

SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Migraitan 50mg Film-coated Tablets

Sumibril 50mg Film-coated Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each film-coated tablet contains Sumatriptan succinate equivalent to 50mg sumatriptan

Excipient with known effect: Each tablet contains 22mg lactose monohydrate. For the full list of excipients, see Section 6.1.

3. PHARMACEUTICAL FORM

Film-coated tablet (Tablet)

Peach coloured, capsule shaped (about 10.5mm X 4.3mm), biconvex film coated tablets (tablets) with BL embossing on one side and plain on the other.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

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

4.2 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 Sumibril/Migraitan 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 100mg) 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

Paediatric population

The efficacy and safety of sumatriptan (film-coated) tablets/dispersible tablets in children aged less than 10 years have not been established. No clinical data are available in this age group.

The efficacy and safety of sumatriptan (film-coated) tablets/dispersible tablets in children 10 to 17 years of age have not been demonstrated in the clinical trials performed in this age group. Therefore the use of Sumatriptan (film-coated) tablets/dispersible tablets in children 10 to 17 years of age is not recommended (see section 5.1).

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

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1

Sumibril/Migraitan must not be used prophylactically.

- 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 Section 4.5)
- Monoamine oxidase inhibitors (MAOIs). Sumibril/Migraitan must not be used within 2 weeks of discontinuation of therapy with MAOIs.

- Any 5-HT₁ receptor agonist (triptan).

Sumibril/Migraitan 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

4.4 Special warnings and precautions for use

Sumibril/Migraitan 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).

Sumibril/Migraitan 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 Sumibril/Migraitan, the attack may be treated with simple analgesics. Further, the diagnosis of migraine should be reconsidered with a doctor.

The recommended dose of Sumibril/Migraitan 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 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 Sumibril/Migraitan should be taken until considered appropriate by a doctor.

Sumibril/Migraitan 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 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 Sumibril/Migraitan is contraindicated in these patients (see Section 4.3)

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.

Prolonged use of any type of painkiller for headaches can make them 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) the regular use of headache medication. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine.

4.5 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.

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-HT₁ receptor agonist. The increased risk of coronary vasospasm is a theoretical possibility and therefore concomitant administration is contra-indicated (see Section 4.3, Contra-indications).

The period of time that should elapse between the use of sumatriptan and ergotamine-containing preparations or another triptan/5-HT₁ 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-HT₁ 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-HT₁ 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 pharmacodynamics interaction between sumatriptan and tricyclic anti-depressants.

4.6 Fertility, pregnancy and lactation

Pregnancy

Sumibril/Migratan is not 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, embryo-fetal viability might be affected in the rabbit (see Section 5.3).

Lactation

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.

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 when skilled tasks are to be performed 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 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 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 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.

Reporting of Suspected Adverse Reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the Yellow Card Scheme at:

www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

4.9 Overdose

Symptoms and Signs

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

There have been some reports of over dosage with Sumatriptan. Doses in excess of 400 mg orally were not associated with side effects other than those mentioned in Section 4.8

Treatment

If over dosage 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 Sumatriptan.

5 PHARMACOLOGICAL PROPERTIES

5.1 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.

A number of placebo-controlled clinical studies assessed the safety and efficacy of oral sumatriptan in approximately 800 children and adolescent migraineurs aged 10-17 years. These studies failed to demonstrate relevant differences in headache relief at 2 hours between placebo and any sumatriptan dose. The undesirable effects profile of oral sumatriptan in adolescents aged 10-17 years was similar to that reported from studies in the adult population.

5.2 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.

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 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

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

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Lactose monohydrate
Microcrystalline cellulose

Pregelatinised starch
Croscarmellose sodium
Magnesium stearate
Hypromellose
Titanium dioxide E171
Purified talc
Macrogol
Iron oxide red E172
Iron oxide yellow E172

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

4 years

6.4 Special precautions for storage

This medicinal product does not require any special storage conditions.

6.5 Nature and contents of container

Alu / Alu blister packs, pack size of 2 ,6, 12 and 18 tablets.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

None

7 MARKETING AUTHORISATION HOLDER

Bristol Laboratories Limited
Unit 3, Canal side, Northbridge Road,
Berkhamsted, Herts, HP4 1EG.
United Kingdom.

8 MARKETING AUTHORISATION NUMBER(S)

PL 17907/0240

**9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE
AUTHORISATION**

08/05/2009

10 DATE OF REVISION OF THE TEXT

21/06/2018