IRBIS 150 & IRBIS 300

(Irbesartan Tablets 150mg & Irbesartan Tablets 300mg)

DESCRIPTION

IRBIS 150

White to off white coloured, capsule shaped, biconvex, film coated tablets debossed with '159' on one side and H on the other side.
Each film coated tablet contains Irbesartan 150 mg.

IRBIS 300

White to off white coloured, capsule shaped, biconvex, film coated tablets debossed with '160' on one side and H on the other side.
Each film coated tablet contains Irbesartan 300 mg.

PHARMACODYNAMICS

Pharmacotherapeutic group: Angiotensin-II antagonists, ATC code C09C A04.

Mechanism of action:

Irbesartan is a potent, orally active, selective angiotensin-II receptor (type AT1) antagonist.

It is expected to block all actions angiotensin-II mediated by the AT1 receptor, regardless of the source or route of synthesis of angiotensin-II. The selective antagonism of the angiotensin-II (AT1) receptors results in increases in plasma renin levels and angiotensin-II levels, and a decrease in plasma aldosterone concentration. Serum potassium levels are not significantly affected by irbesartan alone at the recommended doses. Irbesartan does not inhibit ACE (kininase-II), an enzyme which generates angiotensin-II and also degrades bradykinin into inactive metabolites. Irbesartan does not require metabolic activation for its activity.

PHARMACOKINETICS

After oral administration, irbesartan is well absorbed studies of absolute bioavailability gave values of approximately60 – 80%. Concomitant food intake does not significantly influence the bioavailability of irbesartan. Plasma protein binding is approximately 96%, with negligible binding to cellular blood components. The volume of distribution is 53 – 93 liters. Following oral or intravenous administration of 14C irbesartan, 80-85% of the circulating plasma radioactivity is attributable to unchanged irbesartan. Irbesartan is metabolized by the liver via glucuronide conjugation and oxidation.

The major circulating metabolite is irbesartan glucuronide (approximately 6%). In vitro studies indicate that irbesartan is primarily oxidized by the cytochrome P450 enzyme CYP2C9; isoenzyme CYP3A4 has negligible effect.

Renal impairment:

In patients with renal impairment or those undergoing haemodialysis, the pharmacokinetic parameters of irbesartan are not significantly altered. Irbesartan is not removed by haemodialysis.

Hepatic impairment:

In patients with mild to moderate cirrhosis, the pharmacokinetic parameters of irbesartan are not significantly altered. Studies have not been performed in patients with severe hepatic impairment

INDICATION

Therapeutic indications

Treatment of essential hypertension

Treatment of diabetic nephropathy with an elevated serum creatinine and proteinuria (> 300 mg/day) in patients with type 2 diabetes and hypertension. In this population, Irbesartan reduces the rate of progression of nephropathy as measured by the occurrence of doubling of serum creatinine or end-stage renal disease (need for dialysis or renal transplantation).

RECOMMENDED DOSE

In the hypertensive type 2 diabetic patients, therapy should be initiated at 150 mg irbesartan once daily and titrated up to 300mg once daily as the preferred maintenance dose for treatment of renal disease. The demonstration of renal benefit of Irbesartan 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. A lower starting dose (75 mg) should be considered for patients undergoing haemodialysis

ROUTE OF ADMINISTRATION

Oral

CONTRAINDICATIONS

Hypersensitivity to the active substance, or to any of the excipients. Second and third trimesters of pregnancy.

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 and 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 of the artery to a single functioning kidney are treated with drugs that affect the renin angiotensin-aldosterone system.

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 diseases

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 favorable in women and non-white subjects (see pharmacodynamics properties).

Hyperkalemia

As with other drugs that affect the renin-angiotensin aldosterone system, hyperkalemia 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 (see interaction with other medicinal products and other forms of interaction).

Lithium

The combination of lithium and Irbesartan is not recommended see interaction with other medicinal products and other forms of interaction).

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 response to antihypertensive drugs acting through inhibition of the renin-angiotensin system. Therefore, the use of Irbesartan is not recommended.

INTERACTION WITH OTHER MEDICAMENTS

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 (see special warnings and special precautions for use).

Potassium supplements and potassium-sparing diuretics

Based on experience with the use of other drugs that affect the renin angiotensin system, concomitant use of potassium-sparing diuretics, potassium supplements, salt substitutes containing potassium or other drugs that may increase serum potassium levels (e.g. heparin) may lead to increases in serum potassium and is, therefore, not recommended (see special warnings and special precautions for use).

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 to irbesartan so far.

Therefore, this combination in not recommended (see special warnings and special precautions for use).

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 preexisting 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

In clinical studies, the pharmacokinetic of irbesartan is not affected by hydrochlorothiazide. Irbesartan is mainly metabolized by CYP2C9 and to a lesser extent by glucuronidation. No significant pharmacokinetic or pharmacodynamics interactions were observed when irbesartan was coadministered with warfarin, a drug metabolized by CYP2C9. The effects of CYP2C9 induce such as rifampicin on the pharmacokinetic of irbesartan has not been evaluated. The pharmacokinetic of digoxin was not altered by coadministration of irbesartan.

PREGNANCY AND LACTATION

pregnancy

The use of AIIRAs is not recommended during the first trimester of pregnancy (see special warnings and precautions for use).

The use of AIIRAs is contraindicated during the second and third trimesters of pregnancy (see contraindications and special warnings and precautions for use).

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 antihypertensive treatments which have an established safely 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 9renal failure, hypotension, hyperkalemia) (see preclinical safety data). 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 (see contraindications and special warnings and precautions for use).

Lactation

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 new born or preterm infant.

SIDE EFFECTS

The frequency of adverse reactions listed below is defined using the following convention:
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)
within each frequency grouping, undesirable effects are presented in order of decreasing seriousness. Adverse reactions additionally reported from post marketing experience are also listed. These adverse reactions are derived from spontaneous reports.

Immune system disorders:

Not known: hypersensitivity reactions such as angioedema, rash, urticaria

Metabolism and nutrition disorders:

Not known: hyperkalaemia

Nervous system disorders:

Common: dizziness, orthostatic dizziness*

Not known: vertigo, headache

Ear and labyrinth disorder:

Not known: tinnitus

Cardiac disorders:

Uncommon: tachycardia

Vascular disorders:

Common: orthostatic hypotension*

Uncommon: flushing

Respiratory, thoracic and mediastinal disorders:

Uncommon: cough

Gastrointestinal disorders:

Common: nausea/vomiting

Uncommon: diarrhoea, dyspepsia/heartburn

Not known: dysgeusia

Hepatobiliary disorders:

Uncommon: jaundice

Not known: hepatitis, abnormal liver function

Skin and subcutaneous tissue disorders:

Not known: leukocytoclastic vasculitis

Musculoskeletal and connective tissue disorders:

Common: musculoskeletal pain*

Not known: arthralgia, myalgia (in some cases associated with increased plasma creatine kinase levels), muscle cramps

Renal and urinary disorders:

Not known: impaired renal function including cases of renal failure in patients at risk (see Special warnings and precautions for use)

Reproductive system and breast disorders:

Uncommon: sexual dysfunction

General disorders and administration site conditions:

Common: fatigue

Uncommon: chest pain

SYMPTOMS AND TREATMENT OF OVERDOSE

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 used in the treatment of overdose. Irbesartan is not removed by hemodialysis.

STORANGE CONDITIONS

Store below 30°C

SHELF LIFE
24 months

PRESENTATION

IRBIS 150 and IRBIS 300 is proposed to be marketed in 10 x 10 tablets Blister pack. Irbesartan Tablets packed in blisters (Alu/PVC/PE/PVdC and Alu/PVC/PVdC) will be further packed in preprinted cartons with package leaflet according to the approved pack size

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