Mysimba Abbreviated Prescribing Information. Please refer to the Summary of Product Characteristics for full details.

Mysimba 8 mg/90 mg prolonged-release tablet (8 mg naltrexone hydrochloride, equivalent to 7.2 mg of naltrexone, and 90 mg bupropion hydrochloride. **Therapeutic indications:** As an adjunct to a reduced-calorie diet and increased physical activity, for the management of weight in adult patients (≥18 years) with an initial Body Mass Index (BMI) of: ≥ 30 kg/m2 (obese), or ≥ 27 kg/m2 to < 30 kg/m2 (overweight) in the presence of one or more weight-related co-morbidities (e.g., type 2 diabetes, dyslipidaemia, or controlled hypertension). Treatment with Mysimba should be discontinued after 16 weeks if patients have not lost at least 5% of their initial body weight. **Posology:** Initial treatment, the dose should be escalated over a 4-week period as follows: **Week 1:** One tablet in the morning, **Week 2:** One tablet in the morning and one tablet in the evening, **Week 3:** Two tablets in the morning and one tablet in the evening, **Week 4** and onwards: Two tablets in the morning and two tablets in the evening. The maximum recommended daily dose of Mysimba is two tablets taken twice daily. The need for continued treatment should be evaluated after 16 weeks and re-evaluated annually. The cardiovascular risks of Mysimba when given for longer than a year have not been fully determined. Discontinue Mysimba after one year if patients do not maintain at least a 5% weight loss; conduct annual assessments for cardiovascular risk and weight maintenance before continuing treatment. **Missed dose:** If a dose is missed, patients should not take an additional dose, but take the prescribed next dose at the usual time. **Special populations:** Naltrexone/bupropion should be used with caution in patients **over 65 years of age and is not recommended in patients over 75 years of age**. Naltrexone/bupropion is contraindicated in patients with **end-stage renal failure**. In patients with moderate or severe renal impairment, the maximum recommended daily dose for naltrexone/bupropion is two tablets (one tablet in the morning and one tablet in the evening). It is recommended that patients with moderate or severe renal impairment initiate treatment with one tablet in the morning for the first week of treatment and escalate to one tablet in the morning and one tablet in the evening from week 2 onwards. For individuals who are at elevated risk for renal impairment, in particular patients with diabetes or elderly individuals, estimated glomerular filtration rate (eGFR) should be assessed prior to initiating therapy with naltrexone/bupropion. Patients with **hepatic impairment** Naltrexone/bupropion is **contraindicated** in patients with severe or moderate hepatic impairment. For with mild hepatic impairment, the maximum recommended daily dose for naltrexone/bupropion is two tablets. Degree of hepatic impairment should be assessed using the Child-Pugh score. **Paediatric population children and adolescents below 18:** Contraindicated. **Method of administration:** The tablets should be swallowed whole with some water and food and should not be cut, chewed or crushed. **Contraindications:** Hypersensitivity to the active substance(s) or to any of the excipients, uncontrolled hypertension, current seizure disorder or a history of seizures, a known central nervous system tumour, undergoing acute alcohol or benzodiazepine withdrawal, history of bipolar disorder, receiving any concomitant treatment containing bupropion or naltrexone, current or previous diagnosis of bulimia or anorexia nervosa, currently dependent on chronic opioids or opiate agonists, or patients in acute opiate withdrawal, receiving concomitant administration of monoamine oxidase inhibitors (MAOI). **Special warnings and precautions for use:** The safety and tolerability of naltrexone/bupropion should be assessed at regular intervals. **Suicide and suicidal behaviour, Seizures and associated conditions:** The co-administration of antipsychotics, antidepressants, antimalarials, tramadol, theophylline, systemic steroids, quinolones and sedating antihistamines may lower the seizure threshold, and the consumption of alcohol during naltrexone/bupropion treatment should be minimised or avoided. Patients receiving opioid analgesics. **Allergic reactions have been reported:** A patient should stop taking naltrexone/bupropion and consult a doctor if experiencing allergic or

anaphylactoid/anaphylactic reactions during treatment**. Severe cutaneous adverse reactions (SCARs):** such as Stevens-Johnson syndrome (SJS) and acute generalised exanthematous pustulosis (AGEP), which can be life-threatening or fatal, have been reported in association with naltrexone/bupropion treatment. Patients should be advised of the signs and symptoms and monitored closely for skin reactions. If signs and symptoms suggestive of these reactions appear, naltrexone/bupropion should be withdrawn immediately and an alternative treatment considered (as appropriate). If the patient has developed a serious reaction such as SJS
or AGEP with the use of naltrexone/bupropion, the treatment must not be restarted in this patient at any time. **Elevation of blood pressure** was observed in naltrexone/bupropion Phase 3 clinical trials and if the blood pressure increase continues treatment should be stopped. **Cardiovascular disease:** There is no clinical experience establishing the safety of naltrexone/bupropion in patients with a recent history of myocardial infarction, unstable heart disease or NYHA class III or IV congestive heart failure however use should be with caution. **Brugada Syndrome**: Caution is advised in patients with Brugada syndrome or a family history of cardiac arrest or sudden death. Acute Generalised Exanthematous Pustulosis (AGEP)**Hepatotoxicity:** In naltrexone/bupropion completed clinical studies, where naltrexone hydrochloride daily doses ranged from 16 mg to 48 mg, drug-induced liver injury (DILI) was reported. A patient with suspected DILI should stop taking naltrexone/bupropion. **Serotonin Syndrome:** There have been post-marketing reports of serotonin syndrome when co-administered with a serotonergic agent. if concomitant treatment with other serotonergic agents is warranted, careful observation of the patient is advised, and treatment discontinuation should be considered if symptoms develop. Data in animals suggest a potential for abuse of bupropion. studies in humans use in humans have shown that bupropion has low abuse potential. **Influence on the ability to drive and use machines:** Naltrexone/bupropion has been associated with somnolence and episodes of loss of consciousness. **Patients must be advised to exercise caution while driving or operating** machines during treatment. **Lactose:** Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption use contraindicated**.** Consult educational materials before prescribing. **Patients should be advised to carry the patient card with them at all times. Interaction with other medicinal products and other forms of interaction:** Monoamine oxidase inhibitors (MAOI), Opioid analgesics must not be used. Drugs metabolised by cytochrome P450 (CYP) enzymes and OCT2 substrates have potential for interaction. **Fertility, pregnancy and lactation**: **Pregnancy** limited data available and the drug should not be used in pregnant or women trying to become pregnant. **Breast-feeding:** Naltrexone and bupropion and their metabolites are excreted in human milk and use is contraindicated. **Fertility:** No data available. **Undesirable effects:** The most frequent adverse reactions in clinical studies were nausea (very common), constipation (very common), vomiting (very common), dizziness (common), and dry mouth (common). The most frequent adverse reactions leading to discontinuation with naltrexone/bupropion were nausea (very common), headache (very common), dizziness (common) and vomiting (very common). **Overdose:** There is no clinical experience with overdose with combined use of bupropion and naltrexone. **Excipients: Tablet core:** contains Lactose monohydrate (For a full list see the SmPC). **Shelf life**: 30 months. **Storage:** Do not store above 30°C. Nature and contents of container: PVC/PCTFE/PVC/Aluminium blisters. **Pack sizes:** 28, 112 tablets. **MARKETING AUTHORISATION HOLDER: Orexigen Therapeutics Ireland Limited**, 2nd Floor, Palmerston House, Fenian Street, Dublin 2, Ireland. **MARKETING AUTHORISATION NUMBER(S):** EU/1/14/988/001-002. **DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION**: **26 March 2015.** Date of latest

renewal: **16 January 2020.** Detailed information on this medicinal product is available on www.hpra.ie. Adverse events should be reported to Orexigen Therapeutics Ireland Limited (+3531800849099) or use the link to report directly to Currax.MI@primevigilance.com . Cost NWP**: €83.00** IE-MYS-164(5) **Preparation Date:** July 2025