# hovid-Irbesartan Tablet

VIIRBE01-PC3

## DESCRIPTION

**hovid-Irbesartan Tablet 150 mg:**
Caplet-shaped, white to off-white, 11.55 mm long, 6.35 mm wide, film-coated tablet, bevel-edged with shallow convex faces, thickness of 4.80 - 5.00 mm and "HD" embossed on one face.

**hovid-Irbesartan Tablet 300 mg:**
Caplet-shaped, white to off-white, 16.00 mm long, 8.00 mm wide, film-coated tablet, bevel-edged with shallow convex faces, thickness of 5.45 - 5.65 mm and "HOVID" embossed on one face.

## COMPOSITION

**hovid-Irbesartan Tablet 150 mg:**
Each tablet contains: Irbesartan 150 mg

**hovid-Irbesartan Tablet 300 mg:**
Each tablet contains: Irbesartan 300 mg

## ACTION AND PHARMACOLOGY

Irbesartan is a nonpeptide competitive angiotensin II antagonist that selectively blocks the binding of angiotensin II to the AT 1 receptor. In the renin-angiotensin system, angiotensin I is converted by angiotensin-converting enzyme (ACE) to form angiotensin II. Angiotensin II stimulates the adrenal cortex to synthesize and secrete aldosterone, which decreases the excretion of sodium and increases the excretion of potassium. Angiotensin II also acts as a vasoconstrictor in vascular smooth muscle. Irbesartan, by blocking the binding of angiotensin II to the AT 1 receptor, promotes vasodilation and decreases the effects of aldosterone. The negative feedback regulation of angiotensin II on renin secretion also is inhibited, but the resulting rise in plasma renin concentrations and consequent rise in angiotensin II plasma concentrations do not counteract the blood pressure–lowering effect that occurs

## PHARMACOKINETICS

- **Absorption:** Irbesartan is rapidly absorbed from the gastrointestinal tract with an oral bioavailability of 60 to 80%. Peak plasma concentrations of irbesartan occur 1.5 to 2 hours after an oral dose. Irbesartan may be dosed without regards to meals
- **Distribution:** Irbesartan is about 96% bound to plasma proteins.
  The volume of distribution is 53 - 93 litres
- **Metabolism:** Irbesartan is metabolised in the liver via glucuronide conjugation and oxidation, primarily by the cytochrome P450 isoenzyme CYP2C9, to inactive metabolites. The major circulating metabolite is irbesartan glucuronide (approximately 6%).
- **Elimination:** It is excreted as unchanged drug and metabolites in the bile and in urine. The terminal elimination half-life is about 11 to 15 hours. The total body clearance is 157 - 176 ml/min.

## INDICATION

- Treatment of essential hypertension.
- Treatment of diabetic nephropathy with an elevated serum creatinine and proteinuria (>300mg / 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)

## CONTRAINDICATIONS

Hypersensitivity to the active substance, or to any of the excipients.

Second and third trimesters of pregnancy.

## WARNINGS AND PRECAUTIONS

**Pregnancy:** Fetotoxic, especially during second and third trimesters; when pregnancy is diagnosed, treatment should be discontinue use as soon as possible and, if appropriate, alternative therapy should be started

Severe heart failure, oliguria, progressive azotemia, acute renal failure, and death have been reported with similarly acting drugs

Volume or salt-depleted patients (eg, vigorous diuresis, salt restriction, diarrhoea, vomiting or hemodialysis); increased risk of hypotension; correct volume depletion prior to therapy initiation or initiate at lower dose; medical management needed if hypotension occurs.

Special caution is indicated in patients suffering from aortic or mitral stenosis, or obstructive hypertrophic cardiomyopathy.

Potassium and creatinine serum levels monitoring is recommended when Irbesartan is used in patients with impaired renal function

Hyperkalaemia may occur during the treatment with irbesartan. Close monitoring of serum potassium in patients at risk is recommended

Patients with primary aldosteronism generally will not respond to antihypertensive medicinal products acting through inhibition of the renin-angiotensin system. Therefore, the use of Irbesartan is not recommended.

Renal artery stenosis, bilateral or unilateral; increases in serum creatinine and BUN have been reported

**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.

**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 antihypertensive agent, excessive blood pressure decrease in patients with ischaemic cardiopathy or ischaemic cardiovascular disease could result in a myocardial infarction or stroke.

**Effects on the ability to drive and use machines:** 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

## PREGNANCY AND LACTATION

**Pregnancy**
It is not recommended during the first trimester of pregnancy and is contraindicated during the second and third trimesters of pregnancy

XXX

**Lactation**
Available evidence and/or expert consensus is inconclusive or is inadequate for determining infant risk when used during breastfeeding. Weigh the potential benefits of drug treatment against potential risks before prescribing this drug during breastfeeding.

## 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:**
  Concurrent use may result in hyperkalemia.
- **Non-steroidal anti-inflammatory drugs(NSAIDs):**
  Concurrent use with non-steroidal anti-inflammatory drugs may result in decreased antihypertensive effects and an increased risk of renal impairment. 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.
- **Lithium:**
  The combination of lithium and Irbesartan is not recommended. If the combination proves necessary, careful monitoring of serum lithium levels is recommended.
- Concurrent use of irbesartan and mifepristone may result in increased exposure to irbesartan.
- Concurrent use of amiodarone and irbesartan may result in increased plasma levels of irbesartan.
- Concurrent use of Ma Huang and yohimbine and angiotensin II receptor antagonists may result in reduced effectiveness of angiotensin ii receptor antagonists.

## MAIN SIDE/ADVERSE EFFECTS

- **Investigations:** hyperkalaemia, increases in plasma creatine kinase
- **Cardiac disorders:** tachycardia
- **Vascular disorders:** orthostatic hypotension, flushing
- **Nervous system disorders:** headache, dizziness
- **Respiratory, thoracic and mediastinal disorders:** cough, upper respiratory infection
- **Gastrointestinal disorders:** nausea, vomiting, diarrhoea, dyspepsia/heartburn, dysgeusia
- **General disorders and administration site conditions:** fatigue
- **Renal and urinary disorders:** impaired renal function including cases of renal failure in patients at risk
- **Skin and subcutaneous tissue disorders:** urticaria, leukocytoclastic vasculitis
- **Musculoskeletal and connective tissue disorders:** arthralgia, myalgia (in some cases associated with increased plasma creatine kinase levels), rhabdomyolysis, muscle cramps
- **Immune system disorders:** hypersensitivity reactions such as angioedema, rash, urticaria
- **Hepato-biliary disorders:** hepatitis, abnormal liver function, cholestasis, jaundice
- **Hematologic disorders:** thrombocytopenia
- **Reproductive system and breast disorders:** sexual dysfunction
- **Ear and labyrinth disorders:** tinnitus

## OVERDOSE AND TREATMENT

**Symptoms:** Mild hypotension and tachycardia, hypokalemia, asymptomatic hypoglycemia, muscle cramps and dizziness have been reported. Bradycardia might also occur from overdose.

**Treatment:** The patient should be closely monitored, and the treatment should be symptomatic and supportive. Activated charcoal may be useful in the treatment of overdose. As Irbesartan is highly protein bound; hemodialysis is unlikely to be of any benefit.

## DOSAGE AND ADMINISTRATION

Oral

The usual recommended initial and maintenance dose is 150 mg once daily, with or without food.

Irbesartan at a dose of 150 mg once daily generally provides a better 24 hour blood pressure control than 75 mg. However, initiation of therapy with 75 mg could be considered, particularly in haemodialysed patients and in the elderly over 75 years.

In patients insufficiently controlled with 150 mg once daily, the dose of Irbesartan can be increased to 300 mg, or other antihypertensive agents can be added. In particular, the addition of a diuretic such as hydrochlorothiazide has been shown to have an additive effect with Irbesartan

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.

**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

**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.

**Elderly patients:** although consideration should be given to initiating therapy with 75 mg in patients over 75 years of age, dosage adjustment is not usually necessary for the elderly.

**Paediatric patients:** irbesartan is not recommended for use in children and adolescents due to insufficient data on safety and efficacy.

Note: The information given here is limited. For further information, consult your doctor or pharmacist.

Storage:
Store below 30°C.

Presentation/ Packing:
Blister pack of 10's, 30's and 100's.

Product Registration Holder: HOVID Bhd.
121, Jalan Tunku Abdul Rahman, 30010 Ipoh, Malaysia.

Manufactured by: HOVID Bhd.
Lot 56442, 7 1/2 Miles, Jalan Ipoh/Chemor,
31200 Chemor, Malaysia.

Information date: December 2016