Aprovel ® Abridged Prescribing Information:

1. NAME & PRESENTATION: Aprovel 150 mg – 300 mg film-coated tablets, each film-coated tablet contains 150 mg or 300 mg of irbesartan.

2. Therapeutic INDICATIONS: Aprovel is indicated in adults for the treatment of essential hypertension. It is also indicated for the treatment of renal disease in adult patients with hypertension and type 2 diabetes mellitus as part of an antihypertensive medicinal product regimen

3. DOSAGE & METHOD OF ADMINISTRATION: The usual recommended initial and maintenance dose is 150 mg once daily, with or without food. Aprovel 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 haemodialysis patients and in the elderly over 75 years. In patients insufficiently controlled with 150 mg once daily, the dose of Aprovel 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 Aprovel.

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.

4. SPECIAL POPULATION: 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.

4. CONTRA-INDICATIONS: Hypersensitivity to the active substance or to any of the excipients listed in section. Second and third trimesters of pregnancy. The concomitant use of Aprovel with aliskiren-containing products is contraindicated in patients with diabetes mellitus or renal impairment**.** Older people 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 older people. Paediatric population The safety and efficacy of Aprovel in children aged 0 to 18 has not been established. Currently available data are described in section 4.8, 5.1 and 5.2 but no recommendation on a posology can be made.

WARNINGS & PRECAUTIONS: 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, diarrhoea or vomiting. Such conditions should be corrected before the administration of Aprovel. 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 Aprovel, a similar effect should be anticipated with angiotensin-II receptor antagonists. when Aprovel 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 Aprovel in patients with a recent kidney transplantation.

6. INTERACTIONS: Diuretics and other antihypertensive agents, Aliskiren-containing products and ACE-inhibitors, Potassium supplements and potassium-sparing diuretics, Non-steroidal anti-inflammatory drugs.

7. PREGNANCY AND LACTATION: The use of AIIRAs is not recommended during the first trimester of pregnancy, use of AIIRAs is contraindicated during the second and third trimesters of pregnancy. Because no information is available regarding the use of Aprovel during breast-feeding, Aprovel is not recommended and alternative treatments with better established safety profiles during breast-feeding are preferable, especially while nursing a newborn or preterm infant.

8. EFFECTS ON ABILITY TO DRIVE: irbesartan is unlikely to affect the ability to drive and use machines. When driving vehicles or operating machines, it should be taken into account that dizziness or weariness may occur during treatment.

9. ADVERSE REACTIONS: **Very common**: Hyperkalaemia* occurred more often in diabetic patients treated with irbesartan than with placebo. In diabetic hypertensive patients with microalbuminuria and normal renal function, hyperkalaemia (≥ 5.5 mEq/L) occurred in 29.4% of the patients in the irbesartan 300 mg group and 22% of the patients in the placebo group. In diabetic hypertensive patients with chronic renal insufficiency and overt proteinuria, hyperkalaemia (≥ 5.5 mEq/L) occurred in 46.3% of the patients in the irbesartan group and 26.3% of the patients in the placebo group. **Common**: significant increases in plasma creatine kinase were commonly observed (1.7%) in irbesartan treated subjects. None of these increases were associated with

identifiable clinical musculoskeletal events. In 1.7% of hypertensive patients with advanced diabetic renal disease treated with irbesartan.

10.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 Aprovel. 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.

11.Pharmacodynamics: irbesartan is a potent, orally active, selective angiotensin-II receptor (type AT1) antagonist. It is expected to block all actions of 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.

12. MARKETING AUTHORIZATION HOLDER: Sanofi Clir SNC 54, rue La Boétie F-75008 Paris - France. Abbreviated Prescribing Information based on the EU SmPC as of July 2018 . Always refer to the full Summary of Product Characteristics (SmPC) before prescribing.