DATA SHEET

SUMATRIPTAN

Sumatriptan Succinate immediate release tablets 50 mg and 100 mg

Qualitative and quantitative composition

Sumatriptan tablets are presented as;

Sumatriptan tablets (50 mg)
Pink colored, capsule shaped, biconvex, film coated tablet plain on both sides.
Each film-coated tablet contains Sumatriptan succinate equivalent to 50 mg Sumatriptan.

Sumatriptan tablets (100 mg)
White to off white, capsule shaped, biconvex, film coated tablet plain on both sides.
Each film-coated tablet contains Sumatriptan succinate equivalent to 100 mg Sumatriptan.

Sumatriptan immediate release tablets containing sumatriptan (as the succinate salt) as active ingredient.

Sumatriptan immediate release tablets also contain lactose, microcrystalline cellulose, croscarmellose sodium, hypromellose and magnesium stearate as excipients. The 50 mg tablets also contain OPADRY complete film coating system 03K54036 PINK. The 100 mg tablets also contain OPADRY complete film coating system 03A58900 WHITE.

Sumatriptan-AP tablets are presented in blister pack in cartons.

Pharmaceutical form

Tablets

Clinical particulars

Therapeutic Indications
Sumatriptan tablets are indicated for the acute relief of migraine attacks with or without aura.

Posology and Method of Administration

Sumatriptan tablets should not be used prophylactically.

It is advisable that Sumatriptan tablets 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 recommended adult dose of oral Sumatriptan tablets is a single 50mg tablet. Some patients may require 100mg.

If a patient does not respond to the first dose of Sumatriptan tablets, a second dose should not be taken for the same attack. Sumatriptan tablets 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 300mg is taken in any 24 hour period.

The tablets should be swallowed whole with water.

Children:-
The safety and effectiveness of sumatriptan in children has not yet been established.

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.

Contraindications

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 previous 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

Sumatriptan 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 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 serotonin syndrome (including altered mental status, autonomic instability, 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/SNRI is clinically warranted, appropriate observation of the patient is advised (see Interaction with Other Medicaments and Other Forms of Interaction).
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 medicine, eg. impaired hepatic or renal function.
Sumatriptan should be used with caution in patients with a history of seizures or other risk factors which lower the seizure 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.

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.

The recommended dose of Sumatriptan tablets should not be exceeded.

Pregnancy and Lactation

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.

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.

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.

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.

Interaction with other medicaments and other forms of interaction

There is no evidence of interactions with propanolol, 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 contraindicated (see Contraindications). Rarely an interaction may occur between sumatriptan and SSRIs (see Special Warnings and Special Precautions for Use).

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).

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. The data from clinical trials are estimates. 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.

Respiratory, Thoracic and Mediastinal Disorders

Common:	Dyspnoea.
Gastrointestinal Disorders	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 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

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 (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 Contraindications, Warnings and Precautions).

Vascular disorders

Very rare:	Hypotension, Raynaud's phenomenon.

Gastrointestinal Disorders

Very rare:	Ischaemic colitis.

Overdose

Doses in excess of 16mg subcutaneously and 400mg orally were not associated with side effects other than those mentioned. Patients have received single injections of up to 12mg subcutaneously 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-($5HT_1D$) receptor agonist with no effect at other 5HT receptor ($5HT_2$ -$5HT_7$) subtypes. The vascular $5HT_1D$ 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 antimigraine action of sumatriptan in humans.

Clinical response begins 10-15 minutes following a 6mg subcutaneous injection, and around 30 minutes following a 100mg oral dose.

Although the recommended dose of oral Sumatriptan tablets is 50mg, migraine attacks vary in severity both within and between patients. Doses of 25-100mg have shown greater efficacy than placebo in clinical trials, but 25mg is statistically significantly less effective than 50 and 100mg.

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 100mg dose the mean maximum plasma concentration is 54ng/mL.

Mean absolute oral bioavailability is 14% partly due to pre-systemic metabolism and partly due to incomplete absorption.

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

Elimination

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.

Special patient populations

Hepatic impairment

Following oral administration, pre-systemic clearance is reduced in patients with hepatic impairment resulting in increased plasma levels of sumatriptan.

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 100mg 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 particulars

Incompatibilities

None reported.

Shelf Life

3 years

Special Precautions for Storage

Store below 25ºC

Package Quantities

Sumatriptan tablets are packed in blister packs in cartons.

Sumatriptan tablets 50 mg is available in packs containing 2 and 4 tablets in foil blisters. Sumatriptan tablets 100 mg is available in packs containing 2 tablets in foil blisters.

Further Information

Nil.

Medicine classification

Prescription Only Medicine

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DATE OF PREPARATION

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