Product: Irbesartan + Amlodipine (Aprovasc)
Strengths: 150 mg/ 5 mg Film-Coated Tab (DR-XY45509), 300 mg/ 5 mg Film-Coated Tab (DR-XY45507), 300 mg/ 10 mg Film-Coated Tab (DR-XY45508) Presentation: Alu/White Opaque PVC/PE/PVDC blister pack x 7's (Box of 28's)
I: Treatment of essential hypertension. Indicated in patients whose blood pressure is not adequately controlled on Irbesartan or Amlodipine monotherapy
D: Recommended is one tab per day. Should be administered in patients whose BP is not adequately controlled on monotherapy with Irbesartan or Amlodipine or for continuation of therapy for patients receiving Irbesartan and Amlodipine as separate tabs. Max. recommended dose is 300mg/10 mg per day. No dosage adjustment is necessary for the elderly and/or patients with impaired renal function. Safety and efficacy in children has not been established.
Administer with caution in patients with hepatic insufficiency. Can be used with or without food.
C: Hypersensitivity to either or both active substances or to any of the excipients; hypersensitivity to dihydropyridines; cardiogenic shock, clinically significant aortic stenosis, unstable angina (excl. Prinzmetal's angina); Pregnancy and Lactation. Do NOT co-administer with aliskiren-containing medicines in patients with diabetes or with moderate to severe renal impairment (GFR <60mL/min/1.73m2). Do NOT co-administer with ACE Inhibitors in patients with diabetic nephropathy
W: Symptomatic hypotension, as with ACEIs, may be expected in sodium/volume-depleted patients. Fetal/Neonatal morbidity and mortality. Patients with heart failure and/or hepatic impairment. Safety and efficacy of this drug in hypertensive crisis has not been established.
P: Dual blockade of the RAAS combining Irbesartan/Amlodipine with an ACE Inhibitor or aliskiren is not recommended.
Int: Aliskiren-containing medicinal products in patients with DM or moderate to severe renal impairment, combination with ACEIs in patients with diabetic nephropathy. Concomitant use of potassium-sparing diuretics, potassium supplements, or salt substitutes containing potassium. Patients who are elderly, volume depleted (incl. those on diuretic therapy), or with compromised renal function, coadministration of NSAIDs, including COX-2 inhibitors, with angiotensin II receptor antagonists, may result in deterioration of renal function, including possible acute renal failure. Lithium.
For Amlodipine alone:
Sildenafil.
AE: dizziness, headache, somnolence, nausea/ vomiting, fatigue, edema, palpitations, flushing, abdominal pain, vertigo, upper abdominal pain, nausea, tongue disorder, peripheral edema, glossodynia, cough, contact dermatitis, hot flush, palpitations, orthostatic hypotension, gingival swelling, proteinuria PK: The 3 fixed-dose combinations of Irbesartan/ Amlodipine (150/5, 300/5, 300/10) are bioequivalent to the free dose combinations in terms of rate and extent of absorption. The mean half-life for Irbesartan and Amlodipine, given alone or in combination, are similar: 17.6h vs 17.7h for Irbesartan, and 58.5h vs 52.1h for amlodipine. For Irbesartan: Irbesartan is rapidly and completely absorbed with peak plasma concentration occurring at 1.5-2h after oral administration. The absolute oral BA is 60-80%. Food does not affect the BA. Irbesartan is approximately 96% protein-bound in plasma and has negligible binding to cellular components of blood. For Amlodipine: Amlodipine is well absorbed with peak blood levels between 6 and 12h post dose. Absolute BA is between 64-90%. In vitro studies have shown that ~97.5% of circulating amlodipine is bound to plasma proteins.
PD: For Irbesartan: Irbesartan is a specific antagonist of Angiotensin II receptors (AT1 subtype) . Irbesartan blocks the potent vasoconstrictor and aldosteronesecreting effects of ATII by selective-antagonism of the ATII receptors (AT1 subtype) localized on vascular smooth muscle cells and in the adrenal cortex. It has no agonist activity at the AT1 receptor and a much greater affinity (>8500-

fold) for the AT1 receptor than for the AT2 receptor. The blood pressure lowering effect is apparent after the first dose and substantially present within 1-2 wks, with the maximal effect occurring by 4-6wks. In long-term follow-up studies, the effect of irbesartan was maintained for over 1 yr. Once-daily doses of up to 900 mg provided dose-related decreases in BP. Doses of 150-300 mg once daily lower supine or seated BP at trough (i.e., 24h after dosing) by an ave. of 8-13/5-8 mmHg (systolic/diastolic) greater than those associated with placebo. Optimal effects on 24h BP are achieved with once-daily dosing. For Amlodipine: Amlodipine is a dihydropyridine calcium antagonist that inhibits the transmembrane influx of calcium ions into cardiac and vascular smooth muscle. Amlodipine has a direct relaxant effect of vascular smooth muscle thereby providing antihypertensive action. In patients with hypertension, once daily dosing provides clinically significant reductions of blood pressure in both supine and standing positions throughout the 24h interval. In patients with angina, once daily administration increases total exercise time, time to angina onset, and time to 1mm ST segment depression, and decreases both angina attach frequency and glyceryl trinitrate tablet consumption.

CCDS ver 7 | Date of Revision: Sep 2014