6 Fertility, pregnancy and lactation

Pregnancy

Pregnancy category B3.

SUMAGRAN ACTIVE is not to be used in pregnancy or when breastfeeding unless on the advice of the 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 post-natal development. However, embryofoetal viability might be affected in the rabbit (see section 5.3).

Breast-feeding

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.

Fertility

No data available. For pre-clinical fertility data refer to section 5.3.

4.7 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, e.g. driving or operating machinery.

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 (>1/1000, <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 disturbances 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.
Nystagmus, tremor, dystonia, 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 section 4.3 and 4.4).

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

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.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions https://nzphvc.otago.ac.nz/reporting/.

4.9 Overdose

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

There have been some reports of overdosage with sumatriptan. Doses in excess of 400 mg orally were not associated with side effects other than those mentioned in section 4.8.

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.

For further advice on management of overdose please contact the National Poisons Information Centre (0800 POISON or 0800 764 766).

5. Pharmacological Properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Analgesics, selective 5-HT_1 receptor agonists. ATC code: N02CC01

Mechanism of action

Sumatriptan has been demonstrated to be a specific and selective vascular 5-hydroxytryptamine-1 (5-$HT_{1B/D}$) receptor agonist with no effect on other 5-HT receptor (5-HT_2 – 5-HT_7) 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 and/or oedema formation in these vessels is thought to be the underlying mechanism of migraine in humans.

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 migraine headache and the associated symptoms 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.

5.2 Pharmacokinetic properties

The pharmacokinetics of oral sumatriptan do not appear to be significantly affected by migraine attacks.

Absorption

After 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 nanograms/mL.

Mean absolute oral bioavailability is 14% partly due to pre-systemic metabolism and partly due to incomplete absorption. Oral absorption of Sumatriptan is not significantly affected by food.

Distribution

Plasma protein binding is low (14 - 21%); the mean total volume of distribution is 170 litres.

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 5-HT_1 or 5-HT_2 activity. Minor metabolites have not been identified.

Elimination

The elimination 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.

5.3 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, embryo lethality, without marked teratogenic defects, was seen. The relevance for humans of these findings is unknown.

6. Pharmaceutical Particulars

6.1 List of excipients

SUMAGRAN ACTIVE 50 mg tablets contain sumatriptan succinate 70 mg (equivalent to sumatriptan 50 mg). The tablets also contain:

- lactose monohydrate
- microcrystalline cellulose
- croscarmellose sodium
- magnesium stearate
- titanium dioxide
- polydextrose
- hypromellose
- glycerol triacetate
- polyethylene glycol
- iron oxide red
- iron oxide yellow.

SUMAGRAN ACTIVE is gluten free.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

4 years.

6.4 Special precautions for storage

Store at or below 25°C.

6.5 Nature and contents of container

Blister pack, Alu/Alu. Pack-size of 2 film-coated tablets.

6.6 Special precautions for disposal

Not applicable.

7. Medicines Schedule

Restricted Medicine

8. Sponsor Details

Mylan New Zealand Ltd
PO Box 11183
Ellerslie
AUCKLAND
Telephone 09-579-2792
Freephone: 0800 168 169

9. Date of First Approval

26 April 2007

10. Date of Revision of the Text

27 August 2018

Summary table of changes

Section	Summary of new information
-	Revise to SPC format