SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

IPOREL, 75 micrograms, tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

1 tablet contains 75 micrograms clonidine hydrochloride *(Clonidini hydrochloridum).*

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Tablets
White or off-white with a creamy shade, round, biconvex tablet.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications
Primary arterial hypertension and secondary arterial hypertension of all levels of severity.

4.2 Posology and method of administration.

Posology
At the beginning 75 µg 2x a day. When needed, the dose of the medicinal product can be increased gradually every second or third day up to the optimal dose for the patient. Usually, this is 300 µg to 1200 µg daily. In some patients, it might be necessary to use higher dose, e.g. 1800 µg or more.

Treatment with the Iporel medicinal product may be introduced in addition to previous treatment with other antihypertensives. In such cases, it might be necessary to gradually reduce the dose of previously used medicines.
Clonidine can be used in the perianaesthethic period as well as during general anaesthesia in patients who undergo a surgical procedure.
In elderly patients, there is no need to adjust the dose with respect to the normal dose. Clinical trials have not shown any specific adverse events in this group of people.

Paediatric and adolescent population
There is a lack of sufficient data referring to the use of clonidine in children and adolescents below 18 years. Thus, it is not recommended to use clonidine in children and adolescents below 18 years.

4.3 Contraindications
- Hypersensitivity to the active substance(s) or to any of the excipients listed in section 6.1.
- Severe bradyarrythmia in the course of sick sinus syndrome, or second- or third-degree atrioventricular block
- Use in children up to 12 years

4.4 Special warnings and precautions for use
Special care has to be taken when Iporel is used in patients with Raynaud's syndrome or other diseases of the peripheral vessels, in patients with cerebral or coronary vascular insufficiency, in patients with mild or moderate bradyarrythmia (severe bradyarrythmia is contraindicated), such as slow sinus rhythm, in patients with polyneuropathy or constipation.

Patients with a positive history of depression should be carefully monitored during long-term treatment with Iporel, as there are known reports of depressive episodes in clonidine-treated patients.
As with all antihypertensive drugs, treatment with Iporel should be monitored particularly closely in patients with myocardial insufficiency.
Iporel has no therapeutic effect in hypertension in the course of pheochromocytoma. Clonidine - the active substance of Iporel - and its metabolites are excreted mainly in urine. Patients with renal failure show varying susceptibility to the therapeutic effects of clonidine. Hence, meticulous adjustment of dosage to each patient and careful monitoring is necessary.
During routine dialysis only a minimal amount of clonidine is excreted, therefore there is no need to administer additional clonidine after dialysis.
Abrupt withdrawal of clonidine, especially in patients receiving high doses, may cause rebound hypertension. Cases of restlessness, palpitations, nervousness, tremor, headache and gastrointestinal symptoms have also been observed. Patients should be instructed not to discontinue treatment without consulting their doctor. If it is necessary to discontinue the medicinal product, the dose should be gradually reduced. However, if withdrawal symptoms do occur, they can be resolved by re-administration of clonidine or α and β adrenergic receptor blockers.
When co-administered with a β adrenergic receptor blocker, Iporel should not be discontinued until several days after β adrenergic receptor blocker discontinuation.

Paediatric and adolescent population
Iporel should not be used in children and adolescents under 18 years due to inadequate knowledge of the efficacy and safety of clonidine in these patients.

4.5 Interaction with other medicinal products and other forms of interaction
The antihypertensive effect of clonidine is potentiated by other hypotensive drugs. These include diuretics, vasodilators, β adrenergic receptor blockers, calcium antagonists and ACE inhibitors. In contrast, the effect of α_1-adrenergic receptor blockers is difficult to predict.
Tricyclic antidepressants or α adrenergic receptor blockers may attenuate or cancel the antihypertensive effect of clonidine and induce or exacerbate orthostatic hypotension.
Drugs that increase blood pressure or cause retention of sodium ions (Na^+) and water, such as non-steroidal anti-inflammatory drugs, may attenuate the hypotensive effect of clonidine.
α_2-adrenergic receptor blockers may attenuate the effects of clonidine in a dose-dependent manner.
Administration of drugs that have negative chronotropic or dromotropic effects with clonidine, such as β adrenergic receptor blockers or digitalis glycosides, with clonidine increases the risk of developing or exacerbating bradyarrhythmias.
It cannot be excluded that concomitant use of β-adrenergic receptor blockers with clonidine may cause or exacerbate peripheral vascular disease.
Clonidine may increase the central nervous system depressant effects of substances, including alcohol.

4.6 Fertility, pregnancy and lactation
Pregnancy
In some animal studies, clonidine caused an increased incidence of fetal resorption. Appropriate studies in humans have not been performed. It is known, however, that clonidine passes through the placenta and can cause a reduction in fetal heart rate. A postnatal transient rise in blood pressure in the newborn cannot be excluded.
The medicinal product may be used in pregnant women only if, in the opinion of the doctor, this is absolutely necessary. Careful monitoring of mother and baby is recommended.

Breastfeeding

The use of Iporel during breastfeeding is not recommended due to lack of adequate data.
Clonidine passes into breast milk. The concentration in milk is almost twice as high as in plasma.

4.7 Effects on ability to drive and use heavy machinery
The medicinal product may cause drowsiness, dizziness and visual disturbances to the extent that the ability to drive and use machinery is impaired. Patients experiencing these symptoms should not drive or operate any machinery.
Sedation may be exacerbated with concomitant use of central nervous system depressants.

4.8 Adverse reactions
Adverse reactions are listed in order of frequency, starting with the most common:
Very common (≥1/10); Common (≥1/100 to <1/10); Uncommon (≥1/1,000 to <1/100);
Rare (≥1/10,000 to <1/1,000); Very rare (<1/10,000); Not known (frequency cannot be estimated from the available data)

Some patients experience drowsiness, dizziness, dry mouth at the beginning of treatment. These symptoms usually subside as treatment is continued.

Other adverse reactions.
Endocrine disorders
Unknown: gynaecomastia.

Psychiatric disorders
Common: agitation, nervousness, insomnia, malaise.
Frequency not known: depression, headache, night terrors, night restlessness, anxiety, hallucinations, other behavioural disturbances.

Cardiac disorders
Common: orthostatic hypotension, palpitations, tachycardia or bradycardia.
Frequency not known: Raynaud's phenomenon, heart failure, cardiac arrhythmias, sinus bradycardia or atrioventricular block

Gastrointestinal disorders
Common: nausea and vomiting, constipation.
Frequency not known: anorexia, parotitis, pseudo-obstruction of the colon.

Hepatic and biliary tract disorders
Frequency not known: transient elevation of liver enzymes, liver damage.

Skin and subcutaneous tissue disorders
Frequency not known: itching, rash, urticaria, alopecia, vasogenic oedema.

Musculoskeletal and connective tissue disorders
Frequency not known: muscle and joint pain, muscle spasms in the lower limbs.

Renal and urinary disorders
Frequency not known: difficulty passing urine, urinary retention.

Reproductive system and mammary gland disorders
Common: reduced sexual activity, impotence.

General disorders and administration site conditions
Common: weakness, feeling of tiredness.

Frequency not known: weight gain.

Drying of the nasal mucosa and reduced tear secretion (important for contact lens wearers), as well as visual disturbances have also been described.
Cases of fluid retention during the initial phases of treatment have been reported. This is usually a temporary condition that can be corrected by including a diuretic in the treatment.
The medicinal product may cause a transient increase in blood glucose levels during the initial phase of treatment.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. This allows the continuous monitoring of the benefit-to-risk ratio of medicinal product use. Healthcare professionals are asked to report any suspected adverse reactions via the Department for Monitoring Adverse Reactions of the Medicinal Products of the Office for Registration of Medicinal Products, Medical Devices and Biocidal Products.
Al. Jerozolimskie 181C
02-222 Warsaw
Tel.: 22 49-21-301
fax: 22 49-21-309
Website: https://smz.ezdrowie.gov.pl

4.9 Overdose
Symptoms
Overdose may be accompanied by hypotension, bradycardia, drowsiness, irritability, weakness or abolition of reflexes, constriction of pupils, vomiting and hypoventilation. High doses may cause cardiac arrhythmias, coma and apnoea, convulsions, transient increase in blood pressure.
Treatment
In most cases, no treatment beyond general supportive management is required. In cases of severe bradycardia, atropine may be used to increase the heart rate.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties
Pharmacotherapeutic group: antihypertensive drugs; imidazoline receptor agonists; ATC code: C02AC01

Mechanism of action
Clonidine is a presynaptic α_2-adrenergic receptor agonist It inhibits the release of noradrenaline from nerve endings, both peripheral and central, leading to vasodilation and lowering of blood pressure. In higher concentrations it can stimulate α_1-adrenergic receptors, causing a transient increase in blood pressure.

Clonidine makes little or no difference to exercise and postural haemodynamic responses. It practically does not reduce renal flow. A gradual decrease in peripheral resistance was observed during long-term use.

Paediatric and adolescent population
The efficacy of clonidine in the treatment of hypertension was evaluated in five clinical trials involving children and adolescents. Efficacy data support the properties of clonidine in reducing systolic and diastolic blood pressure. However, due to limited data and methodological shortcomings in the studies, no definitive conclusions can be drawn regarding the use of clonidine in children with hypertension.
The efficacy of clonidine has also been evaluated in several clinical trials in children and adolescents with ADHD, Tourette's syndrome and stuttering. Clonidine has not been proven effective in

the treatment of these conditions. There were also two small studies conducted in children and adolescents with migraine, neither of which showed clonidine to be effective.
In clinical studies conducted in children and adolescents, the most common adverse reactions were somnolence, dry mouth, headache, dizziness and insomnia. These adverse effects can have a serious impact on the daily functioning of children.
Overall, the safety and efficacy of clonidine in children and adolescents have not been established (see section 4.2).

5.2 Pharmacokinetic properties
Absorption
Clonidine is well absorbed from the alimentary tract. Maximum plasma concentrations occur 3 to 5 hours after administration.
Metabolism
Clonidine is metabolised in the liver.
Elimination
It is excreted in 65% in the urine, partly unchanged. The half-life is approximately 12 – 13 hours. In renal failure, the half-life can be significantly prolonged – even up to 41 hours.

5.3 Preclinical safety data
There are no preclinical safety data relevant to the prescriber beyond the information contained in the previous sections of the SmPC.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients
Calcium hydrogen phosphate dihydrate
Potato starch
Povidone K-25
Magnesium stearate

6.2 Incompatibilities
Not applicable.

6.3 Shelf life
3 years

6.4 Special precautions for storage
Store below 25ºC.

6.5 Type and contents of container
PVC/Aluminium film blister in a cardboard box.
50 pcs. (2 blisters 25 pcs. each)

6.6 Special precautions for disposal and other handling
No special requirements.

7. MARKETING AUTHORISATION HOLDER

Bausch Health Ireland Limited
3013 Lake Drive
Citywest Business Campus
Dublin 24, D24PPT3
Ireland

8. MARKETING AUTHORISATION NUMBER(S)

Authorisation No. R/2828

9. DATE OF FIRST AUTHORISATION / RENEWAL OF THE AUTHORISATION

Date of first authorisation: 23 November 1987
Date of most-recent renewal:

10. DATE OF APPROVAL OR PARTIAL REVISION OF THE TEXT OF THE SUMMARY OF PRODUCT CHARACTERISTICS