Gizlan®

Irbesartan

DESCRIPTION:
Gizlan® (Irbesartan) belongs to a group of medicines known as angiotensin-II receptor antagonists.
Inactive ingredients: Lactose monohydrate, croscarmellose sodium, pregelatinized starch, poloxamer, microcrystalline cellulose, magnesium stearate, colloidal anhydrous silica, hypromellose, titanium dioxide, talc, macrogol.

PHARMACOLOGY:
Angiotensin-II is a substance produced in the body which binds to receptors in blood vessels causing them to tighten. This results in an increase in blood pressure. Irbesartan prevents the binding of angiotensin-II to these receptors, causing the blood vessels to relax and the blood pressure to lower.
Gizlan® slows the decrease of kidney function in patients with high blood pressure and type 2 diabetes.

INDICATIONS:
Gizlan® is used in:
- Treatment of essential hypertension.
- Treatment of renal disease in patients with hypertension and type 2 diabetes mellitus as part of an antihypertensive medicinal product regimen.

CONTRAINDICATIONS:
Gizlan® is contraindicated:
- In case of hypersensitivity to the active substance, or to any of the excipients.
- During second and third trimesters of pregnancy.

SIDE EFFECTS:
The incidence of adverse events is not related to dose (in the recommended dose range), gender, age, race, or duration of treatment.
In diabetic hypertensive patients with microalbuminuria and normal renal function, orthostatic dizziness and orthostatic hypotension were reported uncommonly in patients.
Terms marked with a star (*) refer to the adverse reactions that were additionally reported in diabetic hypertensive patients with chronic renal insufficiency and overt proteinuria.
The frequency of adverse reactions listed below is defined using the following convention: 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). Within each frequency grouping, undesirable effects are presented in order of decreasing seriousness.
- Investigations: Very common: Hyperkalaemia* occurs more often in diabetic patients treated with irbesartan. In diabetic hypertensive patients with microalbuminuria and normal renal function, hyperkalaemia (≥5.5 mEq/L) is more common in patients treated with irbesartan. In diabetic hypertensive patients with chronic renal insufficiency and overt proteinuria, hyperkalaemia (≥5.5 mEq/L) is more common.
Common: significant increases in plasma creatine kinase are commonly observed in irbesartan treated subjects. No identifiable clinical musculoskeletal events are expected with these increases. In hypertensive patients with advanced diabetic renal disease treated with irbesartan, a decrease in haemoglobin*, which was not clinically significant, is observed.
- Cardiac disorders: Uncommon: tachycardia
- Nervous system disorders: Common: dizziness, orthostatic dizziness*
- Respiratory, thoracic and mediastinal disorders: Uncommon: cough
- Gastrointestinal disorders: Common: nausea/vomiting. Uncommon: diarrhea, dyspepsia/heartburn.
- Musculoskeletal and connective tissue disorders: Common: musculoskeletal pain*
- Vascular disorders: Common: orthostatic hypotension*. Uncommon: flushing
- General disorders and administration site conditions: Common: fatigue Uncommon: chest pain.
- Reproductive system and breast disorders: Uncommon: sexual dysfunction.

The following additional adverse reactions have been reported during post-marketing experience; they are derived from spontaneous reports and therefore, the frequency of these adverse reactions is not known:
- Nervous system disorders: Headache.
- Ear and labyrinth disorders: Tinnitus.
- Gastrointestinal disorders: Dysgeusia.
- Renal and urinary disorders: Impaired renal function including cases of renal failure in patients at risk.
- Skin and subcutaneous tissue disorders: Leukocytoclastic vasculitis.
- Musculoskeletal and connective tissue disorders: Arthralgia, myalgia (in some cases associated with increased plasma creatine kinase levels), muscle cramps.
- Metabolism and nutrition disorders: Hyperkalaemia.
- Immune system disorders: Hypersensitivity reactions such as angioedema, rash, urticaria.
- Hepato-biliary disorders: Hepatitis, abnormal liver function.

WARNINGS AND PRECAUTIONS:
Intravascular volume depletion: symptomatic hypotension, especially after the first dose, may occur in patients who are volume and/or sodium depleted by vigorous diuretic therapy, dietary salt restriction, diarrhea or vomiting. Such conditions should be corrected before the administration of irbesartan.
Renovascular hypertension: there is an increased risk of severe hypotension and renal insufficiency when patients with bilateral renal artery stenosis or stenosis of the artery to a single functioning kidney are treated with medicinal products that affect the renin-angiotensin-aldosterone system. While this is not documented with irbesartan, a similar effect should be anticipated with angiotensin II receptor antagonists.
Renal impairment and kidney transplantation: when irbesartan is used in patients with impaired renal function, a periodic monitoring of potassium and creatinine serum levels is recommended. There is no experience regarding the administration of irbesartan in patients with recent kidney transplantation.
Hypertensive patients with type 2 diabetes and renal disease: the effects of irbesartan both on renal and cardiovascular events were not uniform across all subgroups, in an analysis carried out in the study with patients with advanced renal disease. In particular, they appeared less favourable in women and non-white subjects.
Hyperkalaemia: as with other medicinal products that affect the renin-angiotensin-aldosterone system, hyperkalaemia may occur during the treatment with irbesartan, especially in the presence of renal impairment, overt proteinuria due to diabetic renal disease, and/or heart failure. Close monitoring of serum potassium in patients at risk is recommended.
Lithium: the combination of lithium and irbesartan is not recommended.
Aortic and mitral valve stenosis, obstructive hypertrophic cardiomyopathy: as with other vasodilators, special caution is indicated in patients suffering from aortic or mitral stenosis, or obstructive hypertrophic cardiomyopathy.
Primary aldosteronism: patients with primary aldosteronism generally will not respond to anti-hypertensive medicinal products acting through inhibition of the renin-angiotensin system. Therefore, the use of irbesartan is not recommended.
General: in patients whose vascular tone and renal function depend predominantly on the activity of the renin-angiotensin-aldosterone system (e.g. patients with severe congestive heart failure or underlying renal disease, including renal artery stenosis), treatment with angiotensin converting enzyme inhibitors or angiotensin II receptor antagonists that affect this system has been associated with acute hypotension, azotaemia, oliguria, or rarely acute renal failure. As with any anti-hypertensive agent, excessive blood pressure decrease in patients with ischaemic cardiopathy or ischaemic cardiovascular disease could result in a myocardial infarction or stroke.
As observed for angiotensin converting enzyme inhibitors, irbesartan and the other angiotensin antagonists are apparently less effective in lowering blood pressure in black people than in non blacks, possibly because of higher prevalence of low renin states in the black hypertensive population.
Paediatric patients: irbesartan has been studied in paediatric populations aged 6 to 16 years old but the current data are insufficient to support an extension of the use in children until further data become available.
Use during Pregnancy and lactation:
Pregnancy:
The use of AIIRAs is not recommended during the first trimester of pregnancy. The use of AIIRAs is contraindicated during the second and third trimesters of pregnancy.
Epidemiological evidence regarding the risk of teratogenicity following exposure to ACE inhibitors during the first trimester of pregnancy has not been conclusive; however a small increase in risk cannot be excluded. Whilst there is no controlled epidemiological data on the risk with Angiotensin II Receptor Antagonists (AIIRAs), similar risks may exist for this class of drugs. Unless continued AIIRA therapy is considered essential, patients planning pregnancy should be changed to alternative anti-hypertensive treatments which have an established safety profile for use in pregnancy. When pregnancy is diagnosed, treatment with AIIRAs should be stopped immediately, and, if appropriate, alternative therapy should be started.
Exposure to AIIRA therapy during the second and third trimesters is known to induce human fetotoxicity (decreased renal function, oligohydramnios, skull ossification retardation) and neonatal toxicity (renal failure, hypotension, and hyperkalaemia).
Should exposure to AIIRAs have occurred from the second trimester of pregnancy, ultrasound check of renal function and skull is recommended.
Infants whose mothers have taken AIIRAs should be closely observed for hypotension.
Lactation:
Because no information is available regarding the use of irbesartan during breast-feeding, irbesartan is not recommended and alternative treatments with better established safety profiles during breast-feeding are preferable, especially while nursing a newborn or preterm infant.
Effects on ability to drive and use machines:
No studies on the effects on the ability to drive and use machines have been performed. Based on its pharmacodynamic properties, irbesartan is unlikely to affect this ability. When driving vehicles or operating machines, it should be taken into account that dizziness or weariness may occur during treatment.
Gizlan® contains lactose: If the patient has been told by the doctor that he has intolerance to some sugars, he should contact his doctor before taking this medicinal product.

DRUG INTERACTIONS:
- Diuretics and other antihypertensive agents: other antihypertensive agents may increase the hypotensive effects of irbesartan; however irbesartan has been safely administered with other antihypertensive agents, such as beta blockers, long-acting calcium channel blockers, and thiazide diuretics. Prior treatment with high dose diuretics may result in volume depletion and a risk of hypotension when initiating therapy with irbesartan.
- Potassium supplements and potassium-sparing diuretics: based on experience with the use of other medicinal products that affect the renin- angiotensin system, concomitant use of potassium-sparing diuretics, potassium supplements, salt substitutes containing potassium or other medicinal products that may increase serum potassium levels (e.g. heparin) may lead to increases in serum potassium and is, therefore, not recommended.
- Lithium: reversible increases in serum lithium concentrations and toxicity have been reported during concomitant administration of lithium with angiotensin converting enzyme inhibitors. Similar effects have been very rarely reported with irbesartan so far. Therefore, this combination is not recommended. If the combination proves necessary, careful monitoring of serum lithium levels is recommended.
- Non steroidal anti inflammatory drugs: when angiotensin II antagonists are administered simultaneously with non-steroidal anti-inflammatory drugs (i.e. selective COX 2 inhibitors, acetylsalicylic acid (> 3 g/day) and non-selective NSAIDs), attenuation of the antihypertensive effect may occur.
As with ACE inhibitors, concomitant use of angiotensin II antagonists and NSAIDs may lead to an increased risk of worsening of renal function, including possible acute renal failure, and an increase in serum potassium, especially in patients with poor pre-existing renal function. The combination should be administered with caution, especially in the elderly. Patients should be adequately hydrated and consideration should be given to monitoring renal function after initiation of concomitant therapy, and periodically thereafter.
- Additional information on irbesartan interactions: the pharmacokinetics of irbesartan is not affected by hydrochlorothiazide. Irbesartan is mainly metabolised by CYP2C9 and to a lesser extent by glucuronidation. No significant pharmacokinetic or pharmacodynamic interactions were observed when irbesartan was coadministered with warfarin, a medicinal product metabolised by CYP2C9. The effects of CYP2C9 inducers such as rifampicin on the pharmacokinetic of irbesartan have not been evaluated. The pharmacokinetic of digoxin was not altered by coadministration of irbesartan.

DOSAGE AND ADMINISTRATION:
The usual recommended initial and maintenance dose is 150 mg once daily, with or without food. **Gizlan®** at a dose of 150 mg once daily generally provides a better 24 hour blood pressure control. Than 75mg irbesartan
In patients insufficiently controlled with 150 mg once daily, the dose of **Gizlan®** can be increased to 300 mg, or other anti-hypertensive agents can be added. In particular, the addition of a diuretic such as hydrochlorothiazide has been shown to have an additive effect with **Gizlan®**.
In hypertensive type 2 diabetic patients, therapy should be initiated at 150 mg irbesartan once daily and titrated up to 300 mg once daily as the preferred maintenance dose for treatment of renal disease.
The demonstration of renal benefit of **Gizlan®** in hypertensive type 2 diabetic patients is based on studies where irbesartan was used in addition to other antihypertensive agents, as needed, to reach target blood pressure.
Renal impairment: no dosage adjustment is necessary in patients with impaired renal function.
Hepatic impairment: no dosage adjustment is necessary in patients with mild to moderate hepatic impairment. There is no clinical experience in patients with severe hepatic impairment.
Paediatric patients: irbesartan is not recommended for use in children and adolescents due to insufficient data on safety and efficacy.

OVERDOSAGE:
Experience in adults exposed to doses of up to 900 mg/day for 8 weeks revealed no toxicity. The most likely manifestations of overdose are expected to be hypotension and tachycardia; bradycardia might also occur from overdose. No specific information is available on the treatment of overdose with irbesartan. The patient should be closely monitored, and the treatment should be symptomatic and supportive. Suggested measures include induction of emesis and/or gastric lavage. Activated charcoal may be useful in the treatment of overdose. Irbesartan is not removed by haemodialysis

PRESENTATIONS:
Gizlan® 150 Film Coated Tablets: Packs of 30 and 500 tablets . Each tablet contains 150 mg irbesartan.
Gizlan® 300 Film Coated Tablets: Packs of 30 and 500 tablets . Each tablet contains 300 mg irbesartan.

STORAGE CONDITIONS:
Store below 30°C.

This is a medicament

Medicament is a product which affects your health, and its consumption contrary to instructions is dangerous for you.
Follow strictly the doctor's prescription, the method of use, and the instructions of the pharmacist who sold you the medicament.
The doctor and the pharmacist are experts in medicine, its benefits and its risks.
Do not, by yourself, interrupt the period of treatment prescribed.
Do not repeat the same prescription without consulting your doctor.

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