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

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

4.2 Posology and method of administration

General recommendations with regard to use and administration:
Sumatriptan should not be use prophylactically.

Sumatriptan is recommended as monotherapy for the acute treatment of a migrane attack should not be given concomitantly with ergotamine or derivatives of ergotamine (including methysergide) (see section 4.3)

It is advisable that sumatriptan be given as early as possible after the onset of a migrane headache. It is equally effective at whatever stage of the attack it is administered.

Adults (18-65 years of age)
The recommended dose is a single 50 mg tablet that should be swallowed whole with water. Some patients may require 100mg.
If there is no response to the first tablet, a second tablet should not be taken for the same attack. In these cases the attack can be treated with paracetamol, acetylsalicylic acid, or

non-steroidal anti-inflammatory drugs. Sumatriptan tablets 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 in the next 24 hours. However, this must be at least 2 hours after the first tablet. No more than 300mg should be taken in any 24 hour period.

Paediatric population

The efficacy and safety of sumatriptan 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 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 tablets in children 10 to 17 years of age is not recommended (see section 5.1).

Elderly (over 65 years of age)
Experience of the use of sumatriptan tablets in patients aged over 65 years is limited. Te 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.

Hepatic impairment
Patients with mild to moderate hepatic impairment: low doses of 25-50mg should be considered for these patients.

Renal impairment
Sumatriptan should be used with caution in patients with renal impairment

4.3 Contraindications

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

Previous myocardial infarction, or those who have ischaemic heart disease, coronary vasospasm (Prinzmetal's angina),peripheral vascular disease or
symptoms or signs consistent with ischaemic heart disease.

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

The use of Sumatriptan in patients with moderate and severe hypertension and mild uncontrolled hypertension is contraindicated.

Sumatriptan should not be administered to patients with severe hepatic impairment.
The concomitant administration of ergotamine, or ergotamine derivatives (including methysergide) or any triptan/5-hydroxytryptamine1 (5-HT1) receptor agonist is contraindicated (see section 4.5)

Concurrent administration of reversible (e.g moclobemide) or irreversible (e.g. selegiline) monoamine oxidase inhibitors (MAOIs) and sumatriptan is contraindicated.

Sumatriptan must not be used within 2 weeks of discontinuation of therapy with monoamine oxidase inhibitors.

4.4. Special warnings and precautions for use

Sumatriptan should only be used where a clear diagnosis of migraine
Sumatriptan is not indicated for use in the management of hemiplegic, basilar or ophthalmoplegic migrane.

As with other acute migrane 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 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, which may be intense and involve the throat (see section 4.8).

Where such symptoms are thought to indicate ischaemic heart disease, no further doses of sumatriptan should be given and appropriate medical evaluation should be carried out. 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).

There have been rare postmarketing 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.

Sumatriptan should be administered with caution to patients with conditions that may affect significantly the absorption, metabolism, or excretion of the drug, e.g. 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, as seizures have been reported in association with sumatriptan (see section 4.8).

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 Sumatriptan is contraindicated in these patients (see Section 4.3).

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 medications.

Sumatriptan should not be given to patients with risk factors for ischaemic heart disease, including patients with diabetes and patients who are heavy smokers or users of nicotine substitution therapies, without prior cardiovascular evaluation (see section 4.3). Special consideration should be given to postmenopausal women and males over 40 with these risk factors. These evaluations however, 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.

In rare cases, asthenia, hyperreflexia and incoordination have been described in post-marketing reports following use of a selective serotonin reuptake inhibitor (SSRI) and sumatriptan.

The recommended dose of sumatriptan should not be exceeded.

Sumatiptan Tablets contain Lactose. 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 medicinal products and other forms of interaction

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

Sumatriptan has the potential to interact with MAOIs, ergotamine and derivatives of Ergotamine.
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 with MAOIs and ergotamines 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.
An interaction may occur between sumatriptan and MAOIs and concomitant administration is contraindicated (see section 4.3).

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

4.6. Fertility, Pregnancy and lactation

Pregnancy

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). Administration of sumatriptan should only be considered if the expected benefits to the mother is greater than any possible risk to the fetus.

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

No studies on the effects on the ability to drive and use machines have been performed. Drowsiness may occur as a result of migraine or its treatment with sumatriptan.

This may influence the ability to drive and operate 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) , not known (cannot be estimated from the available data).).
Some of the symptoms reported as undesirable effects may be associated symptoms of migraine.

Immune System Disorders	
Not known:	Hypersensitivity reactions ranging from cutaneous hypersensitivity to anaphylaxis.
Nervous System Disorders	
Common:	Dizziness, drowsiness, sensory disturbance including paraesthesia and hypoaesthesia.
Not known:	Seizures, although some have occurred in patients with either a history of seizures or concurrent conditions predisposing to seizures there arealso reports in patients where no such predisposing factors are apparent; Tremor, dystonia, nystagmus, scotoma.
Eye Disorders	
Not known:	Flickering, diplopia, reduced vision. Loss of vision (usually transient). However, visual disorders may also occur during a migraine attack itself.
Cardiac Disorders	
Not known:	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.
Not known:	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.
Not known:	Ischaemic colitis. Diarrhoea

Musculoskeletal, Connective Tissue and Bone Disorders

Common:	Sensations of heaviness (The following symptom is usually transient and may be intense and can affect any part of the body including the chest and throat). Myalgia
Not known:	Neck stiffness. Arthralgia

General Disorders and Administration Site Conditions

Common:	Pain, sensations of heat or cold, pressure or tightness (The following symptoms are usually transient and may be intense and can affect any part of the body including the chest and throat). Feelings of weakness, fatigue (The following symptoms are mostly mild to moderate in intensity and transient).
Uncommon:	Somnolence (Mostly mild to moderate in intensity and transient)

Investigations

Very rare:	Minor disturbances in liver function tests have occasionally been observed.

Psychiatric disorders

Not known:	Anxiety

Skin and subcutaneous tissue disorders

Not known:	Hyperhidrosis

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.

4.9 Overdose

Symptoms and Signs

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 and 16mg subcutaneously were not associated with side effects other than those mentioned in Section 4.8.

Treatment
If overdosage 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-HT1B/D) receptor agonist with no effect on other 5-HT receptor (5-HT2-5-HT7) subtypes. The vascular 5-HT1B 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 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-HT_1 or 5-HT_2 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, a reduction in the success of insemination was seen on exposure to concentrations higher than the maximum exposure in humans. In rabbits embryolethality was observed, without marked teratogenic effects.

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 and 6 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

20/02/2015