For the use of Registered Medical Practitioner or a Hospital or a Laboratory

Abbreviated Prescribing Information of CYENDIV® (IPF & SSc-ILD)

ACTIVE INGREDIENTS: Each capsule contains 100 mg or 150 mg of nintedanib (free base) corresponding to 120.4 mg or 180.6 mg of nintedanib esilate respectively. **INDICATION:** For the treatment of Idiopathic Pulmonary Fibrosis (IPF), and Systemic Sclerosis associated Interstitial Lung Disease (SSc-ILD). **DOSAGE & ADMINISTRATION:** 150 mg twice daily administered approximately 12 hours apart to be taken orally, preferably with food, swallowed whole with water, and should not be chewed or crushed. If dose is missed, resume administration at the next scheduled time at the recommended dose. Do not exceed maximum daily dose of 300 mg. ***Dose adjustments:*** In addition to symptomatic treatment if applicable, management of adverse reactions could include dose reduction and temporary interruption until specific adverse reaction resolves to levels that allow continuation of therapy. Resume treatment at full dose (150 mg twice daily) or a reduced dose (100 mg twice daily). Discontinue if patient does not tolerate 100 mg twice daily. **SPECIAL POPULATIONS:** ***Renal Impairment:*** Adjustment of starting dose not required in mild or moderate renal impairment. Safety, efficacy, and pharmacokinetics not studied in severe renal impairment (< 30 ml/min CrCL). ***Hepatic Impairment:*** Recommended dose in mild (Child Pugh A) hepatic impairment is 100 mg twice daily. Safety & efficacy not investigated in patients with Child Pugh B & C hepatic impairment, hence use is not recommended. ***Children:*** Safety and efficacy not studied. ***Elderly patients (⩾ 65 years):*** No adjustment of the initial dosing required. ***Race:*** A priori dose adjustments not necessary. ***Body weight:*** A priori dose adjustments not necessary. **CONTRAINDICATIONS:** Pregnancy, hypersensitivity to nintedanib, peanut or soya or to any of the excipients. **SPECIAL WARNINGS AND PRECAUTIONS:** ***Gastrointestinal disorders.*** **Diarrhoea:** In clinical trials, diarrhoea was the most frequently reported gastro-intestinal event; in most patients, the event was mild to moderate, and occurred within the first three months. Treat diarrhoea at first signs with adequate hydration and anti-diarrhoeals, e.g, loperamide. May require treatment interruption; treatment may be resumed at reduced or full dose. Discontinue nintedanib in case of persisting severe diarrhoea despite symptomatic treatment. **Nausea and vomiting**: Mild to moderate nausea and vomiting frequently reported. May require dose reduction or treatment interruption if symptoms persist despite appropriate supportive care. Discontinue nintedanib in case of persisting severe symptoms. Diarrhoea and vomiting may lead to dehydration with or without electrolyte disturbances, which may progress to renal function impairment. ***Hepatic function:*** Cases of drug-induced liver injury have been observed. In the post-marketing period, non-serious and serious cases of drug-induced liver injury, including severe liver injury with fatal outcome, have been reported. The majority of hepatic events occur within the first three months of treatment. Investigate transaminase and bilirubin levels at regular intervals during the first three months of treatment and periodically thereafter (e.g. at each patient visit) or as clinically indicated. Patients with low body weight (< 65 kg), Asians and females have a higher risk of elevations in liver enzymes. Close monitoring recommended. Treatment not recommended in moderate (Child Pugh B) and severe (Child Pugh C) hepatic impairment as safety & efficacy has not been studies in such patients. ***Haemorrhage:*** Non-serious epistaxis most frequent bleeding event. Patients at known risk for bleeding, patients with inherited predisposition to bleeding or patients receiving a full dose of anticoagulative treatment should be treated only if the anticipated benefit outweighs the potential risk. ***Arterial thromboembolic events:*** Caution in patients with higher cardiovascular risk, including known coronary artery disease. Interrupt treatment if signs or symptoms of acute myocardial ischaemia develop. ***Venous thromboembolism:*** Might have an increased risk of thromboembolic events. ***Gastrointestinal perforations:*** Might have an increased risk of gastrointestinal perforations. Exercise particular caution in treating patients with previous abdominal surgery or a recent history of a hollow organ perforation, previous history of peptic ulceration, diverticular disease or receiving concomitant corticosteroids or NSAIDs. Initiate nintedanib at least 4 weeks after major surgery. Discontinue permanently in patients who develop gastrointestinal perforation. ***Wound healing complication:*** Based on mechanism of action, wound healing may be impaired. Initiate or resume (in case of perioperative interruption) treatment based on clinical judgement of adequate wound healing. **DRUG INTERACTIONS:** ***P-glycoprotein (P-gp):*** Substrate of P-gp. Co-administration with potent P-gp inhibitors may increase exposure. Monitor closely for tolerability. May require interruption, dose reduction, or discontinuation for management of adverse reactions. Potent P-gp inducers may decrease exposure. Consider selecting alternate concomitant medication with no or minimal P-gp induction potential. ***Cytochrome (CYP)-enzymes:*** CYP pathways constitute minor extent of the biotransformation. Low likelihood of drug-drug interactions based on CYP metabolism. ***Co-administration with other drugs:*** Co-administration of nintedanib with bosentan did not alter the pharmacokinetics of nintedanib. **PREGNANCY AND LACTATION:** ***Women of childbearing potential:*** Avoid becoming pregnant. Use adequate contraception during and at least 3 months after the last dose. Women using hormonal contraceptives must add a barrier method. ***Pregnancy:*** Not recommended during pregnancy. Conduct pregnancy testing at least prior to treatment and during treatment as appropriate. ***Lactation:*** Risk to the new-borns/infants cannot be excluded. Discontinue breast-feeding during treatment. ***Fertility:*** No evidence of evidence for impairment of male or female fertility based on preclinical investigations. **EFFECTS**

ON ABILITY TO DRIVE AND USE MACHINES: No studies performed. Exercise caution. **ADVERSE REACTIONS:** ***Gastrointestinal disorders:*** Diarrhoea, vomiting, nausea, abdominal pain, pancreatitis, colitis. ***Hepatobiliary disorders:*** Drug induced liver injury, increased hepatic enzymes (AST, ALT, ALKP, GGT), hyperbilirubinemia. ***Vascular disorders:*** Hypertension, bleeding. ***Blood and lymphatic system disorders:*** Thrombocytopenia. ***Metabolism and nutrition disorders:*** Decreased appetite, decreased weight. ***Skin & subcutaneous tissue:*** Rash, pruritus, alopecia. ***Nervous system disorders:*** headache. **OVERDOSAGE:** No specific antidote. Interrupt treatment and initiate general supportive measures. **SHELF LIFE:** 36 months. **STORAGE:** Store at 2° to 8°C. Do not freeze.

Refer to full prescribing information before use. Full prescribing information available on request from: Boehringer Ingelheim India Private Limited, 1102, 11th Floor, Hallmark Business Plaza, Guru Nanak Hospital Road, Near Guru Nanak Hospital, Bandra (East), Mumbai – 400 051.

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