SUMATRIPTAN 50MG TABLETS (PL 18708/0001)
SUMATRIPTAN 100MG TABLETS (PL 18708/0002)

UKPAR

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SUMATRIPTAN 50MG TABLETS (PL 18708/0001)
SUMATRIPTAN 100MG TABLETS (PL 18708/0002)

LAY SUMMARY

On 19th December 2007, the MHRA granted Liconsa SA licences for the medicinal products Sumatriptan 50mg and 100mg Tablets (PL 18708/0001-2). 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 18708/0001)
SUMATRIPTAN 100MG TABLETS (PL 18708/0002)

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 to Liconsa SA (PL 18708/0001-2) on 19th December 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 to be a generic medicinal product 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-HT\textsubscript{1} 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: \([3-[2-(\text{Dimethylamino})\text{ethyl}]-1H-\text{indol-5-yl}]-N-\text{methylmethanesulphonamide}\) hydrogen butanedioate.

Structural formula

![Structural formula of Sumatriptan succinate](image)

Molecular formula: \(C_{18}H_{27}N_{3}O_{6}S\)

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.

All aspects of the manufacture and control of the active sumatriptan succinate are covered by a European Pharmacopoeia Certificate of Suitability.

An appropriate specification is provided for the active substance. Analytical methods have been appropriately validated and are satisfactory for ensuring compliance with the relevant specifications. Batch analysis data are provided and comply with the proposed specification.
Satisfactory specifications and certificates of analysis have been provided for all packaging used. All primary packaging is in compliance with current directives concerning the contact of packaging with food.

Appropriate stability data have been provided for a retest period of 5 years if stored in the proposed packaging.

**Other Ingredients**

Other ingredients consist of pharmaceutical excipients lactose monohydrate, microcrystalline cellulose, croscarmellose sodium, peppermint flavouring, talc, aspartame, povidone and magnesium stearate.

With the exception of peppermint flavouring, all excipients comply with their respective European Pharmacopoeia monographs. Peppermint flavouring complies with a suitable in-house specification.

Lactose monohydrate is the only ingredients that comes from an animal source. The applicant has confirmed that the milk used in the production of lactose monohydrate is sourced from healthy animals under the same conditions as that for human consumption and that the lactose is prepared using only milk and calf rennet.

**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 and are satisfactory.

**Manufacturing Process**

Satisfactory accounts of the manufacturing process for both strengths of the finished product have been provided. Batch formulae have been provided for both strengths. 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
Both strengths of finished product are packaged in aluminium blisters in pack sizes of 2, 3, 4, 6, 12 and 18 tablets. Two additional pack sizes of 8 tablets and 24 tablets are available for the 50mg strength only.

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 proposed packaging will be marketed in the UK. However, they have provided assurances that they will submit mock-ups for assessment before launching any packaging types into the market.

Stability of the product
Stability studies were performed on pilot batches of all strengths of finished product in the packaging proposed for marketing, in accordance with current guidelines. These data support a shelf-life of 3 years for both strengths of product, with the storage conditions “Store in original package”.

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. The marketing authorisation holder has provided a commitment to update the marketing authorisation no later than 1st July 2008 with a package leaflet in compliance with Article 59 of Council Directive 2001/83/EC and that the leaflet shall reflect the results of consultation with target patient groups.

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

The requirements for the proposed products to be generic medicinal products of the 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 claim they are generic medicinal products of 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

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.

Bioequivalence
A single-dose, two-way crossover study was carried out, comparing the plasma pharmacokinetics of test sumatriptan 100mg tablets versus the reference Imigran 100mg Tablets (GlaxoWellcome UK).

Blood samples were taken predose and up to 12 hours post dose, with a washout period of 2 weeks between dosing.

The main pharmacokinetic results are presented below:

<table>
<thead>
<tr>
<th></th>
<th>Cmax (ng/mL)</th>
<th>AUC0-tlast (ng.h/mL)</th>
<th>AUC0-∞ (ng.h/mL)</th>
<th>Tmax (hrs)</th>
<th>T1/2 (hrs)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sumatriptan</td>
<td>46.4 ± 15.6</td>
<td>210.6 ± 73.7</td>
<td>217.2 ± 74.2</td>
<td>2.17 ± 1.39</td>
<td>4.74 ± 3.56</td>
</tr>
<tr>
<td>100mg [Test]</td>
<td></td>
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<tr>
<td>Imigran</td>
<td>45.3 ± 14.0</td>
<td>206.0 ± 67.9</td>
<td>213.9 ± 69.2</td>
<td>2.21 ± 1.20</td>
<td>3.93 ± 2.65</td>
</tr>
<tr>
<td>100mg [Ref]</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test/Ref</td>
<td>102.0%</td>
<td>101.8%</td>
<td>101.3%</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Ratio 90% CI</td>
<td>92.2; 112.9</td>
<td>97.5; 106.4</td>
<td>97.1; 105.6</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

The 90% confidence limits are within the 80% to 125% range, so bioequivalence can be accepted. 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.

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

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

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

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.

PATIENT INFORMATION LEAFLET (PIL)
The PIL has been provided and is consistent the SPC.
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.

APPLICATION FORM (MAA)
The MAA form is satisfactory.

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

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 50mg 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 18708/0001)**
**SUMATRIPTAN 100MG TABLETS (PL 18708/0002)**

**STEPS TAKEN FOR ASSESMENT**

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<tr>
<td>1</td>
<td>The MHRA received the marketing authorisation applications on 5th April 2005</td>
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<tr>
<td>2</td>
<td>Following standard checks and communication with the applicant the MHRA considered the applications valid on 3rd May 2005</td>
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<tr>
<td>3</td>
<td>Following assessment of the applications the MHRA requested further information relating to the quality dossiers on 2nd March 2006, 10th August 2006, 16th August 2006 and 22nd March 2007.</td>
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<tr>
<td>4</td>
<td>The applicant responded to the MHRA’s requests, providing further information on 10th August 2006, 15th August 2006, 26th November 2006 and 23rd July 2007 for the quality dossiers.</td>
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<tr>
<td>5</td>
<td>The applications were determined on 19th December 2007</td>
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SUMATRIPTAN 50MG TABLETS (PL 18708/0001)
SUMATRIPTAN 100MG TABLETS (PL 18708/0002)

STEPS TAKEN AFTER AUTHORISATION - SUMMARY

<table>
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<tr>
<th>Date submitted</th>
<th>Application type</th>
<th>Scope</th>
<th>Outcome</th>
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SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT
Sumatriptan 50 mg Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION
Each Sumatriptan 50 mg tablet contains 50 mg sumatriptan (as succinate). Each tablet also contains lactose monohydrate and Aspartame (E951).

For full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM
Tablet.
50 mg tablet: Scored, oblong, white-cream tablet with characteristic peppermint flavour with the following dimensions: 10 mm x 4 mm.

Tablets should not be broken/divided.

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
Adults
Sumatriptan tablets is indicated for the acute intermittent treatment of migraine. It 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 of oral Sumatriptan 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 tablets should not take a second dose for the same attack. Sumatriptan tablets may be taken for subsequent attacks.

Sumatriptan tablets 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)
The safety and effectiveness of Sumatriptan tablets in children has not yet been established.

Elderly (Over 65)
Experience of the use of Sumatriptan tablets 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.
4.3 Contraindications

Hypersensitivity to any component of the preparation.

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

4.4 Special warnings and precautions for use

Sumatriptan tablets should only be used where there is a clear diagnosis of migraine.

Sumatriptan is not indicated for use in the management of hemiplegic, basilar or ophthalmoplegic migraine.

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, hyperreflexia, 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.

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.

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

This medicinal product contains aspartame, a source of phenylalanine. May be harmful for people with phenylketonuria.

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

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.

Rarely, an interaction may occur between sumatriptan and SSRI's (see Special Warnings and special Precautions for Use).

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 24 hours after treatment.

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

General

The following symptoms are usually transient and may be intense and can affect any part of the body including the chest and throat; pain, sensations of tingling, heat, heaviness, pressure or tightness. The following symptoms are mild to moderate in intensity and transient: flushing, dizziness and feelings of weakness.

Fatigue and drowsiness have been reported.
Cardiovascular
Hypotension, bradycardia, tachycardia, palpitations.
Transient increases in blood pressure arising soon after treatment have been recorded. In extremely rare cases, serious coronary events have been reported which have included cardiac arrhythmias, ischaemic ECG changes, coronary artery vasospasm or myocardial infarction. (see contraindications and Precautions and Warnings).
There have also been rare reports of Raynaud's phenomenon and ischaemic colitis.

Gastrointestinal
Nausea and vomiting occurred in some patients but the relationship to sumatriptan is not clear.

CNS
There have been rare reports of seizures following use of sumatriptan. 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.

Eye Disorders
Patients treated with Sumatriptan tablets rarely exhibit visual disorders like flickering and diplopia. Additionally, cases of nystagmus, scotoma and reduced vision have been observed. Very rarely, loss of vision has occurred, which is usually transient. However, visual disorders may also occur during a migraine attack itself.

Hypersensitivity/skin
Hypersensitivity reactions ranging from cutaneous hypersensitivity to, in rare cases, anaphylaxis.

Laboratory values
Minor disturbances in liver function tests have occasionally been observed.

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 tablets.

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 (5HT1D) receptor agonist with no effect on other 5HT receptor (5-HT2-5-HT7) subtypes. The vascular 5-HT1D 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 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 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.

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

6 PHARMACEUTICAL PARTICULARS
6.1 List of excipients
SUMATRIPTAN 50/100mg tablets
Lactose monohydrate
Cellulose microcrystalline
Crocarmellose sodium
Peppermint flavour
Talc
Aspartame (E951)
Povidone
Magnesium stearate

6.2 Incompatibilities
Not applicable.

6.3 Shelf life
3 years
6.4 Special precautions for storage
Keep in the original package.
No special storage conditions are required.

6.5 Nature and contents of container
Sumatriptan 50 mg: Aluminium / Aluminium blister, containing 2, 3, 4, 6, 8, 12, 18 or 24 tablets.
Not all pack sizes may be marketed.

6.6 Special precautions for disposal
No special requirements.

7 MARKETING AUTHORISATION HOLDER
LABORATORIOS LICONSA,
S.A.Gran Via Carlos III, 98, 7th floor
08028 Barcelona (Spain)

8 MARKETING AUTHORISATION NUMBER(S)
PL 18708/0001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION
19/12/2007

10 DATE OF REVISION OF THE TEXT
19/12/2007
1 NAME OF THE MEDICINAL PRODUCT
Sumatriptan 100 mg Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION
Each Sumatriptan 100 mg tablet contains 100 mg sumatriptan (as succinate). Each tablet also contains lactose monohydrate and Aspartame (E951).

For full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM
Tablet.
100 mg tablet: Scored, oblong, white-cream tablet with characteristic peppermint flavour with the following dimensions: 14 mm x 6 mm.

Tablets should not be broken/divided.

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
Sumatriptan tablets is indicated for the acute intermittent treatment of migraine. It 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 of oral Sumatriptan 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 tablets should not take a second dose for the same attack. Sumatriptan tablets may be taken for subsequent attacks.

Sumatriptan tablets 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)
The safety and effectiveness of Sumatriptan tablets in children has not yet been established.

Elderly (Over 65)
Experience of the use of Sumatriptan tablets 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.
4.3 **Contraindications**

Hypersensitivity to any component of the preparation.

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

4.4 **Special warnings and precautions for use**

Sumatriptan tablets should only be used where there is a clear diagnosis of migraine.

Sumatriptan is not indicated for use in the management of hemiplegic, basilar or ophthalmoplegic migraine.

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.

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.

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

This medicinal product contains aspartame, a source of phenylalanine. May be harmful for people with phenylketonuria.

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
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.

Rarely, an interaction may occur between sumatriptan and SSRI's (see Special Warnings and special Precautions for Use).

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 24 hours after treatment.

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
General
The following symptoms are usually transient and may be intense and can affect any part of the body including the chest and throat; pain, sensations of tingling, heat, heaviness, pressure or tightness. The following symptoms are mild to moderate in intensity and transient: flushing, dizziness and feelings of weakness.

Fatigue and drowsiness have been reported.
Cardiovascular
Hypotension, bradycardia, tachycardia, palpitations. Transient increases in blood pressure arising soon after treatment have been recorded. In extremely rare cases, serious coronary events have been reported which have included cardiac arrhythmias, ischaemic ECG changes, coronary artery vasospasm or myocardial infarction. (see contraindications and Precautions and Warnings). There have also been rare reports of Raynaud's phenomenon and ischaemic colitis.

Gastrointestinal
Nausea and vomiting occurred in some patients but the relationship to sumatriptan is not clear.

CNS
There have been rare reports of seizures following use of sumatriptan. 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.

Eye Disorders
Patients treated with Sumatriptan tablets rarely exhibit visual disorders like flickering and diplopia. Additionally, cases of nystagmus, scotoma and reduced vision have been observed. Very rarely, loss of vision has occurred, which is usually transient. However, visual disorders may also occur during a migraine attack itself.

Hypersensitivity/skin
Hypersensitivity reactions ranging from cutaneous hypersensitivity to, in rare cases, anaphylaxis.

Laboratory values
Minor disturbances in liver function tests have occasionally been observed.

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 tablets.

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 (5HT1D) receptor agonist with no effect on other 5HT receptor (5-HT2-5-HT7) subtypes. The vascular 5-HT1D 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 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 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.

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

6 PHARMACEUTICAL PARTICULARS
6.1 List of excipients
SUMATRIPTAN 50/100mg tablets
Lactose monohydrate
Cellulose microcrystalline
Crocarmellose sodium
Peppermint flavour
Talc
Aspartame (E951)
Povidone
Magnesium stearate

6.2 Incompatibilities
Not applicable.

6.3 Shelf life
3 years
6.4 Special precautions for storage
Keep in the original package.
No special storage conditions are required.

6.5 Nature and contents of container
Sumatriptan 100 mg: Aluminium / Aluminium blister, containing 2, 3, 4, 6, 12 or 18 tablets.
Not all pack sizes may be marketed.

6.6 Special precautions for disposal
No special requirements.

7 MARKETING AUTHORISATION HOLDER
LABORATORIOS LICONSA,
S.A.Gran Via Carlos III, 98, 7th floor
08028 Barcelona (Spain)

8 MARKETING AUTHORISATION NUMBER(S)
PL 18708/0002

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION
19/12/2007

10 DATE OF REVISION OF THE TEXT
19/12/2007
Read all of this leaflet carefully before you start taking this medicine.

- Keep this leaflet. You may need to read it again.
- If you have any further questions please ask your doctor or pharmacist.
- This medicine has been prescribed for you. Do 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 50 mg tablets is and what it is used for
2. Before you take Sumatriptan 50 mg tablets
3. How to take Sumatriptan 50 mg tablets
4. Possible side effects
5. Storing Sumatriptan 50 mg tablets

SUMATRIPTAN 50 mg TABLETS
Composition:
- The active substance is: sumatriptan (as succinate).
  Sumatriptan 50 mg tablets contains 60 mg of sumatriptan (as succinate).
- The other ingredients (excipients) are: lactose monohydrate, cellulose microcrystalline, croscarmellose sodium, peppermint flavour, sac, aspartame (E951), povidone, magnesium stearate.

Marketing Authorisation Holder and Manufacturer:
Marketing Authorisation Holder: LABORATORIOS LICORSA, S.A.
Gran Via Carlos III, 98, 7th floor
08028 Barcelona, SPAIN
Manufacturer: LABORATORIOS LICORSA, S.A.
Avda. Miraclambo, Nº 7, Poligono Industrial Miracampo
19200 Azuqueca de Henares (Guadalajara), SPAIN

1. WHAT SUMATRIPTAN 50 mg TABLETS IS AND WHAT IT IS USED FOR

Sumatriptan 50 mg tablets are scored, oblong, white-cream tablet with characteristic peppermint flavour with the following dimensions: 10 mm x 4 mm. Each pack contains 2, 6 or 12 tablets.

Sumatriptan tablets contain sumatriptan, a medicine developed for the treatment of migraine. The symptoms of migraine may be due to temporary swelling of blood vessels in the head. 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.

2. BEFORE YOU TAKE SUMATRIPTAN 50 mg TABLETS

Please consult your doctor, even if these statements were applicable to you any time in the past.

Do not take Sumatriptan 50 mg tablets:
- If you are allergic (hypersensitive) to sumatriptan, any of the other ingredients of Sumatriptan tablets or to medicines called xanthines.
- If you have history of cerebrovascular accident (CVA) or transient ischaemic attack (TIA).
- If you have severe hepatic impairment.
- If you have moderate and severe hypertension and mild uncontrolled hypertension.
- The concomitant administration of ergotamine or derivatives of ergotamine (including methylergide) is contraindicated.
- If you are taking monoamine oxidase inhibitors. Sumatriptan tablets must not be used within two weeks of discontinuation of therapy with monoamine oxidase inhibitors (MAOIs).

Take special care with Sumatriptan 50 mg tablets:
- Sumatriptan tablets should only be used where there is a clear diagnosis of migraine.
- Sumatriptan is not indicated for use in the management of hypotensive, subarachnoid or subdural haemorrhage.
- 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).
- If you suffer 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 you should consult your doctor.
- 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 if you are a postmenopausal woman or have other risk factors for cardiovascular disease.
- It should be noted that these medicines may not benefit every patient who has migraine 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, hypotension, and incontinence following the use of a selective serotonin reuptake inhibitor (SSRI) and sumatriptan. If you are taking these medicines, you should inform your doctor.
- Sumatriptan should be administered with caution to patients with conditions which may affect significantly the absorption, metabolism or excretion of drugs. A 50 mg dose should be considered in patients with hepatic impairment. If you have improved hepatic or renal function, inform your doctor.
- If you are pregnant or breastfeeding, you should inform your doctor. Patients with known hypersensitivity to sumatriptan 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.
- If you are under treatment with herbal preparations containing St John's Wort (Hypericum perforatum) and are Sumatriptan tablets, undesirable effects may be more common.

Pregnancy
Ask your doctor or pharmacist for advice before using any medicine.

Although the available data do not indicate that direct teratogenic effects are produced under treatment with sumatriptan, these data contain insufficient information to draw definitive conclusions.

Breast-feeding
Ask your doctor or pharmacist for advice before using any medicine.

It has been demonstrated that following subcutaneous administration, sumatriptan is excreted into breast milk. Infant exposure can be minimised by avoiding breast feeding for 24 hours after treatment.
Driving and using machines
Sumatriptan tablets may cause drowsiness. If you are affected do not drive or operate machines.

Important Information about some of the ingredients of Sumatriptan 50 mg tablets.
This medicine contains aspirin, a source of phenylalanine. May be harmful for people with phenylketonuria.
If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicinal product.

Taking other medicines
- Sumatriptan has the potential to interact with monoamine oxidase inhibitors (MAOIs), ergotamine and derivatives of ergotamine. The increased risk of coronary vasospasm is a theoretical possibility and concomitant administration is contra-indicated. (Do not take Sumatriptan 50 mg tablets). 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 4 hours have elapsed following sumatriptan administration. Rarely, an interaction may occur between sumatriptan and selective serotonin reuptake inhibitor (SSRIs) (see Take special care with Sumatriptan 50 mg tablets).

3. HOW TO TAKE SUMATRIPTAN 50 mg TABLETS

Adults
Sumatriptan tablets is indicated for the acute intermittent treatment of migraine. It 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 of oral Sumatriptan is a single 50 mg tablet. Some patients may require 100 mg. 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 tablets should not take a second dose for the same attack. Sumatriptan tablets may be taken for subsequent attacks.

Sumatriptan tablets 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.

Tablets should not be broken/divided and should be swallowed whole with water.

Children (under 15 years of age)
The safety and effectiveness of Sumatriptan tablets in children has not yet been established. The use of Sumatriptan tablets in children is not recommended.

Elderly (over 65)
Experience of the use of Sumatriptan tablets 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.

If you take more Sumatriptan tablets than you should
If you may have taken more Sumatriptan 50 mg tablets than you should, talk to a doctor or pharmacist immediately.

4. POSSIBLE SIDE EFFECTS

Like all medicines, Sumatriptan tablets, can cause side effects, although not everybody gets them. The following side effects can occur:

General
The following symptoms are usually transient and may be intense and can affect any part of the body including the chest and throat, pain, sensations of tingling, heat, heaviness, pressure or tightness. The following symptoms are mild to moderate in intensity and transient: flushing, dizziness and feelings of weakness. Fatigue and drowsiness have been reported.

Cardiovascular
Hypertension, bradycardia, tachycardia, palpitations.
Transient increase in blood pressure arising soon after treatment have been recorded. In extremely rare cases, serious coronary events have been reported which have included cardiac arrhythmias, ischemic ECG changes, coronary artery vasospasm or myocardial infarction. (see Contraindications and Precautions and Warnings).

There have also been rare reports of Raynaud’s phenomenon and ischemic colitis.

Gastrointestinal
Nausea and vomiting occurred in some patients but the relationship to sumatriptan is not clear.

CNS
There have been rare reports of seizures following use of sumatriptan. 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.

Eye Disorders
Patients treated with Sumatriptan tablets rarely exhibit visual disorders like flickering and diplopia. Additionally, cases of nyctagimna, scotoma and reduced vision have been observed. Very rarely, loss of vision has occurred, which is usually transient. However, visual disorders may also occur during a migraine attack itself.

Hypersensitivity/skin
Hypersensitivity reactions ranging from cutaneous hypersensitivity to, in rare cases, anaphylaxis.

Laboratory values
Minor disturbances in liver function tests have occasionally been observed.

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

5. STORING SUMATRIPTAN 50 mg TABLETS

Store the tablets in the original packaging.
Keep out of the reach and sight of children.
There are no special storage conditions instructions.
Do not use Sumatriptan 50 mg tablets after the expiry date on the carton.

Applicable to all medicines
Old and unnecessary medicines can be returned to the chemist/s for destruction.

This leaflet was last approved on XXX.
Read all of this leaflet carefully before you start taking this medicine.

- Keep this leaflet. You may need to read it again.
- If you have any further questions please ask your doctor or pharmacist.
- This medicine has been prescribed for you. Do 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 100 mg tablets is and what it is used for
2. Before you take Sumatriptan 100 mg tablets
3. How to take Sumatriptan 100 mg tablets
4. Possible side effects
5. Storing Sumatriptan 100 mg tablets

SUMATRIPANT 100 mg TABLETS
Composition:
- The active substance is: sumatriptan (as succinate).
- Sumatriptan 100 mg tablets contains 100 mg of sumatriptan (as succinate).
- The other ingredients (excipients) are: lactose monohydrate, cellulose microcrystalline, croscarmellose sodium, peppermint flavour, tangerine, silicon dioxide (E551), povidone, magnesium stearate.

Marketing Authorisation Holder and Manufacturer:
Marketing Authorisation Holder: LABORATORIOS LICONSA, S.A.
Gran Via Carlos III, 58, 5th Floor
08028 Barcelona, SPAIN
Manufacturer: LABORATORIOS LICONSA, S.A.
Avda. Minas de Irati, 2, Building Industrial Minas de Irati
20200 Azcoitia (Guipuzcoa), SPAIN

1. WHAT SUMATRIPANT 100 mg TABLETS IS AND WHAT IT IS USED FOR
Sumatriptan 100 mg tablets are scored, oblong, white-cream tablet with characteristic peppermint flavour with the following dimensions: 14 mm x 6 mm. Each pack contains 6 or 12 tablets.

Sumatriptan tablets contain sumatriptan, a medicine developed for the treatment of migraine. The symptoms of migraine may be due to temporary swelling of blood vessels in the head. 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.

2. BEFORE YOU TAKE SUMATRIPANT 100 mg TABLETS
Please consult your doctor, even if these statements were applicable to you any time in the past.

Do not take Sumatriptan 100 mg tablets:
- If you are allergic (hypersensitive) to sumatriptan, any of the other ingredients of Sumatriptan tablets or to medicines called triptans.
- If you have history of cerebrovascular accident (CVA) or transient ischaemic attack (TIA).
- If you have severe hepatic impairment.
- If you have moderate and severe hypertension and mild uncontrolled hypertension.
- If you are taking monoamine oxidase inhibitors. Sumatriptan tablets must not be used within two weeks of discontinuation of therapy with monoamine oxidase inhibitors (MAOIs).

Take special care with Sumatriptan 100 mg tablets:
- Sumatriptan tablets should only be used when there is a clear diagnosis of migraine.
- Sumatriptan is not indicated for use in the management of hemiplegic, basilar or optocephaloplastic 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).
- If you suffer transient symptoms including chest pain and lightheadness 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 you should consult your doctor.
- 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 if you are a postmenopausal women or a male 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 case reports of patients with weakness, hyper-reflexia, and incoordination following the use of a selective serotonin reuptake inhibitor (SSRI) and sumatriptan. If you are taking these medicines, you should inform your doctor.
- Sumatriptan should be administered with caution to patients with conditions which may affect significantly the absorption, metabolism or excretion of drugs. A 50mg dose should be considered in patients with hepatic impairment. If you have impaired hepatic or renal function, inform your doctor.
- If you are allergic to sulfonamides, you should inform your doctor. Patients with known hypersensitivity to sulfonamides 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.
- If you are under treatment with herbal preparations containing St John’s Wort (hypericum perforatum) and are sumatriptan tablets, undesirable effects may be more common.

Pregnancy
Ask your doctor or pharmacist for advice before using any medicine.

Although the available data do not indicate that direct teratogenic effects are produced under treatment with sumatriptan, these data contain insufficient information to draw definitive conclusions.

Breast-feeding
Ask your doctor or pharmacist for advice before using any medicine.

It has been demonstrated that following subcutaneous administration, sumatriptan is excreted into breast milk. Infant exposure can be minimised by avoiding breast feeding for 24 hours after treatment.
Driving and using machines
Sumatriptan tablets may cause drowsiness. If you are affected do not drive or operate machines.

Important information about some of the ingredients of Sumatriptan 100 mg tablets
This medicine contains aspirin, a source of phenylalanine. May be harmful for people with phenylketonuria. If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicinal product.

Taking other medicines
- Sumatriptan has the potential to interact with monoamine oxidase inhibitors (MAOIs), ergotamine and derivatives of ergotamine. The increased risk of coronary vasospasm is a theoretical possibility and concomitant administration is contraindicated. (Do not take Sumatriptan 100 mg tablets). 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.

Rarely, an interaction may occur between sumatriptan and selective serotonin reuptake inhibitor (SSRIs) (see Take special care with Sumatriptan 100 mg tablets).

3. HOW TO TAKE SUMATRIPTAN 100 mg TABLETS

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

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

The recommended dose of oral Sumatriptan is a single 50 mg tablet. Some patients may require 100 mg. 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 300 mg is taken in any 24 hour period.

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

Sumatriptan tablets 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.

Tablets should not be broken/divided and should be swallowed whole with water.

Children (under 16 years of age)
The safety and effectiveness of Sumatriptan tablets in children has not yet been established. The use of Sumatriptan tablets in children is not recommended.

Elderly (Over 65)
Experience of the use of Sumatriptan tablets 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.

If you take more Sumatriptan tablets than you should
If you may have taken more Sumatriptan 100 mg tablets than you should, talk to a doctor or pharmacist immediately.

4. POSSIBLE SIDE EFFECTS

Like all medicines, Sumatriptan tablets, can cause side effects, although not everybody gets them. The following side effects can occur:

General
The following symptoms are usually transient and may be intense and can affect any part of the body including the chest and throat, pain, sensations of tingling, heat, heaviness, pressure or tightness. The following symptoms are mild to moderate in intensity and transient: flushing, dizziness and feelings of weakness.

Fatigue and drowsiness have been reported.

Cardiovascular
Hypertension, bradycardia, tachycardia, palpitations.

Transient increases in blood pressure arising soon after treatment have been recorded. In extremely rare cases, serious coronary events have been reported which have included cardiac arrhythmias, ischaemic ECG changes, coronary artery vasospasm or myocardial infarction (see contraindications and Precautions and Warnings).

There have also been rare reports of Raynaud’s phenomenon and ischaemic colitis.

Gastrointestinal
Nausea and vomiting occurred in some patients but the relationship to sumatriptan is not clear.

CNS
There have been rare reports of seizures following use of sumatriptan. 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.

Eye Disorders
Patients treated with Sumatriptan tablets rarely exhibit visual disorders like flickering and diplopia. Additionally, cases of nyctalopia, scotoma and reduced vision have been observed. Very rarely, loss of vision has occurred, which is usually transient. However, visual disorders may also occur during a migraine attack itself.

Hypersensitivity/Allergic reactions ranging from cutaneous hypersensitivity to, in rare cases, anaphylaxis.

Laboratory values
Minor disturbances in liver function tests have occasionally been observed.

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

5. STORING SUMATRIPTAN 100 mg TABLETS

Store the tablets in the original packaging. Keep out of the reach and sight of children. There are no special storage conditions. Do not use Sumatriptan 50 mg tablets after the expiry date on the carton.

Applicable to all medicines
Old and unnecessary medicines can be returned to the chemist for destruction.

This leaflet was last approved on XXX.
2 Tablets
SUMATRIPTAN 50 mg tablets
Sumatriptan (as succinate)
SUMATRIPTAN 50 mg tablets
For oral administration
POM

SUMATRIPTAN 50 mg tablets
Sumatriptan (as succinate)
Each tablet contains 50 mg of sumatriptan (as succinate).
Also contains lactose monohydrate and aspartame (E951).
Read the package leaflet before use.

2 Tablets
SUMATRIPTAN 50 mg tablets
Sumatriptan (as succinate)
For oral administration
POM

Medicinal product subject to medical prescription.
Take as directed by your physician.
Keep out of reach and sight of children.
Store in the original package.

Laboratorios Licensa, S.A.
Gran Via Carlos III, 56, 7th floor
08028 Barcelona (Spain)
SUMATRIPTAN 100 mg tablets
Sumatriptan (as succinate)
For oral administration
POM

SUMATRIPTAN 100 mg tablets
Sumatriptan (as succinate)
Each tablet contains 100 mg of sumatriptan (as succinate).
Also contains lactose monohydrate and aspartame (E951).
Read the package leaflet before use.

SUMATRIPTAN 100 mg tablets
Sumatriptan (as succinate)
6 Tablets
For oral administration
POM

Medicinal product subject to medical prescription.
Take as directed by your physician.
Keep out of reach and sight of children.
Store in the original package.
SUMATRIPTAN 100 mg tablets
Sumatriptan (as succinate)
SUMATRIPTAN 100 mg tablets
For oral administration

Each tablet contains 100 mg of sumatriptan (as succinate). Also contains lactose monohydrate and aspartame (E951). Read the package leaflet before use.

12 Tablets
SUMATRIPTAN 100 mg tablets
Sumatriptan (as succinate)
For oral administration

Medicinal product subject to medical prescription. Take as directed by your physician. Keep out of reach and sight of children. Store in the original package.

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