NARAMIG

SCHEDULING STATUS:

S4

PROPRIETARY NAME AND DOSAGE FORM:

NARAMIG® tablet

COMPOSITION:

Each tablet contains 2,5 mg naratriptan as naratriptan hydrochloride.

Excipients:

Tablet core: Microcrystalline cellulose, anhydrous lactose, croscarmellose sodium, magnesium stearate.

Film coat: Methylhydroxypropylcellulose, titanium dioxide (E171), triacetin, Iron oxide yellow (E172), indigo carmine aluminium lake (E132).

PHARMACOLOGICAL CLASSIFICATION:

A 7.3 Vascular medicines, Migraine preparations

PHARMACOLOGICAL ACTION:

Pharmacodynamic properties:

Naratriptan is a selective agonist for the vascular 5-hydroxytryptamine$_1$ (5-HT$_1$) receptor. This receptor is found predominantly in intracranial (cerebral and dural) blood vessels. Naratriptan has high affinity for human cloned 5-HT$_{1B}$ and 5-HT$_{1D}$ receptors; the human 5-HT$_{1B}$ receptor is thought to correspond to the vascular 5-HT$_1$ receptor mediating contraction of intracranial blood

vessels. Naratriptan has little effect at other 5-HT receptor (5-HT_2, 5-HT_3, 5-HT_4 and 5-HT_7) subtypes. In animals, naratriptan selectively constricts the carotid arterial circulation which supplies blood to the extracranial and intracranial tissues such as the meninges. In addition, experimental evidence suggests that naratriptan inhibits trigeminal nerve activity. Both these actions may contribute to the anti-migraine action of naratriptan in humans.

Pharmacokinetic Properties:

Following oral administration, naratriptan is absorbed with maximum plasma concentrations observed at 2-3 hours. After administration of a 2,5 mg naratriptan tablet, C_{max} is approximately 8,3 ng/ml in women and 5,4 ng/ml in men. The mean elimination half-life is 6 hours.

Naratriptan is predominantly excreted in the urine with 50 % of an oral dose recovered as unchanged naratriptan and 30 % recovered as inactive metabolites. *In vitro*, naratriptan is metabolised by a wide range of cytochrome P450 isoenzymes and does not interact with monoamine oxidase.

INDICATIONS:

NARAMIG tablets are indicated for the acute treatment of migraine attacks with or without aura.

CONTRA-INDICATIONS:

Hypersensitivity to any component of the preparation.

NARAMIG should not be used in patients who have had a myocardial infarction or have ischaemic heart disease, or Prinzmetal's angina/coronary vasospasm, or peripheral vascular disease or patients who have symptoms or signs consistent with ischaemic heart disease.

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

The use of NARAMIG in patients with uncontrolled hypertension is contra-indicated.

NARAMIG is contra-indicated in patients with severely impaired renal or hepatic function.

The concomitant administration of ergotamine, derivatives of ergotamine (including methysergide) and other triptans with NARAMIG is not recommended.

WARNINGS AND SPECIAL PRECAUTIONS:

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

Before treating headaches in patients not previously diagnosed as migraineurs, and in migraineurs who present with 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. CVA or TIA).

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

NARAMIG should not be given to patients in whom unrecognised cardiac disease is likely without a prior evaluation for underlying cardiovascular disease. Such patients include postmenopausal women, males over 40 years and patients with risk factors for coronary artery disease. If symptoms consistent with ischaemic heart disease occur appropriate evaluation should be carried out.

The recommended dose of NARAMIG should not be exceeded.

NARAMIG contains a sulphonamide component therefore there is a theoretical risk of a hypersensitivity reaction in patients with known hypersensitivity to sulphonamides.

Caution is recommended in patients performing skilled tasks (e.g. driving or operating machinery) as drowsiness may occur as a result of migraine.

The safety and effectiveness of NARAMIG in the elderly (over 65 years of age) have not been evaluated. There is a moderate decrease (26 %) in clearance with increasing age.

NARAMIG is not recommended for use in children (under 12 years of age) or adolescents (12-17 years of age).

INTERACTIONS:

There is no evidence of interactions with β-blockers, tricyclic antidepressants, selective serotonin reuptake inhibitors, alcohol or food.

NARAMIG does not inhibit monoamine oxidase enzymes; therefore interactions with monoamine oxidase inhibitors are not anticipated. In addition, the limited metabolism of naratriptan and the wide range of cytochrome P450 isoenzymes involved suggest that significant drug interactions with NARAMIG are unlikely.

PREGNANCY AND LACTATION:

The safe use of NARAMIG in pregnant women has not been established.

NARAMIG and/or drug related metabolites are secreted into the milk of lactating rats.

Caution should be exercised when considering administration of NARAMIG to nursing women.

DOSAGE AND DIRECTIONS FOR USE:

It should not be used prophylactically.

NARAMIG tablets should be taken as early as possible after the onset of a migraine headache but may be effective if taken at a later stage.

The tablets should be swallowed whole with water.

The recommended dose of NARAMIG Tablets is a single 2,5 mg tablet.

A minimum interval of four hours should be left between doses.

No more than two 2,5 mg tablets in any 24 hour period.

Maximum total daily dose in renal/hepatic impairment: one 2,5 mg tablet.

If a patient does not respond to the first dose of NARAMIG tablets it is unlikely that a second dose will be of benefit in the same attack.

SIDE 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 (> 1/1 000, < 1/100), rare (> 1/10 000, < 1/1 000) and very rare (< 1/10 000). Common and uncommon frequencies were determined from clinical trial data. Very rare frequencies were generally derived from spontaneous data.

Clinical trial data:

At therapeutic doses of naratriptan, the incidence of side effects reported in clinical trials was similar to placebo.

Nervous system disorders:

Common: tingling

This is usually of short duration, may be severe and may affect any part of the body including the chest or throat.

Gastrointestinal:

Common: nausea and vomiting

Musculoskelatal and connective tissue disorders:

Common: sensations of heaviness

This is usually of short duration, may be severe and may affect any part of the body including the chest or throat.

General disorders and administration site conditions:

The following symptoms are usually of short duration, may be severe and may affect any part of the body including the chest or throat:

Common: pain, sensations of tingling and heat

Uncommon: sensations of pressure or tightness.

Post-marketing data:

Immune system disorders: hypersensitivity reactions ranging from cutaneous hypersensitivity to anaphylaxis

Cardiovascular: coronory artery vasospasm transient ischaemic ECG changes, angina and myocardial infarction (see CONTRA-INDICATIONS, WARNINGS AND SPECIAL PRECAUTIONS and SIDE EFFECTS)

Vascular disorders: peripheral vascular ischaemia

Gastrointestinal disorders: ischaemic colitis.

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT:

Administration of a high dose of 25 mg naratriptan in one healthy male subject increased blood pressure by up to 71 mmHg and resulted in adverse events including light-headedness, tension in the neck, tiredness and a loss of co-ordination. Blood pressure returned to baseline by 8 hours after dosing without other pharmacological intervention.

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

Treatment: If overdosage with naratriptan occurs, the patient should be monitored for at least 24 hours and standard supportive treatment applied as required.

IDENTIFICATION:

NARAMIG tablets are green film-coated, D shaped, biconvex, with 'GX CE5' engraved on the one face.

PRESENTATION:

NARAMIG tablets are packed in double foil blister packs of 2, 4, 6 and 12 tablets.

STORAGE INSTRUCTIONS:

Store below 30 °C.

Protect from light.

Keep out of reach of children.

REGISTRATION NUMBER:

32/7.3/0463

NAME AND BUSINESS ADDRESS OF THE OF THE HOLDER OF THE CERTIFICATE OF REGISTRATION:

GlaxoSmithKline South Africa (Pty) Ltd

39 Hawkins Avenue

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DATE OF PUBLICATION OF THIS PACKAGE INSERT:

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CONFIDENTIAL

1.3 South African labelling and packaging
1.3.1 South African Package Insert
1.3.1.1 Package insert

Namibia: Reg No 04/7.3/0903 NS2

GDS-06

HISTORY:

Amended: 02 April 2002 (Applicant name change)
Amended: 03/05/2004 (In line with GCT-006)
Amended: 06 September 2006 (In response to CC Recommendations dated 10 March 2006)
Amended: 15 May 2007 (Compliant pi as per CC Recommendations dated 24/04/07) Approved 05 October 2007
Amended: 31 August 2011 (Applicant address change Bryanston to CT)
Amended: 25 August 2015. Notification to bring pi in line with Reg 9. Implemented