Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Clonidine hydrochloride 100 micrograms/ 5 ml Oral Solution

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 5 ml of oral solution contains 100 micrograms of clonidine hydrochloride.

Excipients with known effect:
Each 5 ml of oral solution contains 9 mg methyl parahydroxybenzoate (E218).

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Oral solution

A clear colourless solution.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Clonidine Oral Solution is indicated in adults for the treatment of hypertension that has failed to respond adequately to other anti-hypertensives.

4.2 Posology and method of administration

Posology

Adults:
The usual initial dosage is 2.5 ml to 5 ml (50 to 100 micrograms) three times daily with subsequent gradual increments to the level of optimal control generally in the daily dose range of 15 ml to 60 ml (300 to 1200 micrograms) in divided doses although higher levels may be required.

Where clonidine has been added to other anti-hypertensive therapy, dosage of other anti-hypertensive therapy should be gradually reduced as the clonidine is introduced.

Patients undergoing anaesthesia should continue their clonidine treatment before, during and after anaesthesia using oral or intravenous administration according to individual circumstances.

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

Renal impairment:
Dose must be adjusted:

- according to the individual antihypertensive response which can show high variability in patients with renal insufficiency
- according to the degree of renal impairment. (see Section 4.4)

Paediatric Population:
There is insufficient evidence for the use of clonidine in children and adolescents younger than 18 years. Therefore the use of clonidine is not recommended in paediatric subjects under 18 years (see Sections 4.3, 4.4 and 5.1).

Method of administration:
For oral use only.

4.3 Contraindications

Clonidine Oral Solution should not be used

- in children and adolescents below 18 years of age (see Sections 4.2, 4.4 and 5.1)
- in patients with known hypersensitivity to the active ingredient or any of the excipients listed in section 6.1
- in patients with severe bradyarrhythmia resulting from either sick sinus syndrome or AV block of 2nd or 3rd degree.

4.4 Special warnings and precautions for use

Clonidine should only be used with caution in patients with depression or a history thereof, with Raynaud's disease, or other peripheral vascular occlusive disease. The product should only be used with caution in patients with cerebrovascular or coronary insufficiency. Clonidine should also be used with caution in patients with mild to moderate bradyarrhythmia such as low sinus rhythm, and with polyneuropathy or constipation.

As with other antihypertensive drugs, treatment with clonidine should be monitored particularly carefully in patients with heart failure.

In hypertension caused by phaeochromocytoma no therapeutic effect of clonidine can be expected.

Clonidine and its metabolites are extensively excreted in the urine. Dosage must be adjusted
according to the individual antihypertensive response, which can show high variability in patients with renal insufficiency (see Section 4.2); careful monitoring is required. Since only a minimal amount of clonidine is removed during routine haemodialysis, there is no need to give supplemental clonidine following dialysis.

Sudden withdrawal of clonidine should be avoided because of possible rebound, hypertension. Cases of agitation, restlessness, palpitations, nervousness, tremor, headache and abdominal symptoms have also been reported. Patients should be instructed not to discontinue therapy without consulting their physician. When discontinuing therapy the physician should reduce the dose gradually. However, if withdrawal symptoms should nevertheless occur, these can usually be treated with reintroduction of clonidine or with alpha and beta adrenoceptor blocking agents.

If long-term treatment with a beta-receptor blocker has to be interrupted then the beta-receptor blocker should first be phased out gradually, followed by gradual withdrawal of clonidine.
Patients who wear contact lenses should be warned that treatment with clonidine may cause decreased lacrimation.

The use and the safety of clonidine in children and adolescents has little supporting evidence in randomized controlled trials and therefore cannot be recommended for use in this population (see Sections 4.2, 4.3 and 5.1).

In particular, when clonidine is used off-label concomitantly with methylphenidate in children with ADHD, serious adverse reactions, including death, have been observed. Therefore, clonidine in this combination is not recommended.

Excipients warnings
This product contains methyl parahydroxybenzoate (E218), which may cause allergic reactions (possibly delayed).
This medicine contains less than 1mmol sodium (23 mg) per 5 ml, that is to say essentially 'sodium-free'.

4.5 Interaction with other medicinal products and other forms of interaction

The reduction in blood pressure induced by clonidine can be further potentiated by concurrent administration of other hypotensive agents. This can be of therapeutic use in the case of other anti-hypertensive agents such as diuretics, vasodilators, beta-receptor blockers, calcium antagonists and ACE-inhibitors, but the effect of alpha1 - blockers is unpredictable.

The anti-hypertensive effect of clonidine may be reduced or abolished and orthostatic hypotension may be provoked or aggravated by concomitant administration of tricyclic anti-depressants or neuroleptics with alpha-receptor blocking properties.

Substances, which raise blood pressure or induce a sodium ion (Na+) and water retaining effect such as non-steroidal anti-inflammatory agents can reduce the therapeutic effect of clonidine.

Substances with alpha2-receptor blocking properties, such as mirtazapine, may abolish the alpha2-receptor mediated effects of clonidine in a dose-dependent manner.

Concomitant administration of substances with a negative chronotropic or dromotropic effect such as beta-receptor blockers or digitalis glycosides can cause or potentiate bradycardic rhythm disturbances.

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

Based on observations in patients in a state of alcoholic delirium it has been suggested that high intravenous doses of clonidine may increase the arrhythmogenic potential (QT-prolongation, ventricular fibrillation) of high intravenous doses of haloperidol. Causal relationship and relevance for anti-hypertensive treatment have not been established.

The concomitant use of other central nervous system depressants will increase the depressant effect of the drug.

4.6 Fertility, pregnancy and lactation

Pregnancy
There are limited amount of data from the use of clonidine in pregnant women. This product should only be used in pregnancy if considered essential by the physician. 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 new-born cannot be excluded.

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

During pregnancy the oral forms of clonidine should be preferred. Intravenous injection of clonidine should be avoided.

Non-clinical studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity.

Lactation
Clonidine is excreted in human milk. However, there is insufficient information on the effect on newborns. The use of Clonidine Oral solution is therefore not recommended during breastfeeding.

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

No studies on the effects on the ability to drive and use machines have been performed.

However, patients should be advised that they may experience undesirable effects such as dizziness, sedation and accommodation disorder during treatment with Clonidine. If patients experience the above mentioned side effects they should avoid potentially hazardous tasks such as driving or operating machinery.

4.8 Undesirable effects

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

Adverse events have been ranked under headings of frequency using the following convention:
Very common ≥ 1/10
Common ≥ 1/100, <1/10
Uncommon ≥ 1/1000, <1/100
Rare ≥ 1/10000, <1/1000
Very rare <1/10000

Not known Cannot be estimated from the available data

Endocrine disorders:
Gynaecomastia Rare
Psychiatric disorders:
Confusional state Not known
Delusional perception Uncommon
Depression Common
Hallucination Uncommon
Libido decreased Not known
Nightmare Uncommon
Sleep disorder Common

Nervous system disorders:
Dizziness Very common
Headache Common
Paraesthesia Uncommon
Sedation Very common

Eye disorders:
Accommodation disorder Not known
Lacrimation decreased Rare

Cardiac disorders:
Atrioventricular block Rare
Bradyarrhythmia Not known
Sinus bradycardia Uncommon

Vascular disorders:
Orthostatic hypotension Very common
Raynaud's phenomenon Uncommon

Respiratory, thoracic and mediastinal disorders:
Nasal dryness Rare

Gastrointestinal disorders:
Colonic pseudo-obstruction Rare
Constipation Common
Dry mouth Very common
Nausea Common
Salivary gland pain Common
Vomiting Common

Skin and subcutaneous tissue disorders:
Alopecia Rare
Pruritus Uncommon
Rash Uncommon
Urticaria Uncommon

Reproductive system and breast disorders:
Erectile dysfunction Common

General disorders and administration site conditions:
Fatigue Common
Malaise Uncommon

Investigations:
Blood glucose increased Rare
Fluid retention occurs occasionally. Two cases of hepatitis have also been reported.

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 HPRA Pharmacovigilance Website: www.hpra.ie.

4.9 Overdose

Symptoms:
Manifestations of intoxication are due to a generalised sympathetic depression and include pupillary constriction, lethargy, bradycardia, hypotension, hypothermia, somnolence including coma and respiratory depression including apnoea. Paradoxical hypertension caused by stimulation of peripheral alpha1-receptors may occur. Transient hypertension may be seen if the total dose is over 10mg.

Treatment:
Gastric lavage should be performed where appropriate. In most cases all that is required are general supportive measures. Where bradycardia is severe atropine will increase the heart rate.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: antiadrenergic agents, centrally acting, ATC code: C02AC01
Mechanism of action
Clonidine acts primarily on the central nervous system, resulting in reduced sympathetic outflow and a decrease in peripheral resistance, renal vascular resistance, heart rate and blood pressure. Renal blood flow and glomerular filtration rate remain essentially unchanged. Normal postural reflexes are intact and therefore orthostatic symptoms are mild and infrequent. During long term therapy, cardiac output tends to return to control values, while peripheral resistance remains decreased. Slowing of the pulse rate has been observed in most patients given clonidine, but the drug does not alter normal haemodynamic response to exercise.

Clinical efficacy and safety
The efficacy of clonidine in the treatment of hypertension has been investigated in five clinical studies in paediatric patients. The efficacy data confirms the properties of clonidine in reduction of systolic and diastolic blood pressure. However, due to limited data and methodological insufficiencies, no definitive conclusion can be drawn on the use of clonidine for hypertensive children.
The efficacy of clonidine has also been investigated in a few clinical studies with paediatric patients with ADHD, Tourette syndrome and stuttering. The efficacy of clonidine in these conditions has not been demonstrated.

There were also two small paediatric studies in migraine, neither of which demonstrated efficacy. In the paediatric studies the most frequent adverse events were drowsiness, dry mouth, headache, dizziness and insomnia. These adverse events might have serious impact on daily functioning in paediatric patients.
Overall, the safety and efficacy of clonidine in children and adolescents have not been established (see Sections 4.2. 4.3 and 4.4).

5.2 Pharmacokinetic properties

Absorption and distribution
The pharmacokinetics of clonidine is dose-proportional in the range of 75-300micrograms; over this range, dose linearity has not been fully demonstrated. Clonidine is well absorbed and undergoes a minor first pass effect. Peak plasma concentrations are reached within 1-3 h after oral administration. The plasma protein binding is 30-40 %. Clonidine is rapidly and extensively distributed into tissues and crosses the blood-brain barrier, as well as the placental barrier. Clonidine is excreted in human milk. However, there is insufficient information on the effect on newborns.

Metabolism and elimination
The terminal elimination half-life of clonidine has been found to range from 5 to 25.5 hours. It can be prolonged in patients with severely impaired renal function up to 41 hours.

About 70 % of the dose administered is excreted with the urine mainly in the form of unchanged parent drug (40-60 % of the dose). The main metabolite p-hydroxy-clonidine is pharmacologically inactive. Approximately 20 % of the total amount is excreted with the faeces. The pharmacokinetics of clonidine is not influenced by food nor race of the patient,
The antihypertensive effect is reached at plasma concentrations between about 0.2 and 2.0 ng/ml in patients with normal renal function. The hypotensive effect is attenuated or decreases with plasma concentrations above 2.0 ng/ml.

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 SPC.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Methyl parahydroxybenzoate (E218)
Sodium dihydrogen phosphate monohydrate (E339)
Disodium phosphate (E339)
Sucralose (E955)
Purified water

6.2 Incompatibilities

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

6.3 Shelf life

24 months
Discard 30 days after first opening.

6.4 Special precautions for storage

This medicinal product does not require any special storage conditions.
Do not refrigerate or freeze.

6.5 Nature and contents of container

Bottle: Type III amber glass bottle

Closure: Tamper evident, child resistant white plastic cap consists of polypropylene inner, polyethylene outer, expanded polyethylene (EPE) liner.

Dosing Device: A 10ml polypropylene oral syringe with 0.25ml intermediate graduation with an adaptor.

Pack size: 150ml

6.6 Special precautions for disposal

No special requirements for disposal.
Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

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1 WML
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8 MARKETING AUTHORISATION NUMBER

PA22697/020/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 1st August 2025

10 DATE OF REVISION OF THE TEXT