SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Sumatriptan 100 mg Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

100 mg: Each film-coated tablet contains 100 mg of sumatriptan (as sumatriptan succinate).
Excipient(s) with known effect:
100 mg: Each film-coated tablet contains 135.1 mg of lactose (as lactose monohydrate).

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Film-coated tablet.

100 mg: White to off-white, oblong shaped film-coated tablet debossed “100” on one side and plain on the other.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Acute treatment of migraine attacks with or without aura.

4.2 Posology and method of administration

Sumatriptan should not be used prophylactically.

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).

Sumatriptan should be taken as early as possible after the onset of a migraine headache. Sumatriptan is equally effective at whatever stage of attack it is administered.

The following recommended dosages should not be exceeded.

Adults

The recommended dose for adults is a single dose of 50 mg. Some patients may require 100 mg.

If the patient does not respond to the first dose of sumatriptan, a second dose should not be taken for the same attack. In these cases the attack can be treated with paracetamol, acetylsalicylic acid, or non-steroidal anti-inflammatory drugs. Sumatriptan film-coated tablets may be taken for subsequent attacks.

If the patient has responded to the first dose, but the symptoms recur a second dose may be given in next 24 hours, provided that there is a minimum interval of 2 hours between the two doses. No more than 300 mg should be taken in any 24-hour period.

The tablets should be swallowed whole with water.

Paediatric population

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

Elderly (over 65 years of age)

Experience of the use of sumatriptan tablets in patients aged over 65 years is limited. 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

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

Renal insufficiency

See section 4.4.

4.3 Contraindications

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

Sumatriptan should not be given to patients who have had myocardial infarction or who have ischaemic heart disease, Prinzmetal's variant angina/spasms of the coronary artery or 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 cerebovascular accident (CVA) or transient ischaemic attack (TIA).

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

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

Concurrent administration of ergotamine or derivatives of ergotamine (including methysergide) or any triptan/5-hydroxytryptamine1 (5-HT1) receptor agonist with sumatriptan is contraindicated (seesection 4.5).

Concurrent administration of monoamine oxidase inhibitors (MAOIs) 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 should only be used when there is a clear diagnosis of migraine. In case of doubt, patients should be referred to a neurologist.

Before treatment with sumatriptan, it is important to rule out that the patient has a severe neurological condition (eg CVA, TIA) in case of atypical symptoms or that the patient has a diagnosis where the use of sumatriptan is not indicated.

It should be noted that migraineurs may be at increased risk of certain cerebrovascular events (e.g. CVA, TIA).

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

Following administration, sumatriptan can be associated with transient symptoms such as 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 an 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 patients on nicotine substitution therapies without prior cardiovascular evaluation (see section 4.3.). Special consideration should be given to post-menopausal women and to men over the age of 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.

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 re-uptake inhibitors (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 especially at the beginning of treatment and when the dose is increased (see section 4.5).

Sumatriptan should be used with caution to patients with conditions which may affect significantly the absorption, metabolism or excretion of the medicine, such as impaired hepatic or renal function (see section 5.2). Lower doses should be considered in patients with hepatic impairment (Child Pugh grade A or B, see section 5.2 under Special patient populations).

Sumatriptan should be administered 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 cutaneous hypersensitivity to anaphylaxis. Evidence of cross sensitivity is limited, however, caution should be exercised before using sumatriptan in these patients.

If ergotamine is used, Sumatriptan should not be taken earlier than 24 hours after taking ergotamine. Similarly, it must take 6 hours before ergotamine can be taken after taking Sumatriptan.

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 MOH (medication overuse headache) should be suspected in patients who have frequent or daily headaches despite (or because of) the regular use of headache medications.

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 amount of patients (see section 4.3).

The recommended dosage should not be exceeded.

<u>Excipient(s)</u>

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

Sodium
This medicinal product contains less than 1 mmol sodium (23 mg) per film-coated tablet, that is to say essentially 'sodium-free'.

4.5 Interaction with other medicinal products and other forms of interaction

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

There are limited data on an interaction with ergotamine-containing preparations or another triptan/5-HT1 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-HT1 receptor agonist is not known. This will also depend on the doses and type of ergotamine-containing products used. The effects may be additive. It is advised to wait at least 24 hours following the use of ergotamine-containing preparations or another triptan /5-HT1 receptor agonist before administering sumatriptan. Conversely it is advised to wait at least six hours following use of sumatriptan before administering an ergotamine-containing product and at least 24b hours before administering another triptan/5-HT1 receptor agonist.

An interaction may occur between sumatriptan and MAOIs and concomitant administration is contraindicated (see section 4.3)..

There have been rare post-marketing reports describing patients with serotonin syndrome (including altered mental status, autonomic instability and neuromuscular abnormalities) following concomitant use of SSRIs and sumatriptan. Serotonin syndrome has also been reported following concomitant treatment with triptans and SNRIs (see section 4.4).

Furthermore, there is a theoretical possibility of interactions with lithium.

4.6 Fertility, pregnancy and lactation

Pregnancy
Post-marketing data on 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 onperi- 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.

Breast-feeding
It has been demonstrated that following subcutaneous administration sumatriptan is secreted 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 effect on the ability to drive and use machines have been performed.

Drowsiness may occur as a result of migraine or its treatment with sumatriptan. This may influence the ability to drive and 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 including isolated reports), not known (cannot be estimated from the available data)..

Immune system disorders
Not known: Hypersensitivity reactions ranging from cutaneous hypersensitivity (such as urticaria) to anaphylaxis.

Psychiatric disorders
Not known: Anxiety

Nervous system disorders
Common: dizziness, drowsiness, sensory disturbance including paraesthesia and hypoaesthesia
Not known: Seizures, although some have occurred in patients with either a history of seizures or concurrent conditions predisposing to seizures. There are also reports in patients where no such predisposing factors are apparent: tremor, dystonia, nystagmus, scotoma, serotonin syndrome.

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 sections 4.3 and 4.4).

Vascular disorders

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

Not known: Hypotension, Raynaud's phenomenon

Respiratory, thoracic and mediastinal disorders

Common: Dyspnoea

Gastrointestinal disorders

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

Not known: Ischaemic colitis, diarrhoea, dysphagia

Skin and subcutaneous tissue disorders

Not known: Hyperhidrosis

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) , myalgia..

Not known: Neck stiffness, arthralgia

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).

Not known: Pain trauma activated, pain inflammation activated

Investigations

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

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 Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store

4.9 Overdose

Symptoms

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

Management
If overdosage occurs, the patient should be monitored for at least 10 hours and standard supportive treatment applied as required. It is unknown what effect of hemodialysis or peritoneal dialysis has on the plasma concentrations of sumatriptan.

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Analgesics: antimigraine preparations: selective serotonin (5-HT_1) receptor agonists
ATC code: N02CC01

Mechanism of action: Selective 5HT1 (seretonin) receptor agonist without effect on other 5HT receptors (5HT2-5HT7) subtypes. Vascular 5HT1 receptor is found mainly in cranial blood vessels and mediates vasoconstriction. Sumatriptan provides selective vasoconstriction in the carotid artery circulation in animals, but does not alter cerebral blood flow. Circulation in the carotid artery leads blood to extracranial and intracranial tissue, such as the meninges. Vasodilation and / or edema formation in these vessels is thought to be an underlying mechanism in migraine in humans. In addition, data from animal studies suggest that sumatriptan inhibits trigeminal nerve activity. Both cranial vasoconstriction and inhibition of trigeminal nerve activity may contribute to the effect of sumatriptan on migraine in humans.

The clinical response begins about 30 minutes after oral administration of a 100 mg dose.

Sumatriptan also has an effect in the acute treatment of migraine attacks in connection with menstruation.

The safety and efficacy of the standard tablet have been investigated in several placebo-controlled clinical trials in over 650 children and young migraine patients between the ages of 10 and 17 years. The results of these studies showed no difference in pain relief between placebo and sumatriptan after two hours, independent of sumatriptan dose.
The adverse reaction profile of sumatriptan seen in children and adolescents between 10 and 17 years of age was similar to that reported in studies in the adult population.

5.2 Pharmacokinetic properties

Absorption:
Absorbed rapidly after oral administration. 70% of Cmax is reached after 45 minutes. After 100 mg dose, Cmax is 54 ng / ml. Clinical effect is achieved after approx. 30 minutes. Bioavailability: 14% (due to presystemic metabolism and incomplete absorption).

Distribution:
Plasma protein binding: 14-21%. Average distribution volume: 170 liters.

Metabolism:
Sumatriptan is mainly metabolised by oxidative metabolism mediated by monoamine oxidase A. The major metabolite, indole-acetic acid analogue of sumatriptan, is mainly excreted in the urine as free acid and glucuronide conjugate. It has no known 5HT1 or 5HT2 activity.

Elimination:

The half-life is approx. 2 hours. The mean total plasma clearance is 1160 ml / min and the mean renal plasma clearance is approx. 260 ml / min. Non-renal clearance amounts to approx. 80% of total clearance.

The pharmacokinetics of oral sumatriptan are not significantly affected by migraine attacks.

Hepatic impairment
Following oral administration, presystemic clearance is reduced in patients with hepatic impairment (see section 4.4).

5.3 Preclinical safety data

In a rat ferfility study, a reduction in the success of insemination was seen at exposures sufficiently in excess of the maximum human exposure.

In rabbits, embryolethality, without marked teratogenic defects, was seen.
Sumatriptan was devoid of genotoxic and carcinogenic activity in in vitro systems and animal studies.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

100 mg

Core

Lactose monohydrate
Croscarmellose sodium
Cellulose, microcrystalline
Silica colloidal anhydrous
Magnesium stearate

Coating – Opadry II 33G28707 white

Hypromellose E464
Titanium dioxide E171
Lactose monohydrate
Macrogol 3000
Glycerol triacetate

6.2 Incompatibilities

Not applicable

6.3 Shelf life

36 months

6.4 Special precautions for storage

This medicinal product does not require any special storage conditions.

6.5 Nature and contents of container

Transparent or white opaque PVC/PVdC aluminium blisters.
Blisters of 2, 3, 4, 6, 12, 18, 24, 30 and 50 film-coated tablets.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements.

7 MARKETING AUTHORISATION HOLDER

Teva UK Limited,
Ridings Point,
Whistler Drive,
Castleford,
WF10 5HX,
United Kingdom

8 MARKETING AUTHORISATION NUMBER(S)

PL 00289/0589

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

03/03/2010

10 DATE OF REVISION OF THE TEXT

14/05/2023