**Product:** Irbesartan (Aprovel)
**Strengths:** 150 mg Film-Coated Tablet (DRP-5716), 300 mg Film-Coated Tablet (DRP-5715)
**Presentation:** Alu/White Opaque PVC/PVDC blister pack x 14s (Box of 28's)
**I:** Treatment of hypertension; may be used either alone or in combination with other antihypertensive agents (e.g., thiazide diuretics, beta-adrenergic blocking agents, long-acting CCB agents). Treatment of renal disease in patients with hypertension and type 2 diabetes.
**D:** Usual initial dose is 150 mg once daily. Increase to 300 mg daily for patients requiring further reduction in BP. In patients with HTN and Type 2 diabetic renal disease, 300 mg once daily is the preferred maintenance dose. Administer with or without food. Safety and effectiveness in pediatric patients have not been established. No dosage reduction necessary in the elderly, in patients with impaired hepatic function (mild to moderate) & in patients with impaired renal function. Consider a lower initial dose in severely volume-depleted and/or sodium-depleted patients.
**C:** Hypersensitivity to Irbesartan or to any of the excipients; Do NOT co-administer with aliskiren-containing medicines in patients with diabetes or with moderate to severe renal impairment (GFR <60mL/min/1.73m$^2$). Do NOT co-administer with ACE Inhibitors in patients with diabetic nephropathy. Pregnancy and Lactation.
**W/P:** Symptomatic hypotension may occur in patients who are volume and/or sodium depleted by vigorous diuretic therapy, dietary salt restriction, diarrhea or vomiting. Risk of severe hypotension and renal insufficiency in patients with bilateral renal artery stenosis or stenosis of the artery to a single functioning kidney. Recommended periodic monitoring of potassium and creatinine serum levels in patients with impaired renal function. Increased risk of hypotension, hyperkalaemia and decreased renal function (incl. acute renal failure) with concomitant use of ACEIs, AT-II receptor blockers or aliskiren. Risk of hyperkalaemia; patients with primary aldosteronism; caution with use in patients with aortic and mitral valve stenosis, obstructive hypertrophic cardiomyopathy; patients who are elderly, volume-depleted, or with compromised renal function. May induce hypoglycemia, particularly in diabetic patients. Contains Lactose.
**Int:** ACE Inhibitors; Aliskiren-containing medicines; lithium; potassium-sparing diuretics, potassium supplements, salt substitutes containing potassium or other medicinal products; NSAIDs (incl. COX-2 inhibitors); Repaglinide; Insulin and antidiabetics.
**AE:** hyperkalaemia, dizziness, orthostatic dizziness, orthostatic hypotension, nausea/vomiting, musculoskeletal pain, fatigue, increases in plasma creatine kinase
**PK:** Absorption: Irbesartan is an orally active agent and does not require biotransformation for its activity. Peak plasma concentration occurs at 1.5-2 hours after oral administration. Following oral administration, irbesartan is rapidly and completely absorbed. The absolute oral bioavailability of irbesartan is 60-80%. Food does not affect the bioavailability. Distribution: approximately 96% protein-bound in plasma and has negligible binding to cellular components of blood. Volume of distribution is 53-93 liters. Metabolism: Irbesartan is metabolized by the liver via glucuronide conjugation and oxidation. Elimination: excreted by both biliary and renal routes. The terminal elimination half-life (t½) is 11-15 hours. Irbesartan exhibits linear pharmacokinetics over the therapeutic dose range. Steady-state plasma concentrations are attained within 3 days after initiation of a once-daily dosing regimen. Limited accumulation (< 20%) is observed in plasma upon repeated once-daily dosing.
**PD:** Irbesartan is a specific antagonist of Angiotensin II receptors ($AT_1$ subtype). Irbesartan blocks the potent vasoconstrictor and aldosterone-secreting effects of AT-II by selective-antagonism of the ATII receptors ($AT_1$ subtype) localized on vascular smooth muscle cells and in the adrenal cortex. It has no agonist activity at the $AT_1$ receptor and a much greater affinity (>8500-fold) for the $AT_1$ receptor than for the $AT_2$ receptor. Irbesartan blockade of AT1 receptors interrupts the feedback loop within the renin-angiotensin system, resulting in increases in plasma renin levels and angiotensin II levels. Aldosterone plasma concentrations decline following irbesartan administration, however, serum potassium levels are not significantly affected (mean increase of < 0.1 mEq/L) at the recommended doses.

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