

SUMATRIPTAN 50MG TABLETS

PL 08553/0239

&

SUMATRIPTAN 100MG TABLETS

PL 08553/0240

(SUMATRIPTAN SUCCINATE)

UKPAR

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LAY SUMMARY

The Medicines and Healthcare products Regulatory Agency (MHRA) granted Dr Reddy's Laboratories (UK) Ltd. Marketing Authorisations (licences) for the medicinal products Sumatriptan 50mg Tablets (PL 08553/0239) and Sumatriptan 100mg Tablets (PL 08553/0240) on 18th December 2008. These are prescription-only medicines used for the treatment of migraine.

The active ingredient is sumatriptan succinate, one of a group of medicines called 5HT₁ receptor agonists. The symptoms of migraine may be caused by a temporary swelling of blood vessels in your head. This type of medicine works by reducing this swelling.

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

SUMATRIPTAN 50MG TABLETS
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SCIENTIFIC DISCUSSION

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INTRODUCTION

Based on the review of the data on quality, safety and efficacy, the MHRA granted Dr Reddy's Laboratories (UK) Ltd Marketing Authorisations for the medicinal products Sumatriptan 50mg Tablets (PL 08553/0239) and Sumatriptan 100mg Tablets (PL 08553/0240) on 18th December 2008. The products are prescription-only medicines.

These are abridged applications for Sumatriptan 50mg Tablets and Sumatriptan 100mg Tablets. These are two strengths of sumatriptan, submitted under Article 10.1 of Directive 2001/83/EC, as amended, claiming to be generic medicinal versions of their respective reference products, Imigran Tablets 50mg and Imigran Tablets 100mg (PL 10949/0222 & 10949/0231), authorised to Glaxo Wellcome UK Limited. These were the innovator products. The reference products have been authorised in the UK for more than 10 years, so the period of data exclusivity has expired.

Sumatriptan 50mg Tablets and Sumatriptan 100mg Tablets contain the active ingredient sumatriptan, as the succinate. Sumatriptan belongs to a group of medicines known as selective 5-HT₁ receptor agonists, which fall under the pharmacotherapeutic group – anti-migraine preparations. Sumatriptan is indicated for the acute relief of migraine attacks, with or without aura. Sumatriptan should only be used where there is a clear diagnosis of migraine.

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.

These applications for Sumatriptan 50mg Tablets and Sumatriptan 100mg Tablets were submitted at the same time and both are supported by the bioequivalence study presented comparing the applicant's 100mg product with the reference product Imigran Tablets 100mg, Glaxo Wellcome UK Limited. Consequently, all sections of the Scientific Discussion refer to both products.

PHARMACEUTICAL ASSESSMENT

ACTIVE SUBSTANCE

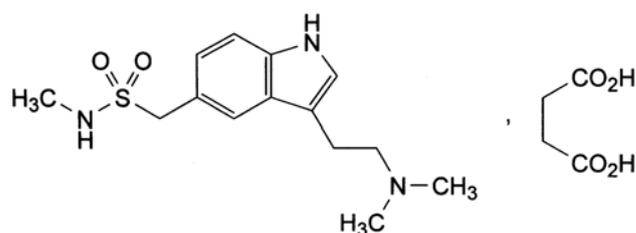
Sumatriptan succinate

Nomenclature:

INN: Sumatriptan succinate

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

Structure:



Molecular formula: $C_{18}H_{27}N_3O_6S$

Molecular weight: 413.5

CAS No: 103628-48-4

Physical form: White or almost white powder

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

The active substance, sumatriptan succinate, is the subject of a European Pharmacopoeia (EP) monograph.

All aspects of the manufacture and control of sumatriptan succinate are supported by an EDQM Certificate of Suitability. This certificate is accepted as confirmation of the suitability of sumatriptan succinate for inclusion in this medicinal product.

Active sumatriptan succinate is stored in appropriate packaging. The primary packaging in direct contact with the active substance satisfies Directive 2002/72/EC (as amended), and is suitable for contact with foodstuffs.

Appropriate stability data have been generated for sumatriptan succinate stored in the proposed packaging. These data demonstrate the stability of the active substance and an appropriate retest period has been set.

DRUG PRODUCT

Description and Composition

Sumatriptan 50mg Tablets are white, round, film-coated, embossed with 'RDY' on one side and '292' on the other side, and contain 50mg of the active ingredient sumatriptan. Sumatriptan 100mg Tablets are white, capsule-shaped, film-coated, embossed with 'RDY' on one side and '293' on the other side, and contain 100mg of the active ingredient sumatriptan.

Other ingredients consist of pharmaceutical excipients, namely lactose monohydrate, microcrystalline cellulose, croscarmellose sodium, anhydrous lactose, and magnesium stearate making up the tablet core; and lactose monohydrate, mannitol (E421), titanium dioxide (E171), triacetin, and talc making up the film coating. Appropriate justification for the inclusion of each excipient has been provided.

All excipients used comply with their respective European Pharmacopoeia monographs. Satisfactory Certificates of Analysis have been provided for all excipients.

The magnesium stearate is of vegetable origin. The only excipient used that contains material of animal or human origin is lactose monohydrate. The applicant has provided a declaration that milk used in the production of lactose monohydrate is sourced from healthy animals under the same conditions as that for human consumption.

There were no novel excipients used and no overages.

Dissolution and Impurity profiles

Satisfactory comparative dissolution data were provided for the test and reference products. The dissolution profiles were found to be similar.

Impurity data were also provided for the Sumatriptan 50mg tablets and the originator product, Imigran 50mg tablets. The impurity profiles were found to be similar, with all impurities within the specification limits.

Pharmaceutical development

Details of the pharmaceutical development of the drug products have been supplied and are satisfactory.

Manufacture

A description and flow-chart of the manufacturing method has been provided.

In-process controls are appropriate considering the nature of the product and the method of manufacture. Process validation studies have been conducted and are satisfactory.

Finished product specification

The finished product specifications proposed for both release and shelf life are acceptable, and provide an assurance of the quality and consistency of the finished products. Acceptance limits have been justified with respect to conventional pharmaceutical requirements and, where appropriate, safety. 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 reference standards used.

Container Closure System

The tablets are presented in PVdC (polyvinylidene chloride) coated PVC (polyvinylchloride) / aluminium blister strips. Both strengths are packed in blister strips of 2, 3, 4 or 6 tablets, which are placed with the Patient Information Leaflet (PIL) into cardboard outer cartons. The finished products are packaged in carton pack sizes of 2, 3, 4, 6, 12 or 18 tablets. The MA Holder has stated that not all pack sizes may be marketed.

Specifications and Certificates of Analysis for all packaging components used have been provided. These are satisfactory. All primary product packaging complies with EU legislation, Directive 2002/72/EC (as amended), and is suitable for contact with foodstuffs.

Stability

Finished product stability studies have been conducted in accordance with current guidelines and results were within the proposed specification limits. Based on the results, a shelf-life of 2 years has been set, which is satisfactory. Storage conditions are 'Keep in the original packaging'.

Bioequivalence Study

A bioequivalence study was presented comparing the test product, Sumatriptan 100mg Tablets, to the reference product, Imigran Tablets 100mg, Glaxo Wellcome UK Limited.

An evaluation of the bioequivalence study is found in the Clinical Assessment section.

Quality Overall Summary

A satisfactory QOS is provided, and has been prepared by an appropriately qualified expert. An appropriate CV for the expert has been supplied.

Product Information

The approved SmPCs, leaflet, and labelling are satisfactory. Colour mock-ups of the labelling have been provided. The labelling is satisfactory and fulfils the statutory requirements for Braille.

Conclusion

The test products are pharmaceutically equivalent to their respective reference products which have been licensed in the UK for over 10 years. The drug products correspond to the current EU definition of a generic medicinal product because they comply with the criteria of having the same qualitative and quantitative composition in terms of the active substance and pharmaceutical form. On this basis, and considering the bioequivalence data provided, the applicant's claim that Sumatriptan 100mg Tablets is a generic medicinal product of Imigran Tablets 100mg is justified.

The pharmaceutical conditions for a biowaiver were met. Therefore, in line with 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 were extrapolated to the 50mg strength product.

All pharmaceutical issues have been resolved and the quality grounds for these applications are considered adequate. It was, therefore, recommended that Marketing Authorisations be granted.

PRECLINICAL ASSESSMENT

These abridged applications for Sumatriptan 50mg Tablets and Sumatriptan 100mg Tablets were submitted according to Article 10.1 of Directive 2001/83/EC, as amended.

No new preclinical data have been supplied with these applications and none are required for applications of this type. A preclinical overview has been written by a suitably qualified person and is satisfactory.

CLINICAL ASSESSMENT

INDICATIONS

Sumatriptan 50mg Tablets and Sumatriptan 100mg Tablets are indicated for the acute relief of migraine attacks, with or without aura. Sumatriptan should only be used where there is a clear diagnosis of migraine.

The indications are consistent with those for the innovator products and are satisfactory.

POSODOLOGY AND METHOD OF ADMINISTRATION

The posology is consistent with that for the innovator products and is satisfactory.

TOXICOLOGY

No new data have been submitted and none are required for applications of this type.

CLINICAL PHARMACOLOGY

Pharmacodynamics

Sumatriptan belongs to a group of medicines known as selective 5-HT₁ receptor agonists (ATC Code N02C C01), which fall under the pharmacotherapeutic group – anti-migraine preparations.

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.

Pharmacokinetics

Following oral administration sumatriptan is rapidly absorbed, 70% of the maximum concentration being reached after approximately 45 minutes. After oral administration of 100 mg the peak plasma concentration is, on average, 54 ng/ml. Absolute bioavailability after oral administration is on average 14%. This is partly due to presystemic metabolism and partly to incomplete absorption. In patients with hepatic insufficiency, presystemic clearance after oral administration is reduced, resulting in an increase in the plasma levels of sumatriptan.

Protein binding is low (14-21%) and the mean volume of distribution is 170 litres. The elimination half-life is approximately 2 hours. Mean total clearance is 1160 ml/minute and mean renal clearance is approximately 260 ml/minute. Non-renal clearance is approximately 80% of total clearance, suggesting that sumatriptan is

primarily cleared through oxidative metabolism mediated by monoamine oxidase A. The major metabolite, the indole acetic acid analogue of sumatriptan, is excreted in the urine as the acid or as the glucuronide conjugate. This metabolite has no known 5HT₁ or 5HT₂ activity. Minor metabolites have not been identified. The pharmacokinetics of the oral administration of sumatriptan do not appear to be influenced by a migraine attack.

Pharmacokinetics - Bioequivalence study

The applicant presented a single bioequivalence study comparing the test product, Sumatriptan 100mg Tablets, to the reference product, Imigran Tablets 100mg (Glaxo Wellcome UK Limited) under fasting conditions. Satisfactory Certificates of Analysis for the test and reference products were provided.

This was a conventional; randomised, single-dose, open-label, two-period, two-way crossover, laboratory-blind study designed to assess the bioavailability of the test product versus the reference product under fasting conditions, conducted in 32 healthy adult human subjects. The study was of an appropriate design and was conducted to principles of Good Clinical Practice.

A single dose of the investigational products was administered orally with 240 ml of water to each subject in each period, after an overnight fast of at least 10 hours. Treatment periods 1 and 2 were separated by a satisfactory washout period of 13 days. Blood samples were obtained at 19 time points up to 12 hours post dose, and plasma sumatriptan content was analysed employing a validated LC-MS/MS method. Plasma samples of all 32 subjects were analysed.

Statistical evaluation was performed for the primary pharmacokinetic parameters for this study; C_{max}, AUC_{0-t}, and AUC_{0-∞}. Bioequivalence of the test product versus the reference product was concluded if the 90% CI fell within the acceptance range, 0.80-1.25 (80%-125%), for log-transformed C_{max}, AUC_{0-t}, and AUC_{0-∞}.

The results are summarised in the table below:

Table: Pharmacokinetic results for a randomised single dose crossover study between the test and reference product. Log transformed. ANOVA. N = 32 healthy adult subjects, dosed fasted; t = 12 hours. 13 days wash out period.

Test parameter	Test product (geometric mean)	Reference product (geometric mean)	Ratio * Test/reference x 100	90% Confidence intervals **
AUC _{0-t} (ng.h/ml)	231	226	102	96.6 – 108
AUC _{0-∞} (ng.h/ml)	243	236	103	97.0 – 109
C _{max} (ng/ml)	54.8	52.1	105	98.0 – 113

* : Point estimate of 'test/reference' mean ratio from analysis of log-transformed data.

** : 90% Confidence interval for the 'test/reference' mean ratio from analysis of variance of log-transformed data.

The 90% confidence intervals for the log-transformed parameters C_{max}, AUC_{0-t} and AUC_{0-∞} of sumatriptan lie within the range 80-125%, such that the test and reference products can be considered bioequivalent after a single dose under fasted conditions.

The multiple dose waiver criteria are met and hence this study is also accepted as demonstrating bioequivalence for the 50mg tablet strength.

EFFICACY

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

Efficacy is reviewed in the clinical overview. The reference products are established and the applications depend upon the bioequivalence study.

SAFETY

No new data are submitted and none are required for applications of this type. Safety is reviewed in the clinical overview. No serious or significant adverse events were reported during the bioequivalence study.

EXPERT REPORT

A satisfactory clinical overview is provided, and has been prepared by an appropriately qualified expert. An appropriate CV for the expert has been supplied.

PRODUCT INFORMATION:

Summary of Product Characteristics (SmPC)

The approved SmPCs are consistent with those for the reference products and are acceptable.

Patient Information Leaflet (PIL)

The final PIL is in line with the approved SmPCs and is satisfactory.

Labelling

Colour mock-ups of the labelling have been provided. The labelling is satisfactory.

CONCLUSIONS

All issues have been adequately addressed by the applicant. The bioequivalence study was of an appropriate design and demonstrates the bioequivalence of the test (Sumatriptan 100mg Tablets) and reference (Imigran 100mg Tablets) products within general acceptance limits.

As the test products, Sumatriptan 50mg Tablets and Sumatriptan 100mg Tablets, meet the criteria 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 were extrapolated to the 50mg strength tablets. It is therefore concluded that the 50mg strength formulation is bioequivalent to its corresponding marketed brand formulation, despite bioequivalence not being assessed explicitly.

Sufficient clinical information has been submitted to support these applications. Marketing Authorisations were, therefore, recommended to be granted on medical grounds.

OVERALL CONCLUSION AND RISK BENEFIT ASSESSMENT

QUALITY

The important quality characteristics of Sumatriptan 50mg Tablets and Sumatriptan 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 reference product Imigran 100mg Tablets (Glaxo Wellcome UK Limited). As the applicant's products were deemed to meet the criteria 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 were extrapolated to the 50mg tablet strength. Thus, no separate bioequivalence studies were necessary for this strength.

No new or unexpected safety concerns arise from these applications.

PRODUCT LITERATURE

The approved SmPCs, PIL and labelling are satisfactory and consistent with those for the reference products Imigran 500mg Tablets and Imigran 100mg Tablets.

A package leaflet has been submitted to the MHRA along with results of consultations with target patient groups ("user testing"), in accordance with Article 59 of Council Directive 2001/83/EC. The results indicate that the package leaflet is well-structured and organised, easy to understand and written in a comprehensive manner. The testing shows that the patients/users are able to act upon the information that the leaflet contains.

The approved labelling artwork complies with statutory requirements. In line with current legislation, the name of the product in Braille appears on the outer packaging and sufficient space has been included for a standard UK pharmacy dispensing label.

RISK BENEFIT ASSESSMENT

The quality of the products is acceptable and no new preclinical or clinical safety concerns have been identified. The bioequivalence study and the valid extrapolation of its results and conclusions support the claim that the applicant's products and their respective reference products are interchangeable. Extensive clinical experience with sumatriptan is considered to have demonstrated the therapeutic value of the active substance. The risk: benefit is, therefore, considered to be positive.

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SUMATRIPTAN 100MG TABLETS

PL 08553/0240

(SUMATRIPTAN SUCCINATE)

STEPS TAKEN FOR ASSESMENT

- 1 The MHRA received the marketing authorisation applications on 4th April 2005
- 2 Following standard checks and communication with the applicant the MHRA considered the applications valid on 19th April 2005
- 3 Following assessment of the applications the MHRA requested further information relating to the quality dossiers on 28th February 2006 and 27th September 2006
- 4 The applicant responded to the MHRA's requests, providing further information for the quality sections on 30th August 2006 and 21st October 2006 respectively
- 5 The applications were determined on 18th December 2008

SUMMARY OF PRODUCT CHARACTERISTICS

The UK Summary of Product Characteristics (SmPC) for Sumatriptan 50 mg tablets is as follows:

1 NAME OF THE MEDICINAL PRODUCT

Sumatriptan 50mg Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each film coated tablet contains 50mg sumatriptan (as the succinate).

Also contains lactose.

For a full list of excipients see section 6.1

3 PHARMACEUTICAL FORM

Tablet

Round white film coated tablets embossed 'RDY' on one face and '292' on the other.

4 CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS

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

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

4.2 POSOLOGY AND METHOD OF ADMINISTRATION

Adults

Sumatriptan 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 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 300 mg 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 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 and adolescents (under 18 years of age)

Sumatriptan has 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 years of age)

Experience of the use of sumatriptan in patients aged over 65 years is limited. The pharmacokinetics do not differ significantly from a younger population but until further

clinical data are available, the use of sumatriptan in patients aged over 65 years is not recommended.

Hepatic insufficiency

Low doses of 25-50 mg should be considered for patients with mild to moderate liver impairment.

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 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 Section 4.5.).

Concurrent administration of monoamine oxidase inhibitors and sumatriptan is contraindicated.

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

Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

Sumatriptan 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 Section 4.8.). 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). 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.

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 but caution should be exercised before using sumatriptan in these patients

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

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

Lactose

Sumatriptan Tablets contain lactose and should therefore not be used in patients with rare genetic disorders such as galactose intolerance, Lapp lactase deficiency or glucose-galactose malabsorption.

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 (see also Contraindications). The increased risk of coronary vasospasm is a theoretical possibility and concomitant administration is contraindicated. (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.

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

Rarely, an interaction may occur between sumatriptan and SSRIs (see Section 4.4.).

4.6 PREGNANCY AND LACTATION

Use during pregnancy

Post-marketing data from the use of sumatriptan during the first trimester in over 1,000 women are available. Although these data contain insufficient information to draw definitive conclusions, they do not 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 fetus.

Use during breast-feeding

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 [4]. 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 and 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 and may be intense and can affect any part of the body including the chest and throat).

Uncommon: 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. Tremor, dystonia.

Eye disorders

Very rare: Flickering, diplopia, reduced vision, nystagmus & scotoma. 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

Patients have received up to 12 mg of sumatriptan, as a single subcutaneous injection without significant undesirable effects. With subcutaneous doses exceeding 16 mg and oral doses exceeding 400 mg, no other undesirable adverse effects have been observed than those mentioned in "section 4.8".

In cases of overdose, the patient must be monitored for at least 10 hours and if necessary, standard supportive treatment must be given.

There is no information on the effect of hemodialysis or peritoneal dialysis on plasma sumatriptan concentrations.

5 PHARMACOLOGICAL PROPERTIES**5.1 PHARMACODYNAMIC PROPERTIES**

Pharmacotherapeutic group: Analgesics: antimigraine preparations: selective 5-HT₁ receptor agonists

ATC Code N02C C01

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 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 100 mg oral dose.

Although the recommended dose of oral sumatriptan is 50 mg, migraine attacks vary in severity both within and between patients. Doses of 25 – 100 mg have shown greater efficacy

than placebo in clinical trials, but 25 mg is statistically significantly less effective than 50 and 100 mg.

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 100 mg dose, the maximum plasma concentration is 54 ng/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 1160 ml/min and the mean renal plasma clearance is approximately 260 ml/min. Non-renal clearance accounts for about 80 % of the total clearance. Sumatriptan is eliminated primarily by oxidative metabolism mediated by monoamine oxidase A. The 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

Tablet core

Lactose monohydrate
Croscarmellose sodium
Microcrystalline cellulose
Anhydrous lactose
Magnesium stearate

Film coating

Lactose monohydrate
Mannitol (E421)
Titanium dioxide (E171)
Triacetin
Talc

6.2 INCOMPATIBILITIES

Not applicable.

6.3 SHELF LIFE

2 years.

6.4 SPECIAL PRECAUTIONS FOR STORAGE

Keep in the original packaging.

6.5 NATURE AND CONTENTS OF CONTAINER

Aluminium foil /PVdC coated PVC blister strips of 2, 3, 4, or 6 tablets in cartons of 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

Dr Reddy's Laboratories (UK) Ltd,
6 Riverview Rd, Beverley, HU17 0LD, UK.

8 MARKETING AUTHORISATION NUMBER(S)

PL 08553/0239

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

18/12/2008

10 DATE OF REVISION OF THE TEXT

18/12/2008

SUMMARY OF PRODUCT CHARACTERISTICS

The UK Summary of Product Characteristics (SmPC) for Sumatriptan 100 mg tablets is as follows:

1 NAME OF THE MEDICINAL PRODUCT

Sumatriptan 100mg Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each film coated tablet contains 100mg sumatriptan (as the succinate).

Also contains lactose.

For a full list of excipients see section 6.1

3 PHARMACEUTICAL FORM

Tablet

Capsule-shaped white film coated tablets embossed 'RDY' on one face and '293' on the other.

4 CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS

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

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

4.2 POSOLOGY AND METHOD OF ADMINISTRATION

Adults

Sumatriptan 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 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 300 mg 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 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 and adolescents (under 18 years of age)

Sumatriptan has 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 years of age)

Experience of the use of sumatriptan in patients aged over 65 years is limited. The pharmacokinetics do not differ significantly from a younger population but until further

clinical data are available, the use of sumatriptan in patients aged over 65 years is not recommended.

Hepatic insufficiency

Low doses of 25-50 mg should be considered for patients with mild to moderate liver impairment.

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 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 Section 4.5.).

Concurrent administration of monoamine oxidase inhibitors and sumatriptan is contraindicated.

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

Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

Sumatriptan 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 Section 4.8.). 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). 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.

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 but caution should be exercised before using sumatriptan in these patients

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

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

Lactose

Sumatriptan Tablets contain lactose and should therefore not be used in patients with rare genetic disorders such as galactose intolerance, Lapp lactase deficiency or glucose-galactose malabsorption.

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 (see also Contraindications). The increased risk of coronary vasospasm is a theoretical possibility and concomitant administration is contraindicated. (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.

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

Rarely, an interaction may occur between sumatriptan and SSRIs (see Section 4.4.).

4.6 PREGNANCY AND LACTATION

Use during pregnancy

Post-marketing data from the use of sumatriptan during the first trimester in over 1,000 women are available. Although these data contain insufficient information to draw definitive conclusions, they do not 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 fetus.

Use during breast-feeding

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 [4]. 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 and 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 and may be intense and can affect any part of the body including the chest and throat).

Uncommon: 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. Tremor, dystonia.

Eye disorders

Very rare: Flickering, diplopia, reduced vision, nystagmus & scotoma. 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

Patients have received up to 12 mg of sumatriptan, as a single subcutaneous injection without significant undesirable effects. With subcutaneous doses exceeding 16 mg and oral doses exceeding 400 mg, no other undesirable adverse effects have been observed than those mentioned in “section 4.8”.

In cases of overdose, the patient must be monitored for at least 10 hours and if necessary, standard supportive treatment must be given.

There is no information on the effect of hemodialysis or peritoneal dialysis on plasma sumatriptan concentrations.

5 PHARMACOLOGICAL PROPERTIES**5.1 PHARMACODYNAMIC PROPERTIES**

Pharmacotherapeutic group: Analgesics: antimigraine preparations: selective 5-HT₁ receptor agonists

ATC Code N02C C01

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 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 100 mg oral dose.

Although the recommended dose of oral sumatriptan is 50 mg, migraine attacks vary in severity both within and between patients. Doses of 25 – 100 mg have shown greater efficacy

than placebo in clinical trials, but 25 mg is statistically significantly less effective than 50 and 100 mg.

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 100 mg dose, the maximum plasma concentration is 54 ng/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 1160 ml/min and the mean renal plasma clearance is approximately 260 ml/min. Non-renal clearance accounts for about 80 % of the total clearance. Sumatriptan is eliminated primarily by oxidative metabolism mediated by monoamine oxidase A. The 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

Tablet core

Lactose monohydrate
Croscarmellose sodium
Microcrystalline cellulose
Anhydrous lactose
Magnesium stearate

Film coating

Lactose monohydrate
Mannitol (E421)
Titanium dioxide (E171)
Triacetin
Talc

6.2 INCOMPATIBILITIES

Not applicable.

6.3 SHELF LIFE

2 years.

6.4 SPECIAL PRECAUTIONS FOR STORAGE

Keep in the original packaging.

6.5 NATURE AND CONTENTS OF CONTAINER

Aluminium foil /PVdC coated PVC blister strips of 2, 3, 4, or 6 tablets in cartons of 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

Dr Reddy's Laboratories (UK) Ltd,
6 Riverview Rd, Beverley, HU17 0LD, UK.

8 MARKETING AUTHORISATION NUMBER(S)

PL 08553/0240

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

18/12/2008

10 DATE OF REVISION OF THE TEXT

18/12/2008

PATIENT INFORMATION LEAFLET

PACKAGE LEAFLET: INFORMATION FOR THE USER Sumatriptan 50mg & 100mg Tablets

Read this entire leaflet before you start taking this medicine:

Keep this leaflet as you may wish to read it again. If you have any further questions, ask your doctor or pharmacist. Remember 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. If any of the side effects are serious or you notice any side effects not listed in this leaflet please tell your doctor or pharmacist.

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. How to store your Sumatriptan Tablets
6. Further information



1. What Sumatriptan Tablets are and what they are used for

Sumatriptan is one of a group of medicines called 5HT₁ receptor agonists that are used to treat migraine. The symptoms of migraine may be caused by a temporary swelling of blood vessels in your head. This type of medicine works by reducing this swelling. Sumatriptan cannot prevent a migraine attack.

2. Before you take Sumatriptan Tablets

If you have been allergic to sumatriptan, sulphonamides or any of the other ingredients in Sumatriptan Tablets, listed in Section 6, do not take this medicine.

You should make sure you have told your doctor or pharmacist about any other medicines that you are taking including any you have bought without a prescription. If you can answer yes to any of the following questions, talk to your doctor before taking this medicine:

- You suffer from heart disease, angina or have had a heart attack in the past
- You have risk factors for heart disorders such as a family history of heart disease, sugar diabetes, have high blood cholesterol, being overweight, smoking regularly, being a male over 40 years old or a postmenopausal woman
- You suffer from any kind of vascular disease
- You suffer from high blood pressure
- You have previously had a stroke or even a temporary form of stroke lasting less than 24 hours (transient ischaemic attack or TIA)
- You suffer from any liver problems
- You are taking or have recently taken any drugs to treat depression including medicines called lithium, Monoamine Oxidase Inhibitors (MAOIs), or other antidepressants called SSRIs (for example citalopram, fluoxetine, fluvoxamine, paroxetine, or sertraline)
- You are taking any medicines to help lose weight or treat epilepsy
- You are taking the herbal remedy St John's Wort (*Hypericum perforatum*)
- You are pregnant, likely to get pregnant or breast feeding
- If you have been told by your doctor that you have intolerance to some sugars.

Your doctor may still want you to take these tablets and will advise you about taking these tablets.

Driving and using machines

You may suffer drowsiness, dizziness or other related symptoms either due to the migraine itself or the use of these tablets. If affected do not operate machinery or drive.

Important information about some of the ingredients of Sumatriptan Tablets

These tablets contain lactose. If you are intolerant of some sugars then consult your doctor before taking these tablets.

3. How to take Sumatriptan Tablets

Sumatriptan tablets are for the treatment of migraine in adults only. The tablets should be swallowed whole with water do not chew or crush the tablets. You should take these tablets as early as possible during a migraine attack although they should still be beneficial no matter when taken during a migraine. Do not take these tablets to prevent a migraine.

The usual dose is one 50mg tablet but you may require a 100mg tablet depending upon your individual response. If you have any liver problems your doctor may advise a lower dose..

This medicine is not recommended in children and the elderly over 65.

If you respond to the first tablet but symptoms return a second tablet may be taken in the next 24 hours provided you allow at least 2 hours between tablets and do not take more than 300mg in 24 hours. If you fail to respond, do not take a second tablet but Aspirin or other pain relief medicines may be used.

If you take more Sumatriptan Tablets than you should: contact your doctor or go to the local hospital accident and emergency department immediately and take this leaflet and any remaining Sumatriptan Tablets with you.

4. Possible side effects

As with all medicines, you may experience some side effects when taking sumatriptan tablets.

If you experience any of the following rare but serious side effects, stop taking these tablets and contact your doctor immediately as you may be allergic to these tablets: severe skin rash or itching, swelling of the face, mouth or lips, difficulty swallowing, difficulty breathing or shortness of breath, chest pain or collapse.

Common side effects: (affecting more than 1% but less than 10% of people)

Tingling, dizziness, drowsiness: temporary increases in blood pressure soon after treatment: flushing: nausea (feeling sick) and vomiting (being sick): feelings of heaviness, pressure or tightness (these usually pass quickly but may be intense and can occur in any part of the body including the chest and throat): feelings of heat or pain:

Uncommon: (between 1 in 100 to one in a 1000)

Feelings of weakness and fatigue (feeling very tired) these are usually mild and pass quickly.

Very rare: (affecting less than 1 in 10,000 people)

Allergic reactions which may be severe (see the beginning of this section): seizures (epileptic fits): involuntary movements: visual disorders including double vision or even a temporary loss of vision (these are rare and may be due to the migraine itself): heart problems which show up as irregular heart beats or a heart attack, an increase or a decrease in heart rate (palpitations): low blood pressure; Raynaud's syndrome (a condition where the fingers and toes become white and numb): inflammation of the colon (this may show as a pain in the lower left side of your belly and bloody diarrhoea): neck stiffness.

Sumatriptan may affect liver function tests. If you have any blood tests to monitor your liver function, tell the doctor or nurse that you are taking these tablets.

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

5. How to store your Sumatriptan Tablets

Keep the blisters in the box. The blisters and box have an expiry date printed on them, do not take these tablets if this date has passed. Keep your tablets in a safe place out of the reach and sight of children. Any unused tablets can be returned to your pharmacist for safe disposal.

6. Further information

What Sumatriptan Tablets contain

Each white film coated tablet contains either 50mg or 100mg of sumatriptan (as the succinate).

Both strengths also contain lactose, powered cellulose, mannitol, titanium dioxide (E171), triacetin, magnesium stearate and talc.

What Sumatriptan Tablets look like

The 50mg strength is a white round tablet embossed with RDY on one face and 292 on the other. The 100mg strength is a white capsule shaped tablet embossed with RDY on one face and 293 on the other.

Contents of the pack

Both strengths are available in packs of 2, 3, 4, 6 and 12 tablets.

The 50mg tablets are also available in packs of 18 tablets.

Marketing Authorisation Holder and Manufacturer:

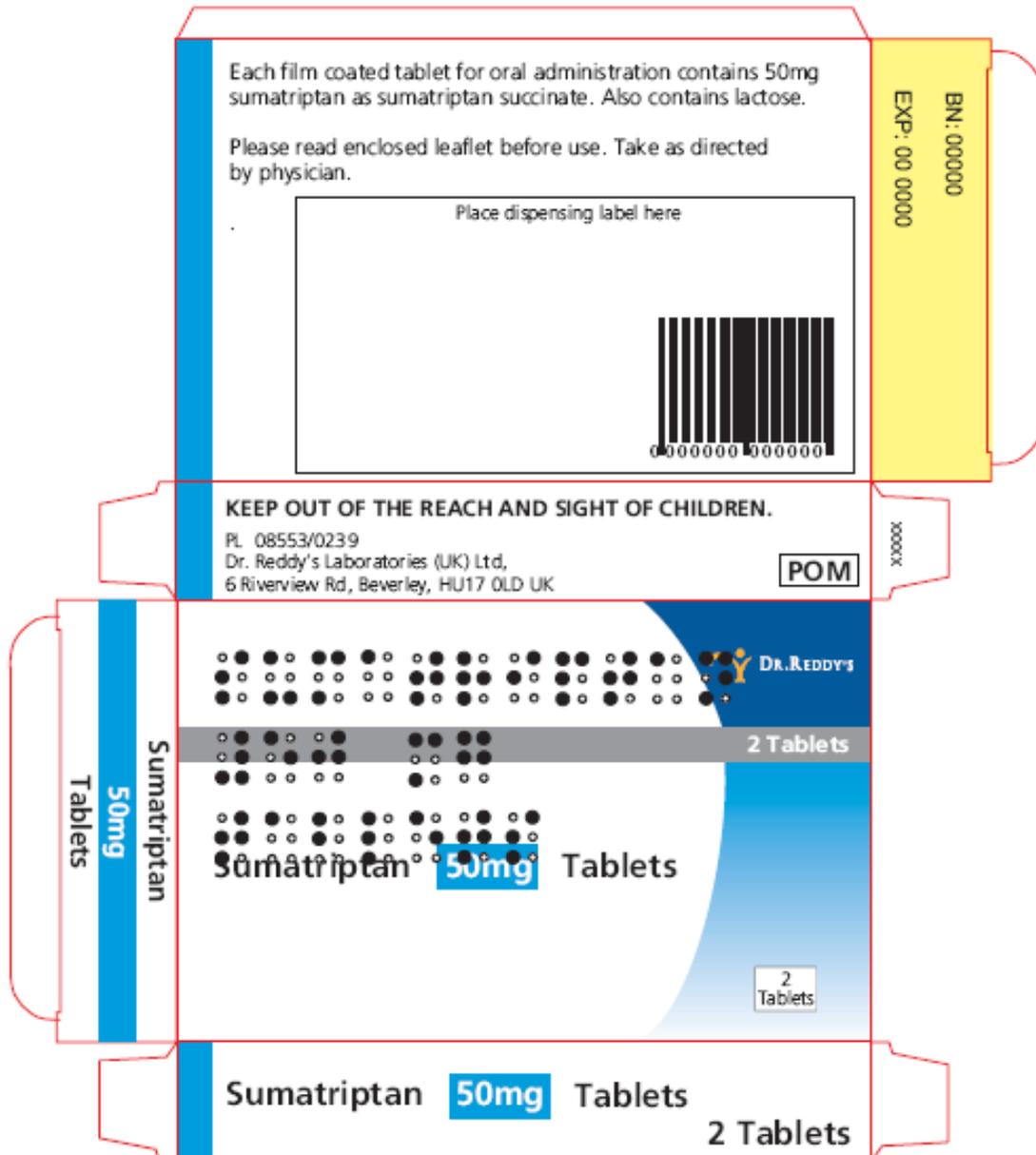
Dr Reddy's Laboratories (UK) Ltd
6 Riverview Rd, Beverley,
HU17 0LD, UK

Sumatriptan 50mg Tablets, PL 08553/0239
Sumatriptan 100mg Tablets, PL 08553/0240
Date of preparation: 10/2006

LABELLING

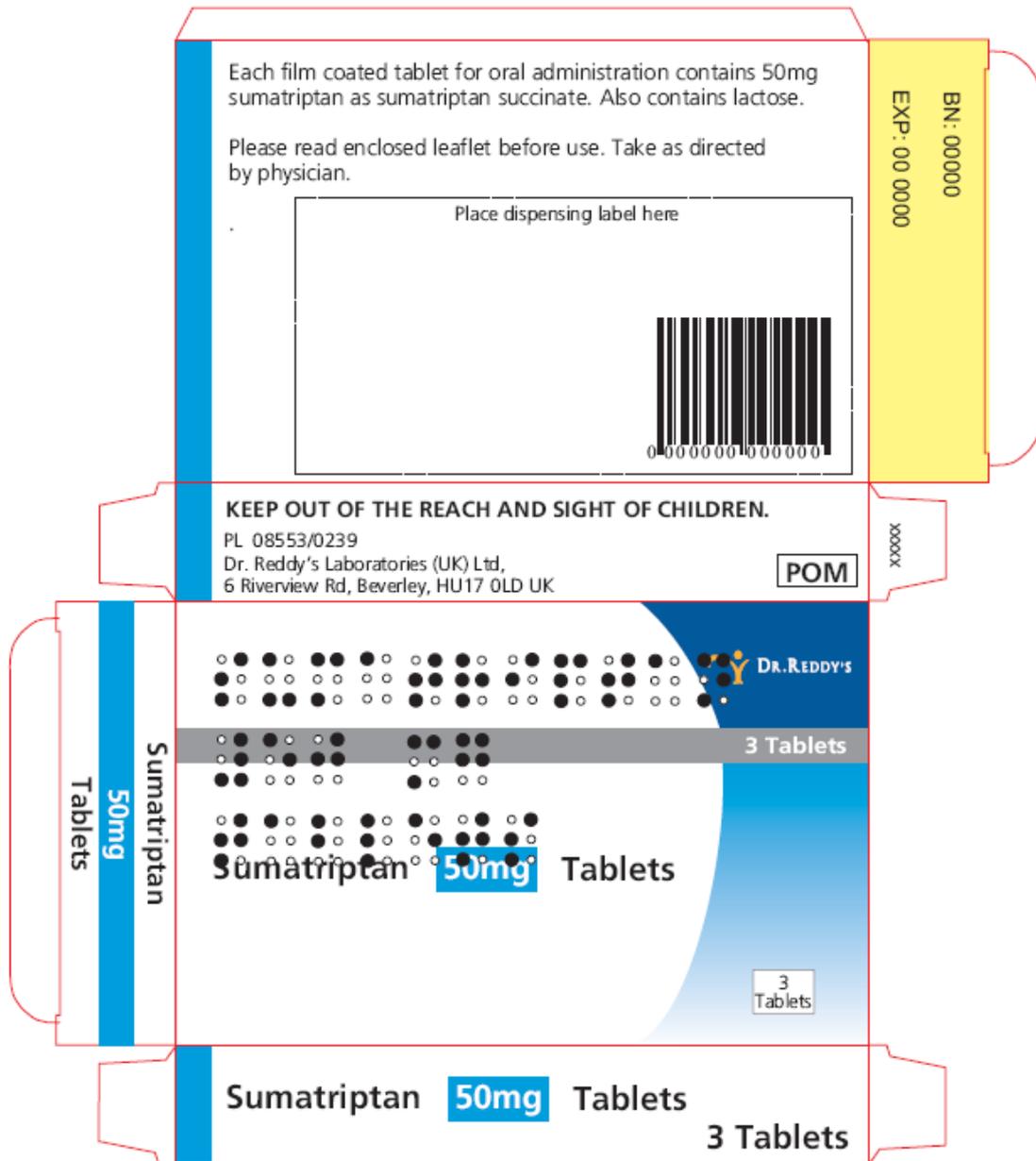
Sumatriptan 50mg Tablets - Carton for blisters, with Braille

Pack size 2



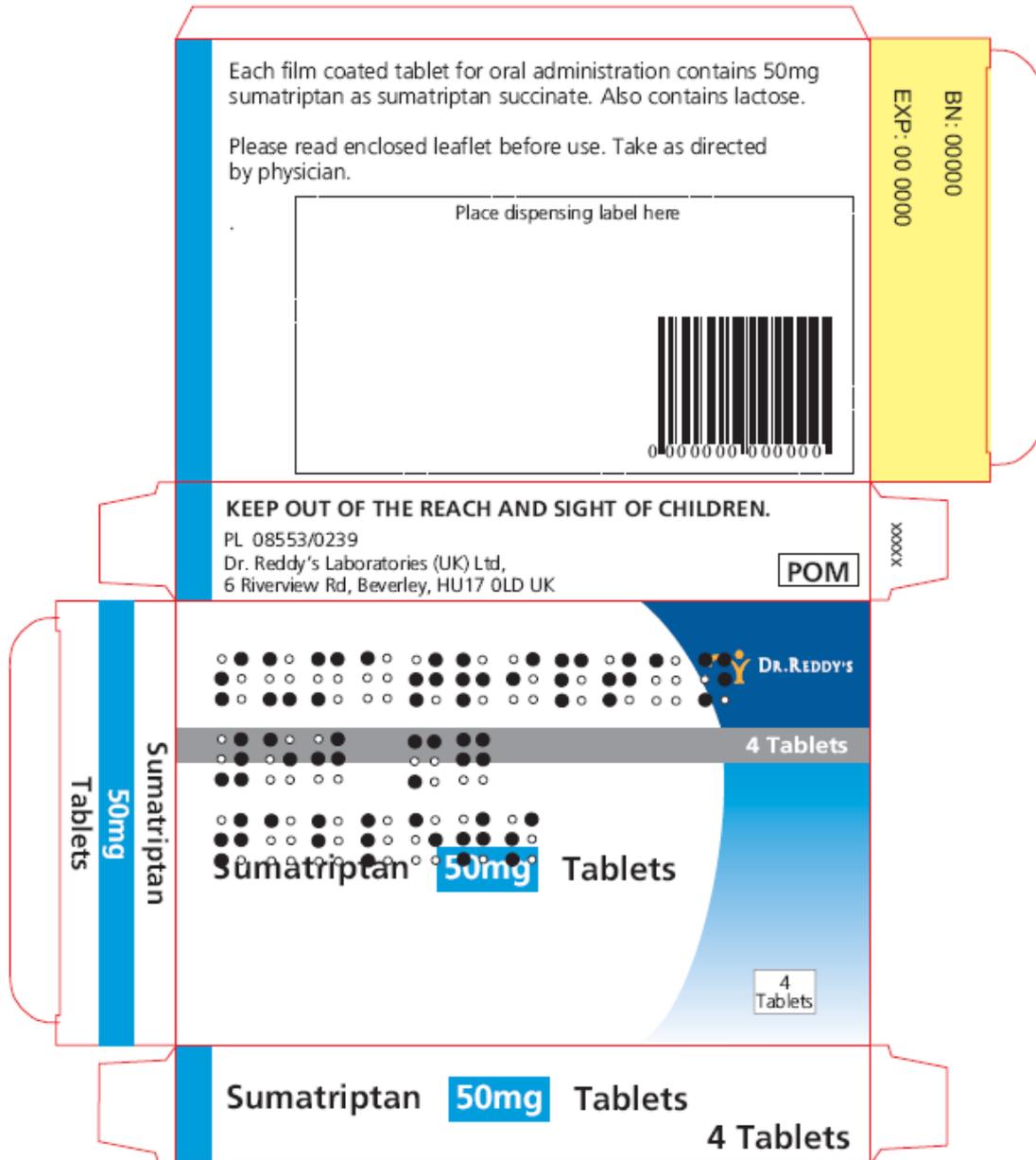
Sumatriptan 50mg Tablets - Carton for blisters, with Braille

Pack size 3



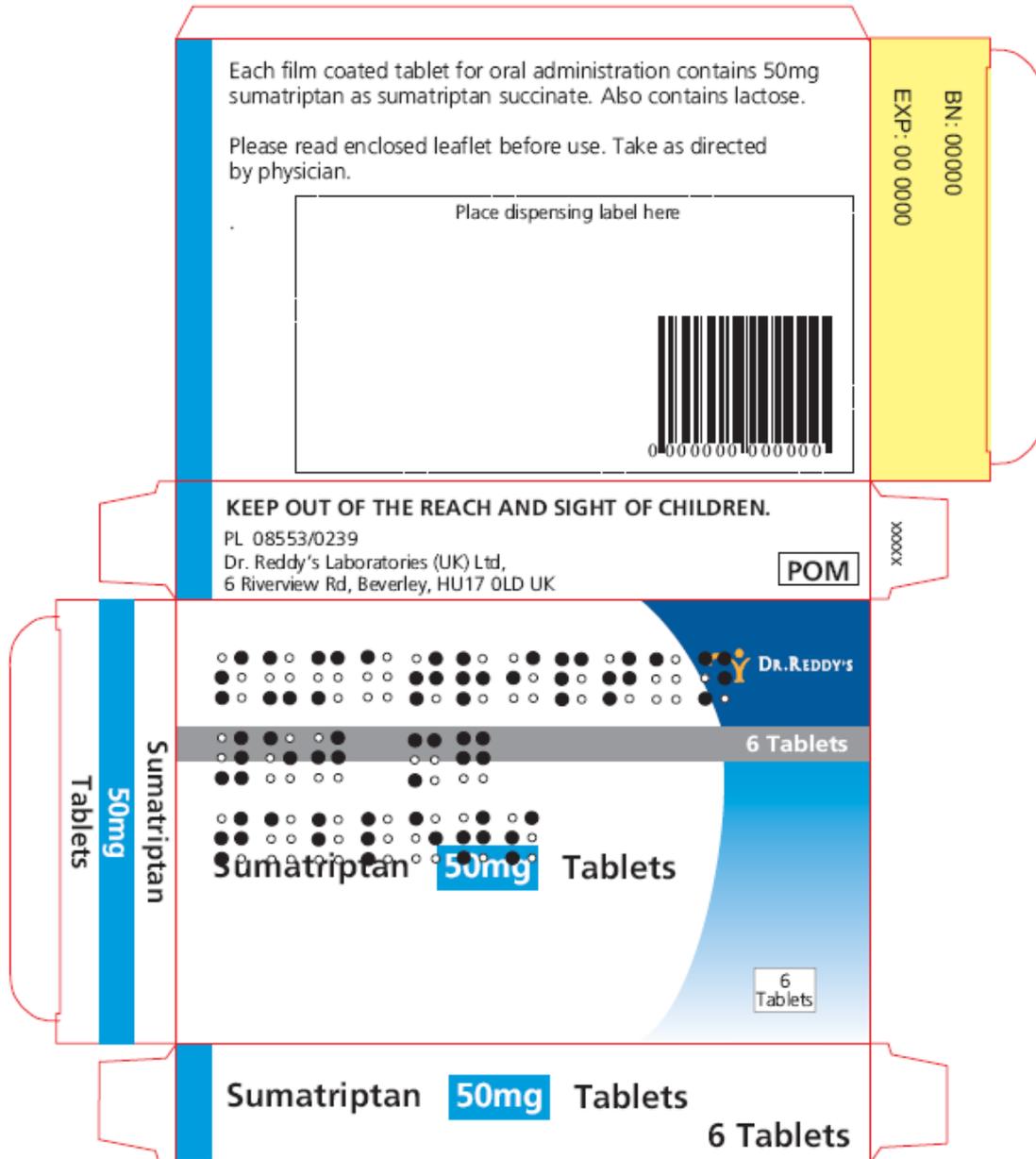
Sumatriptan 50mg Tablets - Carton for blisters, with Braille

Pack size 4



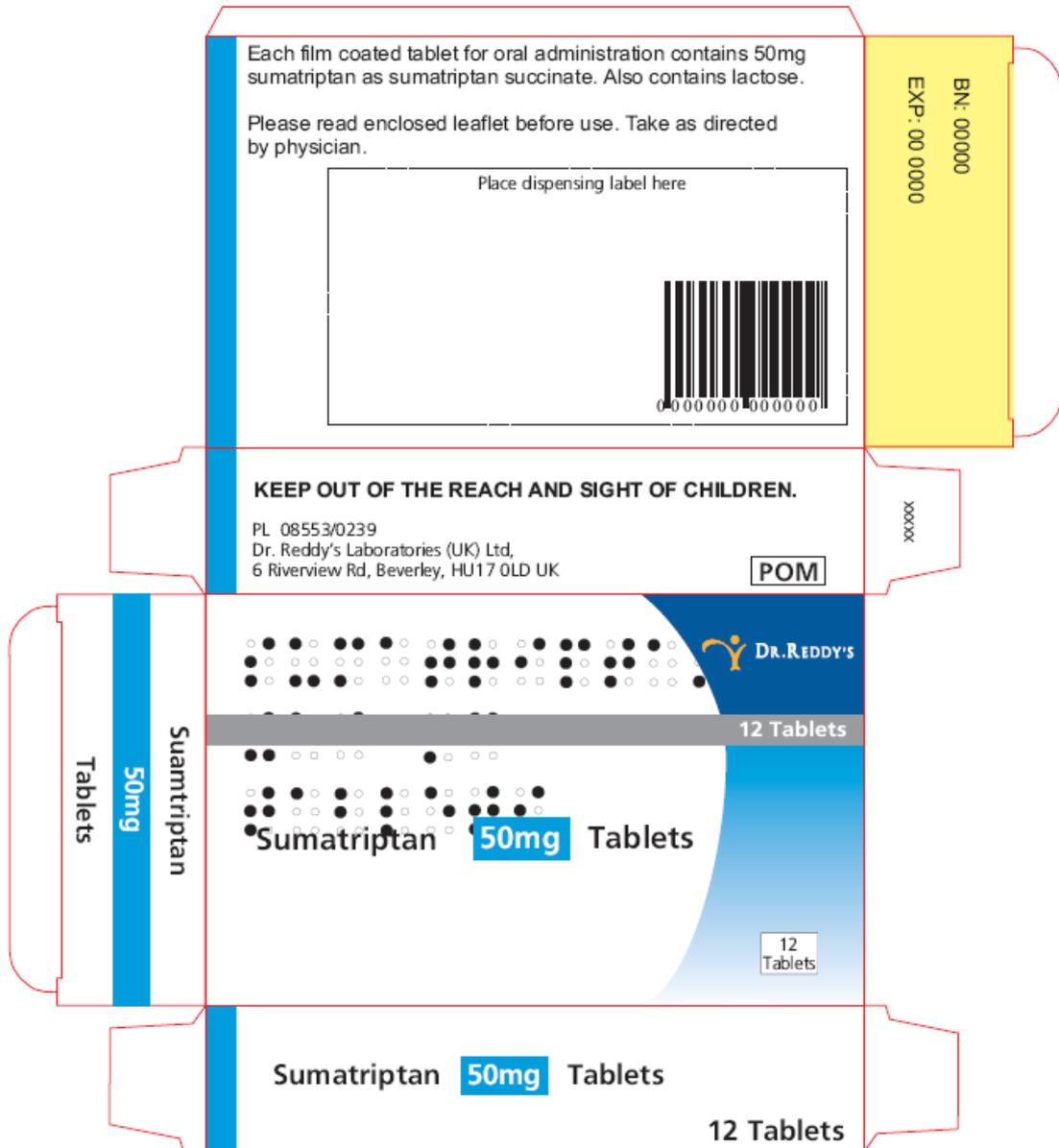
Sumatriptan 50mg Tablets - Carton for blisters, with Braille

Pack size 6



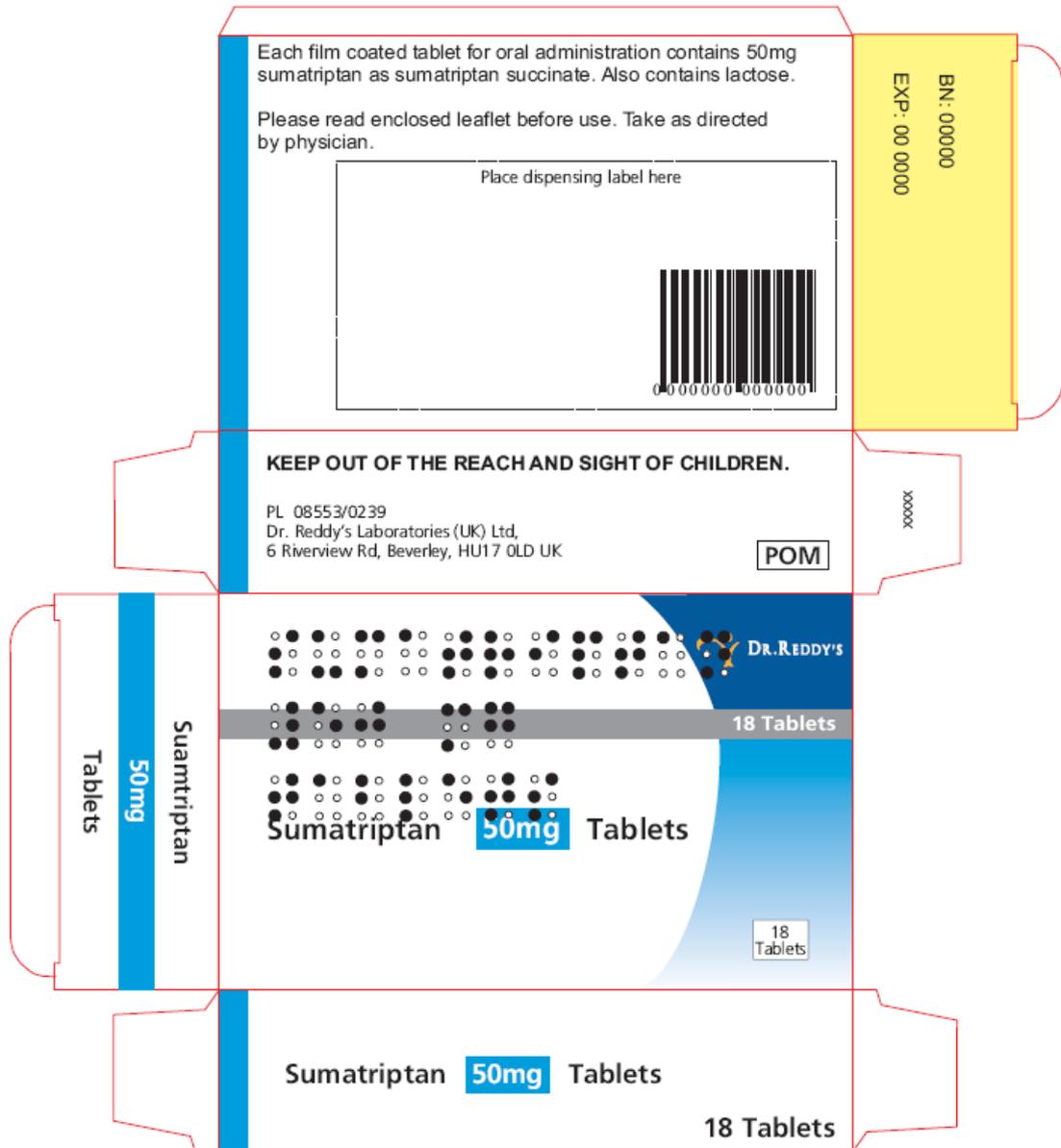
Sumatriptan 50mg Tablets - Carton for blisters, with Braille

Pack size 12

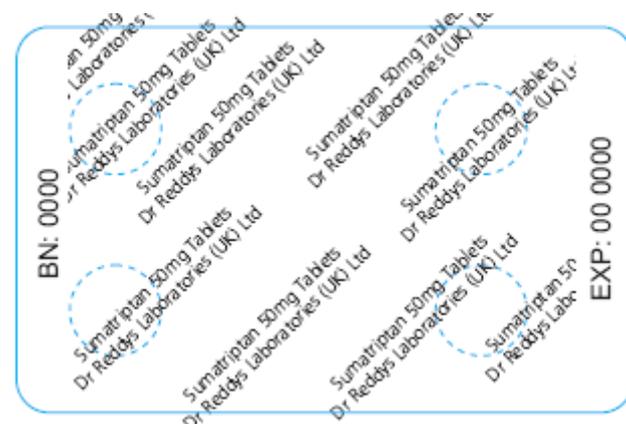
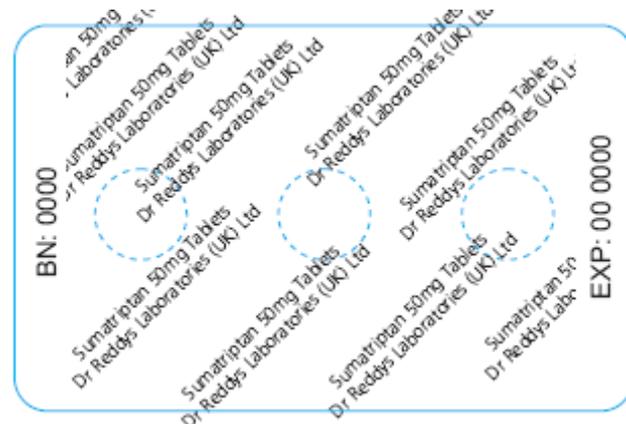
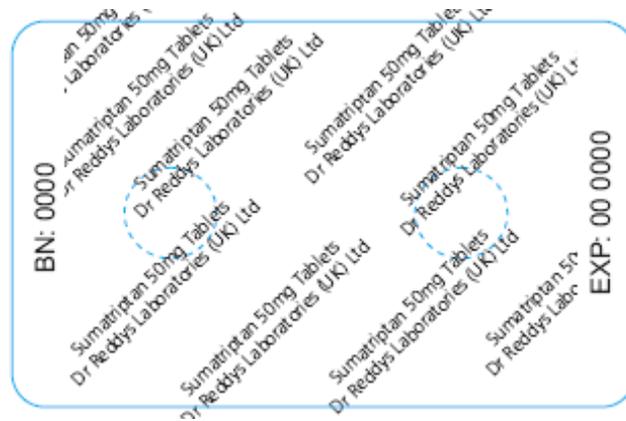


Sumatriptan 50mg Tablets - Carton for blisters, with Braille

Pack size 18

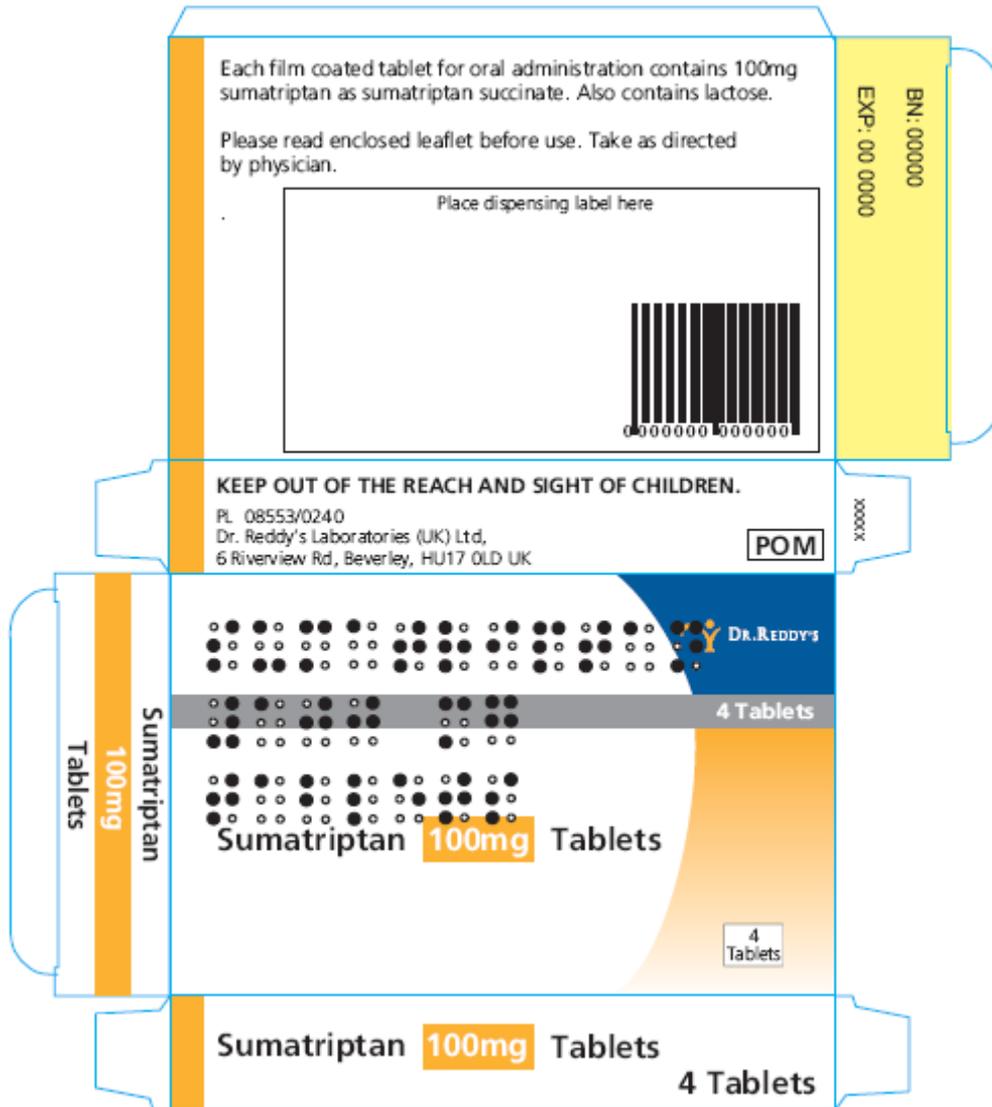


Sumatriptan 50mg Tablets – blister foils for 2, 3, and 4 tablets



Sumatriptan 100mg Tablets - Carton for blisters, with Braille

Pack size 4



Sumatriptan 100mg Tablets – blister foils for 2, 3, 4 and 6 tablets

