SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Sumatriptan 100 mg Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

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

Excipient with known effect:

Contains lactose.

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

3 PHARMACEUTICAL FORM

Coated tablet.
White, oval, biconvex, 8.2x17 mm coated tablets, debossed with ‘SN100’ on one side and plain on the other side.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

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

4.2 Posology and method of administration

For oral use.

Adults:

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

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

The recommended dose is a single 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 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. In these cases the attack can be treated with paracetamol, acetylsalicylic acid, or non-steroidal anti-inflammatory drugs. 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 ergotamine or derivatives of ergotamine (including methysergide) (see section 4.3).

The tablets should be swallowed whole with water.

Paediatric population

The efficacy and safety of sumatriptan tablets in children aged less than 10 years have not been established. No clinical data are available in this age group.

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

Elderly (Over 65 years of age):

Experience of the use of sumatriptan 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 Sumatriptan or to any of the excipients (Listed in section 6.1)
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) or any triptan/5-hydroxytryptamine$_1$ (5-HT$_1$) receptor agonist with sumatriptan is contraindicated (see section 4.5).

Concurrent administration of monoamine oxidase inhibitors and sumatriptan is contraindicated.

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

4.4 Special warnings and precautions for use

Sumatriptan 100 mg Tablets should only be used where there is a clear diagnosis of migraine. Sumatriptan is not indicated for use in the management of hemiplegic, basilar or ophthalmoplegic migraine.

Before treating with sumatriptan, care should be taken to exclude potentially serious neurological conditions (e.g. CVA, TIA) if the patient presents with atypical symptoms or if they have not received an appropriate diagnosis for sumatriptan use.

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, including those patients who are heavy smokers or users of nicotine substitution therapies. without prior cardiovascular evaluation (See Section 4.3). Special consideration should be given to postmenopausal women and males over 40 with these risk factors. These evaluations however, may not identify every patient who has cardiac disease and, in very rare cases, serious cardiac events have occurred in patients without underlying cardiovascular disease.

Sumatriptan should be administered with caution to patients with mild controlled hypertension since transient increases in blood pressure and peripheral vascular resistance have been observed in a small proportion of patients (See section 4.3).

There have been rare post-marketing reports describing patients with serotonin syndrome (including altered mental status, autonomic instability and neuromuscular abnormalities) following the use of a selective serotonin reuptake inhibitor (SSRI) and Sumatriptan.

Serotonin syndrome has been reported following concomitant treatment with triptans and serotonin noradrenaline reuptake inhibitors (SNRIs).

If concomitant treatment with Sumatriptan and an SSRI/SNRI is clinically warranted, appropriate observation of the patient is advised (See section 4.5).

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 (Child Pugh grade A or B; see section 5.2) or renal function (see section 5.2). A 50 mg dose should be considered in patients with hepatic impairment.

Sumatriptan should be used with caution in patients with a history of seizures or other risk factors which lower the seizure threshold, as seizures have been reported in association with Sumatriptan (see section 4.8).

Patients with known hypersensitivity to sulphonamides may exhibit an allergic reaction following administration of Sumatriptan. Reactions may range from cutaneous hypersensitivity to anaphylaxis. Evidence of cross-sensitivity is limited; however, caution should be exercised before using Sumatriptan in these patients.

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

Prolonged use of any type of painkiller for headaches can make them worse. If this situation is experienced or suspected, medical advice should be obtained and treatment should be discontinued. The diagnosis of medication overuse headache (MOH) should be suspected in patients who have frequent or daily headaches despite (or because of) the regular use of headache medications.

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

This medicine contains less than 1 mmol sodium (23 mg) per tablet, that is to say essentially 'sodium-free'.

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.

There are limited data on an interaction with preparations containing ergotamine or another triptan/5-HT_1 receptor agonist. The increased risk of coronary vasospasm is a theoretical possibility and concomitant administration is contraindicated (see section 4.3).
The period of time that should elapse between the use of Sumatriptan and ergotamine containing preparations or another triptan/5-HT_1 receptor agonist is not known. This will also depend on the doses and types of products used. The effects may be additive. It is advised to wait at least 24 hours following the use of ergotamine-containing preparations or another triptan/5-HT_1 receptor agonist before administering Sumatriptan. Conversely, it is advised to wait at least 6 hours following use of Sumatriptan before administering an ergotamine-containing product and at least 24 hours before administering another triptan/5-HT_1 receptor agonist.
An interaction may occur between sumatriptan and monoamine oxidase inhibitors (MAOIs) and concomitant administration is contraindicated (see section 4.3).
There have been rare post-marketing reports describing patients with serotonin syndrome (including altered mental status, autonomic instability and neuromuscular abnormalities) following the use of SSRIs and sumatriptan. Serotonin syndrome has also been reported following concomitant treatment with triptans and SNRIs (See section 4.4).

4.6 Fertility, pregnancy and lactation

Pregnancy

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

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

No studies on the effects on the ability to drive and use machine have been performed. Drowsiness may occur as a result of migraine or its treatment with Sumatriptan. This may influence the ability to drive and to operate machinery.

4.8 Undesirable effects

Adverse events are listed below by system organ class and frequency. Frequencies are defined as: very common (≥1/10), common (≥1/100, <1/10), uncommon (≥1/1000, <1/100), rare (≥1/10,000, <1/1000) and very rare (<1/10,000) and not known (cannot be estimated from the available data). Some of the symptoms reported as undesirable effects may be associated symptoms of migraine.

Clinical Trial Data:

Nervous System Disorders
Common: Dizziness, drowsiness, sensory disturbance including paraesthesia and hypoaesthesia.

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

Respiratory, Thoracic and Mediastinal Disorders
Common: Dyspnoea

Gastrointestinal disorders
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, but may be intense and can affect any part of the body including the chest and throat).
Myalgia

General Disorders and Administration Site Conditions
Common: Pain, sensations of heat or cold, 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).
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
Not known: Hypersensitivity reactions ranging from cutaneous hypersensitivity to anaphylaxis.

Nervous System Disorders
Not known: Seizures (although some have occurred in patients with either a history of seizures or concurrent conditions predisposing to seizures there are also reports in patients where no such predisposing factors are apparent). Tremor, dystonia, nystagmus, scotoma.

Eye disorders
Not known: Flickering, diplopia, reduced vision, loss of vision including reports of permanent defects. However, visual disorders may also occur during a migraine attack itself.

Cardiac disorders
Not known: Bradycardia, tachycardia, palpitations, cardiac arrhythmias, transient ischaemic ECG changes, coronary artery vasospasm, angina, myocardial infarction (see section 4.3 and 4.4).

Vascular disorders
Not known: Hypotension, Raynaud's phenomenon.

Gastrointestinal disorders
Not known: Ischaemic colitis, Diarrhoea, Dysphagia.

Musculoskeletal, connective tissue and bone disorders
Not known: Neck stiffness, Arthralgia

Psychiatric disorders
Not known: Anxiety

Skin and subcutaneous disorders:
Not known: Hyperhidrosis.

General disorders and Administration site conditions
Not known: Pain trauma activated, Pain inflammation activated.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the yellow card scheme at www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App store.

4.9 Overdose

Doses in excess of 400mg orally were not associated with side effects other than those mentioned.

If overdosage occurs, the patient should be monitored for at least ten hours and standard supportive treatment applied as required.

It is unknown what effect haemodialysis or peritoneal dialysis has on the plasma concentrations of sumatriptan.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Analgesics: Selective 5-HT_1 receptor agonists. ATC code: N02CC01

Sumatriptan has been demonstrated to be a specific and selective 5 Hydroxytryptamine1 ($5HT_1D$) receptor agonist with no effect on other 5HT receptor (5-HT_2-5-HT_7) 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 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.

A number of placebo-controlled clinical studies assessed the safety and efficacy of oral sumatriptan standard tablets in over 650 child and adolescent migraineurs aged 10 - 17 years. These studies failed to demonstrate statistically a significant difference in headache relief at 2 hours between placebo and any sumatriptan dose. The undesirable effects profile of oral sumatriptan in children and adolescents aged 10 - 17 years was similar to that reported from studies in the adult population.

5.2 Pharmacokinetic properties

Following oral administration, sumatriptan is rapidly absorbed, 70% of maximum concentration occurring at 45 minutes. After 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.

Special patient populations

Hepatic Impairment

Sumatriptan pharmacokinetics after an oral dose (50 mg) and a subcutaneous dose (6 mg) were studied in 8 patients with mild to moderate hepatic impairment matched for sex, age, and weight with 8 healthy subjects. Following an oral dose, sumatriptan plasma exposure (AUC and Cmax) almost doubled (increased approximately 80%) in patients with mild to moderate hepatic impairment compared to the control subjects with normal hepatic function. There was no difference between the patients with hepatic impairment and control subjects after the s.c. dose. This indicates that mild to moderate hepatic impairment reduces presystemic clearance and increases the bioavailability and exposure to sumatriptan compared to healthy subjects.

Following oral administration, presystemic clearance is reduced in patients with mild to moderate hepatic impairment and systemic exposure is almost doubled.

The pharmacokinetics in patients with severe hepatic impairment have not been studied (see Section 4.3 Contraindications and Section 4.4 Warnings and Precautions).

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 $5HT_1$ or $5HT_2$ 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

Lactose monohydrate
croscarmellose sodium
lactose anhydrous
microcrystalline cellulose
magnesium stearate

Tablet Coat
Lactose monohydrate
mannitol (E421)
titanium dioxide (E171)
talc
triacetin.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

PVC/al blister: 3 years
HDPE bottle with LDPE Cap: 3 years

6.4 Special precautions for storage

This medicinal product does not require any special storage conditions.

6.5 Nature and contents of container

PVC/al blister or HDPE bottle with LDPE Cap

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

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements.

7 MARKETING AUTHORISATION HOLDER

Relonchem Limited,
Cheshire House, Gorsey Lane, Widnes, Cheshire, WA8 0RP, UK.

8 MARKETING AUTHORISATION NUMBER(S)

PL 20395/0064

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

08/11/2024

10 DATE OF REVISION OF THE TEXT

08/11/2024