

SUMATRIPTAN 50MG TABLETS (PL 18866/0039, 0042 and 0045)
SUMATRIPTAN 100MG TABLETS (PL 18866/0040, 0043 and 0046)

UKPAR

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SUMATRIPTAN 50MG TABLETS (PL 18866/0039, 42 and 45)
SUMATRIPTAN 100MG TABLETS (PL 18866/0040, 43 and 46)

LAY SUMMARY

On 14th September 2007, the MHRA granted Rockspring Healthcare Limited (licences) for the medicinal products Sumatriptan 50mg and 100mg Tablets and duplicates (PL 18866/0039, 40, 42, 43, 45 and 46). These are prescription only medicines (POM) that are used for the treatment of migraine.

The symptoms of migraine, which are thought to be due to temporary swelling of blood vessels in the head, may include aura (warning sensations of visual distortion such as flashes of light and zigzag lines or waves). Medicines like Sumatriptan Tablets are believed to work by reducing the size of these blood vessels. These medicines are called 5HT₁ receptor agonists.

No new or unexpected safety concerns arose from these applications and it was therefore judged that the benefits of taking Sumatriptan 50mg and 100mg Tablets outweigh the risks, hence Marketing Authorisations have been granted.

SUMATRIPTAN 50MG TABLETS (PL 18866/0039, 42 and 45)
SUMATRIPTAN 100MG TABLETS (PL 18866/0040, 43 and 46)

SCIENTIFIC DISCUSSION

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INTRODUCTION

Based on the review of the data on quality, safety and efficacy the UK granted marketing authorisations for the medicinal products Sumatriptan 50mg and 100mg Tablets and duplicates to Rockspring Healthcare Limited (PL 18866/0039, 40, 42, 43, 45 and 46) on 14 September 2007. The products are prescription-only medicines.

The applications were submitted as abridged applications according to Article 10.1 of Directive 2001/83/EC, as amended, claiming essential similarity to the original products Imigran 50 and 100 mg Tablets (PL 10949/0222 and 0231), which have been authorised to GlaxoSmithKline in the UK since June 1994.

The products contain the active ingredient sumatriptan succinate and are indicated for the acute relief of migraine attacks, with or without aura. Sumatriptan Tablets should only be used where there is a clear diagnosis of migraine.

Sumatriptan is a vascular 5-HT₁ receptor agonist. The specific subtype receptor it activates is present in the cranial and basilar arteries. Activation of these receptors causes vasoconstriction of the dilated arteries. Sumatriptan has also been shown to reduce the activity of the trigeminal nerve, which accounts for its efficacy in treating cluster headaches.

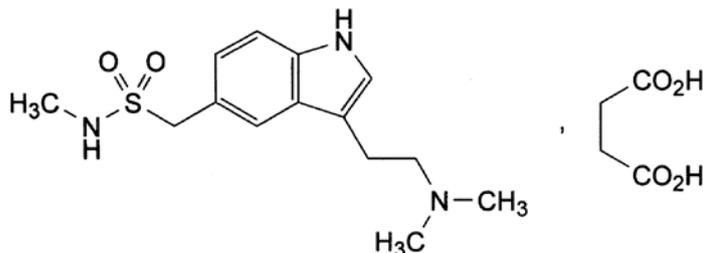
PHARMACEUTICAL ASSESSMENT

Active Substance

INN/Ph.Eur name: Sumatriptan succinate

Chemical name: [3-[2-(Dimethylamino)ethyl]-1*H*-indol-5-yl]-*N*-methylmethanesulphonamide hydrogen butanedioate.

Structural formula



Molecular formula: C₁₈H₂₇N₃O₆S

Molecular weight: 413.5

Polymorphism: There is no evidence of polymorphism.

Chirality: There are no chiral centres present so there is no potential for stereoisomerism.

General Properties

Characters: White to almost white powder, freely soluble in methanol, sparingly soluble in water and methylene chloride.

Solubility: Freely soluble in water, sparingly soluble in methanol, practically insoluble in methylene chloride.

Melting point: 165-167°C.

pH (5% in water): 4.5-5.3

Sumatriptan succinate is the subject of a European Pharmacopoeia monograph.

A Certificate of Suitability has been provided covering the manufacture and control of the drug substance sumatriptan succinate.

Appropriate stability data have been generated showing the active substance to be a physically and chemically stable drug. The data support a retest period of 36 months.

Other Ingredients

Other ingredients consist of pharmaceutical excipients lactose monohydrate, croscarmellose sodium, lactose anhydrous, microcrystalline cellulose, magnesium stearate, water purified, mannitol, titanium dioxide, talc and glycerol triacetate.

All excipients have a respective European Pharmacopoeia monograph.

Satisfactory certificates of analysis have been provided for all ingredients showing compliance with their respective monograph.

Lactose anhydrous and lactose monohydrate are the only ingredients that come from an animal source. The lactose used to produce both is sourced from healthy animals under the same conditions as milk for human consumption.

Pharmaceutical development

The objective of the pharmaceutical development programme was to produce products containing 50mg and 100mg sumatriptan that are tolerable and which could be considered as generic products to the originator products Imigran 50 and 100 mg Tablets.

The rationale for the type of pharmaceutical form developed and formulation variables evaluated during development have been stated and are satisfactory.

The rationale and function of each excipient added is discussed. Levels of each ingredient are typical for a product of this nature and have been optimised on the basis of results from development studies.

Comparative *in vitro* dissolution profiles have been generated for the proposed and originator products with satisfactory results. Comparative impurity studies have also been undertaken.

Manufacturing Process

Satisfactory batch formulae have been provided for the manufacture of both strengths of product, along with an appropriate account of the manufacturing process. The manufacturing process has been validated and has shown satisfactory results at pilot-scale. Additionally, a commitment has been provided that the first full-scale commercial production batches will be validated.

Finished Product Specification

The finished product specifications proposed for both strengths are acceptable. Test methods have been described and have been adequately validated, as appropriate. Batch data have been provided and comply with the release specification. Certificates of analysis have been provided for any working standards used.

Container-Closure System

All strengths of tablet are packaged in either:

1. Polyvinylchloride/aluminium blister strips in pack sizes of 2, 3, 6, 7, 12, 14, 18, 21, 24, 28, 30, 50, 100, 250, 500 and 1000 tablets
2. High-density polyethylene bottle with a low-density polyethylene cap closure in pack sizes of 2, 3, 6, 7, 12, 14, 18, 21, 24, 28, 30, 50, 100, 250, 500 and 1000 tablets.

Satisfactory specifications and certificates of analysis have been provided for all packaging components. All primary packaging complies with the relevant regulations regarding materials for use in contact with food.

The applicant has stated that not all packaging will be marketed in the UK and has provided assurances that they will submit mock-ups before launching any packaging types into the market.

Stability of the product

Stability studies were performed on pilot-scale batches of all strengths of finished product and all packaging types, in accordance with current guidelines. All results from stability studies on pilot batches were within specified limits. These data support a shelf-life of 2 years for product stored in the blister strips and 3 years for product stored in the bottle, with no storage conditions.

The applicant has committed to providing stability data for the first three production-scale batches of each strength of finished product.

Bioequivalence/bioavailability

Satisfactory Certificates of Analysis have been provided for the test and reference batches used in the bioequivalence study.

SPC, PIL, Labels

The SPC, PIL and Labels are pharmaceutically acceptable.

CONCLUSION

It is recommended that Marketing Authorisations are granted for these applications.

The requirements for essential similarity of the proposed and reference products have been met with respect to qualitative and quantitative content of the active substance. In addition, similar dissolution profiles have been demonstrated for the proposed and reference products.

PRECLINICAL ASSESSMENT

These applications for generic products claims essential similarity to Imigran 50 and 100 mg Tablets (GlaxoSmithKline UK), which have been licensed within the EEA for over 10 years.

No new preclinical data have been supplied with these applications and none are required for an application of this type.

CLINICAL ASSESSMENT

1. INTRODUCTION AND BACKGROUND

These are a complex and a standard abridged national applications for Sumatriptan 50mg and 100mg Tablets submitted under Article 10.1 of Directive 2001/83/EC, as amended. The applications cross-refer to Imigran 50 and 100 mg Tablets (GlaxoSmithKline UK), which have been authorised in the EU for more than 10 years.

2. INDICATIONS

For the acute relief of migraine attacks, with or without aura. Sumatriptan Tablets should only be used where there is a clear diagnosis of migraine.

The indications proposed are consistent with those for the originator products and are, therefore, satisfactory.

3. DOSE & DOSE SCHEDULE

For oral use.

Adults:

Sumatriptan Tablets are indicated for the acute intermittent treatment of migraine. Sumatriptan should not be used prophylactically.

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

The recommended dose is a single 50mg tablet. Some patients may require 100mg. 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 and no more than 300mg is taken in any 24 hour period.

Patients who do not respond to the prescribed dose of sumatriptan should not take a second dose for the same attack. Sumatriptan may be taken for subsequent attacks.

Sumatriptan is recommended as monotherapy for the acute treatment of migraine and should not be given concomitantly with other acute migraine therapies. If a patient fails to respond to a single dose of Sumatriptan Tablets there are no reasons, either on theoretical grounds or from limited clinical experience, to withhold products containing aspirin or non-steroidal anti-inflammatory drugs for further treatment of the attack.

The tablets should be swallowed whole with water.

Children (under 18 years of age):

Sumatriptan tablets have not been studied in children under 12 years of age. The available clinical trial data in adolescents (12 to 17 years of age) do not support the use of oral sumatriptan in this age group (see section 5.1). The use of sumatriptan tablets in children and adolescents is therefore not recommended.

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 Tablets in patients aged over 65 years is not recommended

The dose and dose schedule proposed are consistent with those for the originator products and are, therefore, satisfactory.

4. CLINICAL PHARMACOLOGY

With the exception of the bioequivalence study comparing the proposed product to Imigran 100mg Tablets, no formal data are provided and none are required for these applications.

4.1 Bioequivalence

A bioequivalence study was carried out, and the test and reference products shown to be bioequivalent (within the customary 90% confidence intervals) for the appropriate pharmacokinetic criteria.

Design:

Single dose, randomised, cross-over, open-label, laboratory-blind study

Test Product: Sumatriptan 100mg tablets

Reference Product: Imigran 100 mg tablets (GlaxoSmithKline UK)

Subjects: 32 finished the study – 18-55yrs, male and female

Washout: 2 weeks

Sampling: 0, 0.166, 0.33, 0.5, 0.75, 1.0, 1.25, 1.75, 2.0, 2.5, 3.0, 3.5, 4.0, 4.5, 5.0, 6.0, 7.0, 8.0, 10.0 and 12 hrs post dose.

Parameters: primary were C_{max} , $AUC_{0-t_{last}}$ and $AUC_{0-\infty}$; secondary were T_{max} and $T_{1/2}$.

Results:

	C_{max} (ng/mL)	$AUC_{0-t_{last}}$ (ng.h/mL)	$AUC_{0-\infty}$ (ng.h/mL)	T_{max} (hrs)	$T_{1/2}$ (hrs)
Sumatriptan 100mg [Test]	54.8 ± 17.4	231 ± 56.7	243 ± 59.4.	1.88	2.54 ± 0.60
Imigran 100mg [Ref]	52.1 ± 12.3	226 ± 58.3	236 ± 60.0	1.25	2.35 ± 0.52
Point Estimate	105%	102%	103%	0.13%	108%
Ratio 90% CI	98.0; 113	96.6; 108	97.0; 109	-0.25; 0.63	103; 113

Conclusion: The extent and rates of absorption, time to T_{max} and $t_{1/2}$ exhibited indicate that two products may be assumed bioequivalent in terms of the customary confidence intervals.

As the two strengths of the proposed product are dose proportional qualitatively and quantitatively, the results of 100mg tablet can be considered applicable to the 50mg tablet.

5. EFFICACY

No new data on the efficacy of sumatriptan are submitted and none are required for this type of application.

6. SAFETY

No new data on the safety of sumatriptan are submitted and none are required for this type of application.

7. EXPERT REPORTS

A clinical expert report is provided, written by an appropriately qualified Doctor. It includes a suitable review of the bioequivalence study.

8. SUMMARY OF PRODUCT CHARACTERISTICS (SPC)

The SPCs are consistent with the approved SPCs for the originator products Imigran 50 and 100 mg Tablets and are satisfactory.

9. PATIENT INFORMATION LEAFLET (PIL)

The PIL has been provided and is consistent the SPC.

10. LABELLING

Labelling text for all strengths are satisfactory. Mock-ups of labelling intended for marketing are satisfactory and comply with current regulations.

The applicant has stated that not all proposed pack sizes will be marketed initially, but has provided assurances that mock-ups will be submitted for assessment before any further pack sizes are marketed.

11. MARKETING AUTHORISATION APPLICATION (MAA) FORMS

The MAA forms are satisfactory.

12. DISCUSSION

Bioequivalence has been satisfactorily demonstrated for the 100mg product in accordance with CPMP criteria. As these products meet all the criteria as specified in the Note for Guidance on the investigation of bioavailability and bioequivalence (CPMP/EWP/QWP/1401/98), the results and conclusions of the bioequivalence study on the 100mg strength can be extrapolated to the 50mg strength tablets.

The SPC and PIL are consistent with those approved in the UK for the originator product Imigran 50 and 100 mg Tablets and are satisfactory.

13. MEDICAL CONCLUSION

Marketing authorisations may be granted for these products.

OVERALL CONCLUSION AND RISK BENEFIT ASSESSMENT

QUALITY

The important quality characteristics of Sumatriptan 50mg and 100mg Tablets are well-defined and controlled. The specifications and batch analytical results indicate consistency from batch to batch. There are no outstanding quality issues that would have a negative impact on the benefit/risk balance.

PRECLINICAL

No new preclinical data were submitted and none are required for applications of this type.

EFFICACY

Bioequivalence has been demonstrated between the applicant's Sumatriptan 100mg Tablets and the originator products Imigran 100mg Tablets (GlaxoSmithKline UK). As these products meet all the criteria as specified in the Note for Guidance on the investigation of bioavailability and bioequivalence (CPMP/EWP/QWP/1401/98), the results and conclusions of the bioequivalence study on the 100mg strength can be extrapolated to the 50mg strength tablets.

No new or unexpected safety concerns arise from these applications.

The SPC, PIL and labelling are satisfactory and consistent with that for Imigran Tablets.

RISK BENEFIT ASSESSMENT

The quality of the product is acceptable and no new preclinical or clinical safety concerns have been identified. The bioequivalence study supports the claim that the applicant's products and the innovator products are interchangeable. Extensive clinical experience with sumatriptan is considered to have demonstrated the therapeutic value of the compound. The risk benefit is, therefore, considered to be positive.

SUMATRIPTAN 50MG TABLETS (PL 18866/0039, 42 and 45)
SUMATRIPTAN 100MG TABLETS (PL 18866/0040, 43 and 46)

STEPS TAKEN FOR ASSESMENT

1	The MHRA received the marketing authorisation applications on 6 th September 2004.
2	Following standard checks and communication with the applicant the MHRA considered the applications valid on 21 st September 2004.
3	Following assessment of the applications the MHRA requested further information relating to the clinical dossiers in 23 rd June 2005, 27 th July 2006, and further information relating to the quality dossiers on 25 th May 2005, 23 rd February 2006, 15 th May 2006 and 27 th July 2006.
4	The applicant responded to the MHRA's requests, providing further information on 28 th April 2006 and 12 th November 2006 for the clinical dossiers, and again on 25 th May 2005, 15 th May 2006, 5 th June 2006 and 12 th November 2006 for the quality dossiers.
5	The applications were determined on 14 th September 2007.

SUMATRIPTAN 50MG TABLETS (PL 18866/0039, 42 and 45)
SUMATRIPTAN 100MG TABLETS (PL 18866/0040, 43 and 46)

STEPS TAKEN AFTER AUTHORISATION - SUMMARY

Date submitted	Application type	Scope	Outcome

SUMMARY OF PRODUCT CHARACTERISTICS**1 NAME OF THE MEDICINAL PRODUCT**

Sumatriptan 50 mg Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 50 mg of sumatriptan as the succinate salt.

For full list of excipients, see section 6.1.

Contains lactose.

3 PHARMACEUTICAL FORM

Coated tablet.

White, oval, biconvex, 6.5x12.7mm coated tablets with score on both sides and side score, embossed with SN on one side and "50" on the other side.

4 CLINICAL PARTICULARS**4.1 Therapeutic indications**

Sumatriptan 50 mg Tablets are indicated for the acute relief of migraine attacks, with or without aura. Sumatriptan 50 mg Tablets should only be used where there is a clear diagnosis of migraine.

4.2 Posology and method of administration

For oral use.

Adults:

Sumatriptan 50 mg Tablets are indicated for the acute intermittent treatment of migraine. Sumatriptan should not be used prophylactically.

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

The recommended dose is a single 50mg tablet. Some patients may require 100mg. 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 and no more than 300mg is taken in any 24 hour period.

Patients who do not respond to the prescribed dose of sumatriptan should not take a second dose for the same attack. Sumatriptan may be taken for subsequent attacks.

Sumatriptan is recommended as monotherapy for the acute treatment of migraine and should not be given concomitantly with other acute migraine therapies. If a patient fails to respond to a single dose of Sumatriptan 50 mg Tablets there are no reasons, either on theoretical grounds or from limited clinical experience, to withhold products containing aspirin or non-steroidal anti-inflammatory drugs for further treatment of the attack.

The tablets should be swallowed whole with water.

Children (under 18 years of age):

Sumatriptan tablets have not been studied in children under 12 years of age. The available clinical trial data in adolescents (12 to 17 years of age) do not support the use of oral sumatriptan in this age group (see section 5.1). The use of sumatriptan tablets in children and adolescents is therefore not recommended.

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 50 mg Tablets in patients aged over 65 years is not recommended

4.3 Contraindications

Hypersensitivity to sumatriptan or to any of the excipients.

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

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

Sumatriptan should not be administered to patients with severe hepatic impairment.

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

The concomitant administration of ergotamine or derivatives of ergotamine (including methysergide) is contraindicated. (See interactions)

Concurrent administration of monoamine oxidase inhibitors and sumatriptan is contraindicated.

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

4.4 Special warnings and precautions for use

Sumatriptan 50 mg 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.

The recommended doses of sumatriptan should not be exceeded. As with other migraine therapies, before treating headaches in patients not previously diagnosed as migraineurs, and in migraineurs who present 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 Side effects). Where such symptoms are thought to indicate ischaemic heart disease, no further doses of sumatriptan should be given and appropriate evaluation should be carried out.

Sumatriptan should not be given to patients with risk factors for ischaemic heart disease without prior cardiovascular evaluation (See Section 4.3 Contraindications). 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.

There have been rare post-marketing reports describing patients with weakness, hyper-reflexia, and incoordination following the use of a selective serotonin reuptake inhibitor (SSRI) and sumatriptan. If concomitant treatment with sumatriptan and an SSRI is clinically warranted, appropriate observation of the patient is advised.

Sumatriptan should be administered with caution to patients with conditions which may affect significantly the absorption, metabolism or excretion of drugs, e.g. impaired hepatic or renal function. A 50mg dose should be considered in patients with hepatic impairment.

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).

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.

As with other acute migraine treatments, chronic daily headache/exacerbation of headache has been reported with overuse of sumatriptan, which may necessitate a drug withdrawal.

Patients with rare hereditary problems of fructose or galactose intolerance, Lapp 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. Sumatriptan has the potential to interact with MAOIs, ergotamine and derivatives of ergotamine. The

increased risk of coronary vasospasm is a theoretical possibility and concomitant administration is contra-indicated. (see also contraindications).

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.

As interaction may occur between sumatriptan and monoamine oxidase inhibitors and concomitant administration is contraindicated (see contraindications). Rarely, an interaction may occur between sumatriptan and SSRIs (see Special Warnings and special Precautions for Use).

Undesirable effects may be more common during concomitant use of triptans and herbal preparations containing St John's Wort (*Hypericum perforatum*).

4.6 **Pregnancy and lactation**

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 point to 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, embryofoetal viability might be affected in the rabbit (see section 5.3). Administration of sumatriptan should only be considered if the expected benefit to the mother is greater than any possible risk to the foetus.

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 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.

Clinical Trial Data

Nervous System Disorders

Common: Tingling, dizziness, drowsiness.

Vascular disorders

Common: Transient increases in blood pressure arising soon after treatment. Flushing.

Gastrointestinal

Common: Nausea and vomiting occurred in some patients but it is unclear if this is related to sumatriptan or the underlying condition.

Musculoskeletal and Connective Tissue Disorders

Common: Sensations of heaviness (usually transient and may be intense but can affect any part of the body including the chest and throat).

General Disorders and Administration Site Conditions

Common: Pain, sensations of heat, pressure or tightness (these events are usually transient but may be intense and can affect any part of the body including the chest and throat).

Common: Feelings of weakness, fatigue (both events are mostly mild to moderate in intensity and transient).

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 rare cases of 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.
Very rare: Tremor, dystonia, nystagmus, scotoma.

Eye disorders

Very rare: Flickering, diplopia, reduced vision, loss of vision including reports of permanent defects. 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, myocardial infarction (see Contraindications, Warnings and Precautions).

Vascular disorders

Very rare: Hypotension, Raynaud's phenomenon.

Gastrointestinal

Very rare: Ischaemic colitis

Musculoskeletal, connective tissue and bone disorders

Very rare: Neck stiffness.

4.9 Overdose

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

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.

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-Hydroxytryptamine₁ (5HT_{1D}) receptor agonist with no effect on other 5HT receptor (5-HT₂-5-HT₇) subtypes. The vascular 5-HT_{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 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 is 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 in an attack.

Clinical response begins around 30 minutes following a 100mg oral dose.

Although the recommended dose of oral sumatriptan 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.

Five placebo-controlled clinical studies assessed the safety and efficacy of oral sumatriptan in approximately 600 adolescent migraineurs aged 12 - 17 years. These studies failed to demonstrate a statistically significant difference in headache relief at 2 hours between placebo and any sumatriptan dose. The undesirable effects profile of oral sumatriptan in adolescents aged 12 - 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 100mg dose, the maximum plasma concentration is 54ng/ml. Mean absolute oral bioavailability is 14% partly due to presystemic metabolism and partly due to incomplete absorption. The elimination phase half-life is approximately 2 hours, although there is an indication of a longer terminal phase. Plasma protein binding is low (14-21%), mean volume of distribution is 170 litres. 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. 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 5HT1 or 5HT2 activity. Minor metabolites have not been identified. The pharmacokinetics of oral Sumatriptan do not appear to be significantly affected by migraine attacks.

In a pilot study, no significant differences were found in the pharmacokinetic parameters between the elderly and young healthy volunteers.

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 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
croscarmellose sodium
lactose anhydrous
microcrystalline cellulose
magnesium stearate

Tablet Coat

Lactose monohydrate
mannitol
titanium dioxide E171
talc
triacetin.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

PVC/al blister: 2 years

HDPE bottle with LDPE Cap: 3 years

6.4 Special precautions for storage

This medicinal product does not require any special storage conditions.

6.5 Nature and contents of container

PVC/al blister or HDPE bottle with LDPE Cap

Pack sizes: 2, 3, 6, 7, 12, 14, 18, 21, 24, 28, 30, 50, 100, 250, 500 or 1000 Tablets.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements.

7 MARKETING AUTHORISATION HOLDER

Rockspring Healthcare Limited
38/40 Chamberlayne Rd.
London
NW10 3JE
United Kingdom

8 MARKETING AUTHORISATION NUMBER(S)

PL 18866/0039
PL 18866/0042
PL 18866/0045

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

14/09/2007

10 DATE OF REVISION OF THE TEXT

14/09/2007

1 NAME OF THE MEDICINAL PRODUCT

Sumatriptan 100 mg Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 100 mg of sumatriptan as the succinate salt.

For a full list of the excipients, see section 6.1.

Contains lactose.

3 PHARMACEUTICAL FORM

Coated tablet.

White, oval, biconvex, 8.2x17mm coated tablets, embossed with 'SN' on one side and "100" on the other side.

4 CLINICAL PARTICULARS**4.1 Therapeutic indications**

Sumatriptan 100 mg Tablets are indicated for the acute relief of migraine attacks, with or without aura. Sumatriptan 100 mg Tablets should only be used where there is a clear diagnosis of migraine.

4.2 Posology and method of administration

For oral use.

Adults:

Sumatriptan 100 mg Tablets are indicated for the acute intermittent treatment of migraine. Sumatriptan should not be used prophylactically.

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

The recommended dose is a single 50mg tablet. Some patients may require 100mg. 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 and no more than 300mg is taken in any 24 hour period.

Patients who do not respond to the prescribed dose of sumatriptan should not take a second dose for the same attack. Sumatriptan may be taken for subsequent attacks.

Sumatriptan is recommended as monotherapy for the acute treatment of migraine and should not be given concomitantly with other acute migraine therapies. If a patient fails to respond to a single dose of Sumatriptan 100 mg Tablets there are no reasons, either on theoretical grounds or from limited clinical experience, to withhold products containing aspirin or non-steroidal anti-inflammatory drugs for further treatment of the attack.

The tablets should be swallowed whole with water.

Children (under 18 years of age):

Sumatriptan tablets have not been studied in children under 12 years of age. The available clinical trial data in adolescents (12 to 17 years of age) do not support the use of oral sumatriptan in this age group (see section 5.1). The use of sumatriptan tablets in children and adolescents is therefore not recommended.

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 100 mg Tablets in patients aged over 65 years is not recommended.

4.3 Contraindications

Hypersensitivity to sumatriptan or to any of the excipients.

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

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

Sumatriptan should not be administered to patients with severe hepatic impairment.

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

The concomitant administration of ergotamine or derivatives of ergotamine (including methysergide) is contraindicated. (See interactions)

Concurrent administration of monoamine oxidase inhibitors and sumatriptan is contraindicated.

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

4.4 Special warnings and precautions for use

Sumatriptan 100 mg 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.

The recommended doses of sumatriptan should not be exceeded. As with other migraine therapies, before treating headaches in patients not previously diagnosed as migraineurs, and in migraineurs who present 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 Side effects). Where such symptoms are thought to indicate ischaemic heart disease, no further doses of sumatriptan should be given and appropriate evaluation should be carried out.

Sumatriptan should not be given to patients with risk factors for ischaemic heart disease without prior cardiovascular evaluation (See Section 4.3 Contraindications). 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.

There have been rare post-marketing reports describing patients with weakness, hyper-reflexia, and incoordination following the use of a selective serotonin reuptake inhibitor (SSRI) and sumatriptan. If concomitant treatment with sumatriptan and an SSRI is clinically warranted, appropriate observation of the patient is advised.

Sumatriptan should be administered with caution to patients with conditions which may affect significantly the absorption, metabolism or excretion of drugs, e.g. impaired hepatic or renal function. A 50mg dose should be considered in patients with hepatic impairment.

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).

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.

As with other acute migraine treatments, chronic daily headache/exacerbation of headache has been reported with overuse of sumatriptan, which may necessitate a drug withdrawal.

Patients with rare hereditary problems of fructose or galactose intolerance, Lapp 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. Sumatriptan has the potential to interact with MAOIs, ergotamine and derivatives of ergotamine. The increased risk of coronary vasospasm is a theoretical possibility and concomitant administration is contra-indicated. (see also contraindications).

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.

As interaction may occur between sumatriptan and monoamine oxidase inhibitors and concomitant administration is contraindicated (see contraindications). Rarely, an interaction may occur between sumatriptan and SSRIs (see Special Warnings and special Precautions for Use).

Undesirable effects may be more common during concomitant use of triptans and herbal preparations containing St John's Wort (*Hypericum perforatum*).

4.6 **Pregnancy and lactation**

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 point to 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, embryofetal viability might be affected in the rabbit (see section 5.3). Administration of sumatriptan should only be considered if the expected benefit to the mother is greater than any possible risk to the foetus.

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 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.

Clinical Trial Data

Nervous System Disorders

Common: Tingling, dizziness, drowsiness.

Vascular disorders

Common: Transient increases in blood pressure arising soon after treatment. Flushing.

Gastrointestinal

Common: Nausea and vomiting occurred in some patients but it is unclear if this is related to sumatriptan or the underlying condition.

Musculoskeletal and Connective Tissue Disorders

Common: Sensations of heaviness (usually transient and may be intense but can affect any part of the body including the chest and throat).

General Disorders and Administration Site Conditions

Common: Pain, sensations of heat, pressure or tightness (these events are usually transient but may be intense and can affect any part of the body including the chest and throat).

Common: Feelings of weakness, fatigue (both events are mostly mild to moderate in intensity and transient).

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 rare cases of 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.
Very rare: Tremor, dystonia, nystagmus, scotoma.

Eye disorders

Very rare: Flickering, diplopia, reduced vision, loss of vision including reports of permanent defects. 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, myocardial infarction (see Contraindications, Warnings and Precautions).

Vascular disorders

Very rare: Hypotension, Raynaud's phenomenon.

Gastrointestinal

Very rare: Ischaemic colitis

Musculoskeletal, connective tissue and bone disorders

Very rare: Neck stiffness.

4.9 Overdose

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

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.

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-Hydroxytryptamine₁ (5HT_{1D}) receptor agonist with no effect on other 5HT receptor (5-HT₂-5-HT₇) subtypes. The vascular 5-HT_{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 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 is 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 in an attack.

Clinical response begins around 30 minutes following a 100mg oral dose.

Although the recommended dose of oral sumatriptan 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.

Five placebo-controlled clinical studies assessed the safety and efficacy of oral sumatriptan in approximately 600 adolescent migraineurs aged 12 - 17 years. These studies failed to demonstrate a statistically significant difference in headache relief at 2 hours between placebo and any sumatriptan dose. The undesirable effects profile of oral sumatriptan in adolescents aged 12 - 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 100mg dose, the maximum plasma concentration is 54ng/ml. Mean absolute oral bioavailability is

14% partly due to presystemic metabolism and partly due to incomplete absorption. The elimination phase half-life is approximately 2 hours, although there is an indication of a longer terminal phase. Plasma protein binding is low (14-21%), mean volume of distribution is 170 litres. 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. 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 5HT1 or 5HT2 activity. Minor metabolites have not been identified. The pharmacokinetics of oral Sumatriptan do not appear to be significantly affected by migraine attacks.

In a pilot study, no significant differences were found in the pharmacokinetic parameters between the elderly and young healthy volunteers.

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 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
croscarmellose sodium
lactose anhydrous
microcrystalline cellulose
magnesium stearate

Tablet Coat

Lactose monohydrate
mannitol
titanium dioxide E171
talc
triacetin.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

PVC/al blister: 2 years

HDPE bottle with LDPE Cap: 3 years

6.4 Special precautions for storage

This medicinal product does not require any special storage conditions.

6.5 Nature and contents of container

PVC/al blister or HDPE bottle with LDPE Cap

Pack sizes: 2, 3, 6, 7, 12, 14, 18, 21, 24, 28, 30, 50, 100, 250, 500 or 1000 Tablets.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements.

7 MARKETING AUTHORISATION HOLDER

Rockspring Healthcare Limited

38/40 Chamberlayne Rd.
London
NW10 3JE
United Kingdom

- 8 MARKETING AUTHORISATION NUMBER(S)**
PL 18866/0040
PL 18866/0043
PL 18866/0046
- 9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION**
14/09/2007
- 10 DATE OF REVISION OF THE TEXT**
14/09/2007

PATIENT INFORMATION LEAFLET

Read all of this leaflet carefully before you start using this medicine.

- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor or your pharmacist.
- This medicine has been prescribed for you personally and you should not pass it on to others. It may harm them, even if their symptoms are the same as yours.

In this leaflet:

1. What Sumatriptan Tablets are and what they are used for
2. Before you take Sumatriptan Tablets
3. How to take Sumatriptan Tablets
4. Possible side effects
- 5 Storing Sumatriptan Tablets

The name of your medicine is

Sumatriptan 50 mg Tablets

Sumatriptan 100 mg Tablets

- Each tablet contains either 50mg or 100mg sumatriptan (as the succinate)
- The other ingredients are lactose monohydrate, croscarmellose sodium, anhydrous lactose, microcrystalline cellulose, magnesium stearate, mannitol, titanium dioxide E171, talc, triacetin.

Marketing Authorisation Holder

Rockspring Healthcare Limited, 38/40 Chamberlayne Rd., London NW10 3JE, United Kingdom.

Manufacturer

Actavis hf, Reykjavikurvegur 78, IS-220 Hafnarfjordur, Iceland.

1. WHAT SUMATRIPTAN TABLETS ARE AND WHAT THEY ARE USED FOR

Sumatriptan Tablets have been developed for the treatment of migraine. The symptoms of migraine, which are thought to be due to temporary swelling of blood vessels in the head, may include aura (warning sensations of visual distortion such as flashes of light and zigzag lines or waves). Medicines like Sumatriptan Tablets are believed to work by reducing the size of these blood vessels. These medicines are called 5HT₁ receptor agonists.

If you are not sure why Sumatriptan Tablets have been prescribed for you ask your doctor.

The following pack sizes are available 2, 3, 6, 7, 12, 14, 18, 21, 24, 28, 30, 50, 100, 250, 500 or 1000 Tablets. (* only the marketed pack sizes will be stated on the printed leaflets)

2. BEFORE YOU TAKE SUMATRIPTAN TABLETS

Do not take Sumatriptan Tablets if you:

- are allergic to sumatriptan or any of the other ingredients in Sumatriptan Tablets. You may be allergic if after taking sumatriptan, you suddenly experience feelings of tightness in the throat or chest, swelling of the tongue, lips or eyelids, difficulty in breathing or swallowing, a widespread feeling of warmth, flushing or itching of the skin and/or a rash like 'hives', progressing to feeling faint or loss of consciousness. Should any of these occur, stop taking the sumatriptan tablets and get medical assistance immediately
- have had a heart attack or suffer from any heart disease
- have symptoms that might indicate heart disease, such as chest pain or a sensation of pressure or tightness in your chest.
- have high blood pressure, or if your blood pressure is high despite medication
- have poor blood circulation in your legs that causes cramp-like pain when you walk too far (peripheral vascular disease)
- have a history of stroke or transient ischaemic attack (TIA, a minor form of stroke that lasts less than 24 hrs).
- have severe liver problems
- are taking any medicines for your migraine which contain ergotamine or ergotamine derivatives, such as ergotamine tartrate or methysergide maleate (in which case, you should stop taking them at least 24 hours before taking Sumatriptan Tablets)
- are taking any medicines on a doctor's prescription for the treatment of depression such as lithium, MAOIs or SSRIs (including citalopram, fluoxetine, fluvoxamine, paroxetine and sertraline) or if you have taken an MAOI in the last 2 weeks

If you think you may have any of these problems contact your doctor before taking sumatriptan.

Before prescribing sumatriptan, your doctor will establish whether your headache is caused by migraine and not by any other condition.

Take special care with Sumatriptan Tablets:

You should tell your doctor before starting sumatriptan if any of these apply to you:

- if you know that you have problems with your liver or kidneys;
- if you have been diagnosed with epilepsy or any other disease that reduces the threshold for epileptic fits;
- if you know that you are allergic to antibacterial medicines that belong to the group of sulphonamides;
- if you are being treated for high blood pressure as in a small number of cases sumatriptan has been seen to increase blood pressure;
- if you experience pain and/or tightness in the chest or throat. These effects are usually short lasting. If they however persist and you are concerned, or they become severe, contact your doctor immediately for advice;
- if you experience chronic daily headaches. Taking sumatriptan too often may result in developing a chronic headache. In such cases you should contact your doctor as you may have to stop taking sumatriptan;
- if you are considered to be at risk of developing heart disease (e.g. diabetic or a heavy smoker), and particularly if you are a post-menopausal woman or a man over 40 years with these risk factors, your doctor should check your heart function before prescribing sumatriptan. In very rare cases serious heart conditions have occurred after taking sumatriptan, even if no signs of any heart disease were found. Contact your doctor for advice if you have any concerns.

Taking other medicines :

Certain medicines may influence the effectiveness of sumatriptan, and sumatriptan may influence the effectiveness of other medicines. Contact your doctor if you take:

- other medicines for migraine, such as ergotamine or similar medicines;
- medicines to treat depression (MAO inhibitors or serotonin re-uptake inhibitors);
- medicines to treat manic/depressive (bipolar) disorders, such as lithium.

During concomitant use of sumatriptan and herbal preparations containing St. John's Wort (*Hypericum perforatum*) side effects may become more common

Please tell your doctor or pharmacist if you are taking or have recently taken any other medicines, including medicines obtained without a prescription.

Pregnancy and Breast-feeding

Sumatriptan Tablets should not be taken if you are pregnant, likely to become pregnant or if you are breast-feeding, unless advised to do so by your doctor. Breastfeeding should be avoided for 12 hours after a dose and during this time any breast milk expressed should be discarded.

Driving and using machines:

Sumatriptan Tablets may cause drowsiness. If you are affected do not drive or operate machinery.

3. HOW TO TAKE SUMATRIPTAN TABLETS

Always take Sumatriptan Tablets exactly as your doctor has instructed you. You should check with your doctor or pharmacist if you are unsure.

ONE tablet should be taken at the first sign of a migraine attack, although it will still be effective if taken at a later stage. If this tablet does not make your migraine better do not take any more tablets for this attack because it is unlikely that a second dose will work. Sumatriptan Tablets can be used for your next attack.

If, after your first dose, your migraine goes away but then returns, you may take another tablet, provided it is at least **two hours** since you took the first tablet.

DO NOT TAKE MORE THAN 300 mg of Sumatriptan in any 24-hour period. Swallow each tablet whole with water. Do not chew or crush them.

Sumatriptan Tablets should not be used in children under 18 years of age.

There is little experience of Sumatriptan Tablets in those over 65 years of age so it is not usually prescribed for this age group.

If you have the impression that the effect of Sumatriptan Tablets is too strong or too weak, talk to your doctor or pharmacist.

How quickly will the treatment start to work?

It takes Sumatriptan Tablets about 30 minutes to start working. If the tablets do not ease your migraine, then you may take your usual 'pain killers', provided they do not contain ergotamine or its derivatives. Wait at least six hours after taking a Sumatriptan tablet before taking any medicines containing ergotamine or its derivatives.

If you take more Sumatriptan Tablets than you should:

It is important to keep to the dose on the label or follow the instructions above. Taking more than this could make you ill. If an overdose is taken, **DO NOT DELAY**, ask your doctor what to do or contact your nearest accident and emergency department.

4. POSSIBLE SIDE EFFECTS

Most people taking this medicine find it causes no problems, however a few people may find that they have side effects.

Common side effects (could happen to between 1 in 10 and 1 in 100 people taking it):

- Flushing (redness of the face lasting a few minutes), dizziness, feelings of weakness, tiredness and drowsiness (IMPORTANT if you are driving or working a machine)
- Short lasting increases in blood pressure soon after taking the medicine
- Feeling sick (nausea) or being sick (vomiting) - when not part of migraine attack
- Pain, sensations of tingling, heat, heaviness and pressure or tightness. If these effects continue or are particularly severe, especially chest or heart pain which spreads to the arms, tell your doctor **immediately** as there have been rare reports of such problems being caused by a heart attack.

Very rare side effects (could happen to less than 1 in 10,000 people taking it):

- Visual disturbances including flickering, double vision and reduced vision. There have been cases where permanent vision defects have occurred
- lowering of blood pressure that can lead to feeling of faintness especially on standing up
- Slowing or quickening in the speed of your heart beat, palpitations (feeling of fast heart beat), changes in heart rhythm
- Shaking, tremors or uncontrolled movements
- Stiffness in the neck
- If you have a blood test to check how your liver is working and have taken Sumatriptan tablets, tell your doctor as it may affect the results.

If you have any of these side effects mentioned above you do not have to stop taking Sumatriptan tablets unless they persist or you find them too unpleasant, but you should contact your doctor as soon as possible.

The following side effects are very rare but you should contact your doctor **immediately** and do **not** take any more Sumatriptan tablets unless your doctor tells you to do so.

- Sudden wheeziness, fluttering or tightness in the chest, swelling of eyelids, face or lips, skin rash - red spots or hives (skin lumps), which may be signs of an allergic reaction
- Fits (usually in people with a history of epilepsy)
- Inflammation of the colon (part of the intestine), which may present as lower left-sided abdominal pain and/or bloody diarrhoea
- Raynaud's phenomenon (a painful condition causing the fingers or toes to turn white, then blue and red)

If you notice any other side effects not mentioned in this leaflet, please inform your doctor or pharmacist.

5. STORING SUMATRIPTAN TABLETS

Keep out of the reach and sight of children.

This medicinal product does not require any special storage conditions.

Do not use after the expiry date stated on the label.

This leaflet was last approved on February 2007

Packaging

**Example of packaging approved for the 50mg strength tablets:
Sumatriptan 50mg Tablets (PL 18866/0039)**



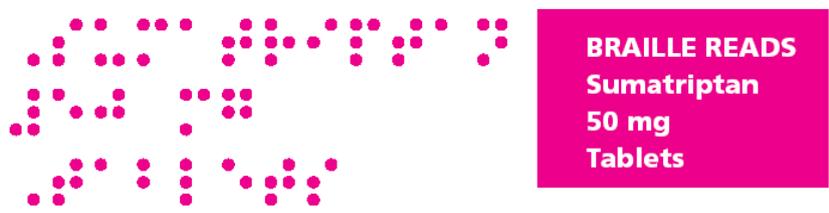
The batch number and Expiry Date will be embossed on to the actual blister pack.

Sumatriptan 50mg Tablets - Blister Foil Mock-up 18866/0039

<p>Sumatriptan 50 mg Tablets</p> <p>(Sumatriptan succinate)</p> <p>xx Tablets</p> <p>Each coated tablet contains: 50 mg Sumatriptan as sumatriptan succinate Also contains lactose and mannitol.</p> <p>ROCKSPRING HEALTHCARE LTD.</p>		<p>For oral use only.</p> <p>Use as directed by your doctor.</p> <p>KEEP OUT OF THE REACH AND SIGHT OF CHILDREN.</p> <p>Product Licence Holder: Rockspring Healthcare Limited 38/40 Chamberlayne Road London NW10 3JE United Kingdom PL 18866/0039</p> <p>POM</p>
<p>Expiry Date:</p>		
<p>Batch No:</p>		

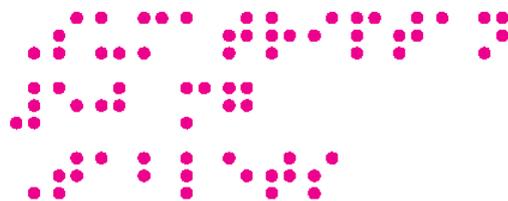
The batch number and Expiry Date will be embossed on to the actual label.

Sumatriptan 50mg Tablets PP Bottle label mock-up PL 18866/0039:
xx: 2, 3, 6, 7, 12, 14, 18, 21, 24, 28, 30, 50, 100, 250, 500 and 1000 Tablets.
Only the marketed pack size will be stated on the actual printed label.



The batch number and Expiry Date will be embossed on to the actual cartons.

PL 18866/0039 Sumatriptan 50 mg Tablets
Blister Carton mock-up



BRILLE READS
Sumatriptan
50 mg
Tablets

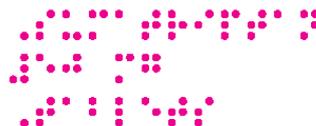
The batch number and Expiry Date will be embossed on to the actual cartons.

PL 18866/0039 Sumatriptan 50 mg Tablets
 Blister Carton mock-up



The batch number and Expiry Date will be embossed on to the actual cartons.

PP Bottle - carton mock-up PL 18866/0039:
 xx: 2, 3, 6, 7, 12, 14, 18, 21, 24, 28, 30, 50, 100, 250, 500 and 1000 Tablets.
 Only the marketed pack size will be stated on the actual printed cartons.



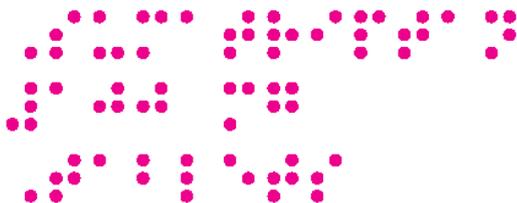
BRaille READS
Sumatriptan
50 mg
Tablets

**Example of packaging approved for the 100mg strength tablets:
Sumatriptan 100mg Tablets (PL 18866/0040)**

Sumatriptan 100 mg Tablets	For oral use only.
(Sumatriptan succinate) xx Tablets Each coated tablet contains: 100 mg Sumatriptan as sumatriptan succinate Also contains lactose and mannitol.	Use as directed by your doctor.
	KEEP OUT OF THE REACH AND SIGHT OF CHILDREN.
Expiry Date:	Product Licence Holder: Rockspring Healthcare Limited 38/40 Chamberlayne Road London NW10 3JE United Kingdom PL 18866/0040
Batch No:	<div style="border: 1px solid black; padding: 2px; display: inline-block;">POM</div>

The batch number and Expiry Date will be embossed on to the actual label.

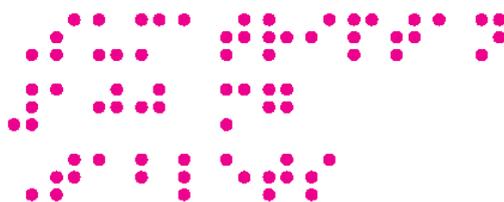
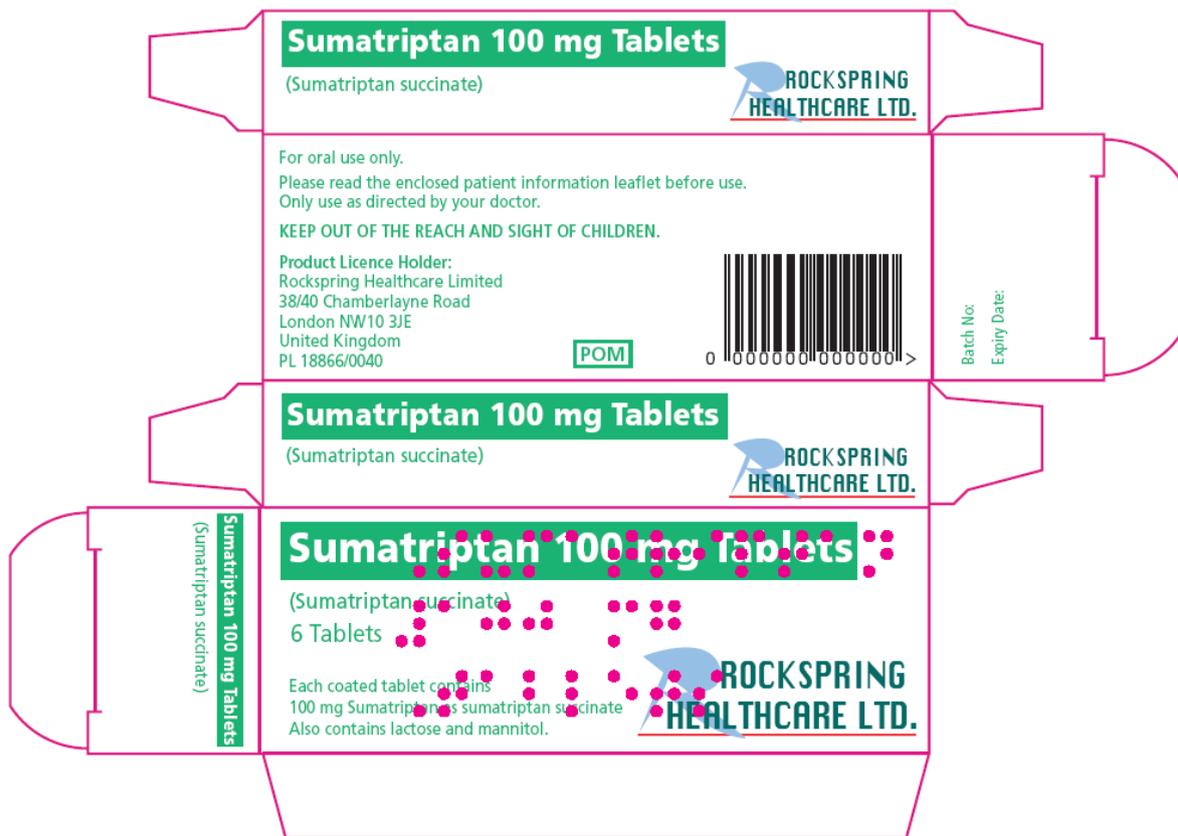
Sumatriptan 100mg Tablets PP Bottle label mock-up PL 18866/0040:
 xx: 2, 3, 6, 7, 12, 14, 18, 21, 24, 28, 30, 50, 100, 250, 500 and 1000 Tablets.
 Only the marketed pack size will be stated on the actual printed label.



BRILLE READS
Sumatriptan
100 mg
Tablets

The batch number and Expiry Date will be embossed on to the actual cartons.

PL 18866/0040 Sumatriptan 100 mg Tablets
 Blister Carton mock-up



BRAILLE READS
Sumatriptan
100 mg
Tablets

The batch number and Expiry Date will be embossed on to the actual cartons.

PL 18866/0040 Sumatriptan 100 mg Tablets
 Blister Carton mock-up



The batch number and Expiry Date will be embossed on to the actual cartons.

PP Bottle - carton mock-up PL 18866/0040:
 xx: 2, 3, 6, 7, 12, 14, 18, 21, 24, 28, 30, 50, 100, 250, 500 and 1000 Tablets.
 Only the marketed pack size will be stated on the actual printed cartons.



BRAILLE READS
Sumatriptan
100 mg
Tablets