Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Clonidine Hydrochloride 25 microgram Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains clonidine hydrochloride 25 micrograms.

Excipients:

Clonidine Hydrochloride 25 microgram Tablets contain 48 mg lactose monohydrate per tablet.

For full list of excipients, see Section 6.1.

3 PHARMACEUTICAL FORM

Tablet.

White to off-white circular tablet, engraved with ‘CD 25’ on one side.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

a) The prophylactic management of migraine or recurrent vascular headache.

b) The management of vasomotor conditions commonly associated with the menopause and characterised by flushing.

4.2 Posology and method of administration

Adults over 18 years:

Initially 2 tablets twice daily. If after two weeks there has been no remission, increase to 3 tablets twice daily.

The duration of treatment depends upon the severity of the condition.

If symptoms continue to occur the patient should be informed that it may take 2 - 4 weeks until Clonidine Hydrochloride 25 microgram Tablets are fully effective.

Children and Adolescents:

There is insufficient information for the application of Clonidine in children and adolescents younger than 18 years. Therefore the use of Clonidine is not recommended in paediatric subjects under 18 years.

Elderly:

No specific information on the use of this product in the elderly is available.

Patients with renal impairment

Clonidine Hydrochloride should be used with caution in patients with renal insufficiency. Careful monitoring of blood pressure is required.

4.3 Contraindications

Clonidine Hydrochloride 25 microgram Tablets should not be used in patients with severe bradyarrhythmia resulting from either sick-sinus syndrome or AV block of 2nd or 3rd degree, or in patients with known hypersensitivity to the active ingredient, clonidine, or other components of the product.

4.4 Special warnings and precautions for use

Clonidine Hydrochloride 25 microgram Tablets should be used with caution in patients with cerebrovascular disease, coronary insufficiency, heart failure, occlusive peripheral vascular disorders, such as Raynaud's disease, constipation or those with a history of depression.

At doses higher than those recommended above, clonidine is an effective antihypertensive agent. Caution should therefore be observed where antihypertensive agents are being used, as potentiation of the hypotensive effect may occur. Provided the recommended dosage regimen is followed, no difficulty with hypotension should arise during the routine management of patients with either migraine or menopausal flushing.

Depending on the dose given, clonidine hydrochloride can cause bradycardia. In patients with pre-existing cardiac conduction abnormalities, arrhythmias have been observed after high doses of clonidine hydrochloride.

Patients with renal failure require extreme care. (See Section 4.2).

Patients should be instructed not to discontinue therapy without consulting their physician. Following sudden discontinuation of Clonidine after prolonged treatment with high doses, agitation, restlessness, palpitations, rapid rise in blood pressure, nervousness, tremor, headache or nausea have been reported. When discontinuing therapy with Clonidine, the physician should reduce the dose gradually over 2-4 days.

Patients who wear contact lenses should be warned that treatment with clonidine may cause decreased lacrimation.

Serious adverse events, including sudden death, have been reported in concomitant use with methylphenidate. The safety of using methylphenidate in combination with clonidine has not been systematically evaluated.

Where clonidine is already being used for the management of hypertension, Clonidine Hydrochloride 25 microgram Tablets therapy is not indicated.
Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

4.5 Interaction with other medicinal products and other forms of interaction

Concurrent administration of antihypertensive agents, vasodilators or diuretics may lead to an increased hypotensive effect.

Substances with alpha$_2$-receptor blocking properties, such as mirtazapine, may abolish the alpha$_2$-receptor mediated effects of clonidine in a dose-dependent manner.

Concomitant use of beta-blockers and/or cardiac glycosides can cause bradycardia or dysrhythmia (AV-block) in isolated cases.

It cannot be ruled out that concomitant administration of a beta-receptor blocker will cause or potentiate peripheral vascular disorders.

If during combined treatment with a beta-blocker there is a need to interrupt or discontinue antihypertensive therapy, the beta-blocker must always be discontinued slowly first (reducing the dose gradually to avoid sympathetic hyperactivity), and then the Clonidine Hydrochloride 25 microgram Tablets, which should also be reduced gradually over several days if previously given in high doses.

Orthostatic hypotension may be provoked or aggravated by concomitant administration of tricyclic antidepressants or neuroleptics with alpha-receptor blocking properties.

As the effects of clonidine can be antagonised by tricyclic anti-depressants, it may be necessary to adjust the dosage of Clonidine Hydrochloride 25 microgram Tablets, if these agents are administered concurrently.

Although there is no experience from clinical trials, the effect of tranquillisers, hypnotics or alcohol could theoretically be potentiated by Clonidine Hydrochloride 25 microgram Tablets.

4.6 Fertility, pregnancy and lactation

Clonidine Hydrochloride 25 microgram Tablets should not be used in pregnancy, especially the first trimester, unless the expected benefit is thought to outweigh any possible risk to the foetus.

In animal studies involving doses higher than the equivalent maximum therapeutic dose in man, effects on foetal development were only seen in one species. Foetal malformations did not occur.

Careful monitoring of mother and child is recommended.

Clonidine passes the placental barrier and may lower the heart rate of the foetus. Post partum a transient rise in blood pressure in the newborn cannot be excluded.

There is no adequate experience regarding the long-term effects of prenatal exposure.

Clonidine is excreted in human milk. The use of Clonidine Hydrochloride 25 microgram Tablets during lactation is not recommended due to a lack of supporting information.

Fertility

No clinical studies on the effect on human fertility have been conducted with clonidine. Non-clinical studies with clonidine indicate no direct or indirect harmful effects with respect to the fertility index.

4.7 Effects on ability to drive and use machines

Because of different individual reactions including drowsiness, dizziness, accommodation disorder, the ability to drive or operate machinery may be impaired, particularly in the initial phase of treatment with Clonidine Hydrochloride 25 microgram Tablets.

4.8 Undesirable effects

Most adverse effects are mild and tend to diminish with continued therapy.

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), very rare (< 1/10,000) and unknown (cannot be calculated from the available data).

Cardiac disorders:

Bradyarrhythmia: not known

sinus bradycardia:uncommon

AV-block: rare

Nervous system disorders:

Dizziness, Sedation: very common

Headache: common

Paraesthesia: uncommon

Eye disorders:

Reduced lachrymal flow (caution: contact lens wearers): rare.

Accommodation disorder: not known

Respiratory, thoracic and mediastinal disorders:

Nasal dryness: rare

Gastrointestinal disorders:

Dry mouth: very common

Constipation, Nausea, Salivary gland pain, Vomiting: common

Colonic pseudo-obstruction: rare

Pain in the parotid gland: very rare.

Skin and subcutaneous tissue disorders:

Pruritus, Rash, Urticaria: uncommon

Alopecia: rare

Vascular disorders:

Orthostatic hypotension, but only following the first administration of high doses*: very common*

Raynaud's phenomenon: uncommon

Disturbances in peripheral blood flow: rare.

General disorders and administration site conditions:

Fatigue common

Malaise uncommon

Reproductive system and breast disorders:

Impotence: rare.

Endocrine disorders:

Gynaecomastia: rare

Psychiatric disorders:

Sleep disorder, depression: common

Hallucination, delusional perception, nightmare: uncommon

Confusional state, libido decreased: not known

Investigations:

Blood glucose increased: rare

Reporting of suspected adverse reactions

If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: www.hpra.ie; E-mail: medsafety@hpra.ie. By reporting side effects you can help provide more information on the safety of this medicine.

Healthcare professionals are asked to report any suspected adverse reactions via Yellow Card Scheme at: www.mhra.gov.uk/yellowcard.

4.9 Overdose

Symptoms:

Manifestations of intoxication are due to generalised sympathetic depression and include pupillary constriction, sedation to coma, hypotension, orthostatic hypotension, bradycardia, hypothermia, apnoea, occasionally vomiting, very occasionally hypertension, dryness of the mouth.

Treatment:

Gastric lavage and/or administration of activated charcoal should be performed where appropriate. In most cases all that is required are general supportive measures.

Supportive care may include atropine sulfate for symptomatic bradycardia, and intravenous fluids and/or inotropic sympathomimetic agents for hypotension. Severe persistent hypertension may require correction with alpha-adrenoceptor blocking drugs.

Naloxone may be a useful adjunct for the management of clonidine-induced respiratory depression.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

ATC code N02C X02

Clonidine is an antihypertensive agent which acts centrally by stimulating alpha$_2$-adrenergic receptors and producing a reduction in sympathetic tone, resulting in a fall in diastolic and systolic blood pressure and a reduction in heart rate.

Treatment with Clonidine Hydrochloride 25 microgram Tablets diminishes the responsiveness of peripheral vessels to constrictor and dilator stimuli, thereby preventing the vascular changes associated with migraine. The same direct action on peripheral vessels moderates the vascular changes associated with menopausal flushing.

5.2 Pharmacokinetic properties

Clonidine is well absorbed from the gastro-intestinal tract. Peak plasma concentrations are observed 3 to 5 hours post administration, decreasing with a half life of up to approximately 23 hours. Clonidine is metabolised in the liver. About 65% is excreted in the urine, partly as unchanged clonidine and about 20% is excreted in the faeces.

5.3 Preclinical safety data

There are no preclinical data of relevance to the prescriber which are additional to that already included in other sections of the SmPC.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Microcrystalline cellulose

Maize starch

Pregelatinised maize starch

Lactose monohydrate

Talc

Sodium starch glycolate Type A

Magnesium stearate (E470b)

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

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/aluminium blister.

Each box contains 112 tablets (4 blister strips of 28 tablets each).

6.6 Special precautions for disposal

No special requirements.

7 MARKETING AUTHORISATION HOLDER

Teva B.V.
Swensweg 5
2031GA Haarlem
Netherlands

8 MARKETING AUTHORISATION NUMBER

PA1986/058/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of First Authorisation: 12th December 2008

Date of Last Renewal: 29th April 2013

10 DATE OF REVISION OF THE TEXT

August 2018