Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard. Adverse events should also be reported to Teva UK Limited on 0207 540 7117 or medinfo@tevauk.com

Please refer to the Summary of Product Characteristics (SmPC) for full details of Prescribing Information.

Amitriptyline Film-coated Tablets Abbreviated Prescribing Information **Presentation:** Each film-coated tablet contains 10mg, 25mg and 50mg amitriptyline hydrochloride Ph. Eur. **Indications:** For the treatment of major depressive disorder in adults. The treatment of neuropathic pain in adults. The prophylactic treatment of chronic tension type headache (CTTH) in adults. The prophylactic treatment of migraine in adults. The treatment of nocturnal enuresis in children aged 6 years and above when organic pathology, including spina bifida and related disorders, have been excluded and no response has been achieved to all other non-drug and drug treatments, including antispasmodics and vasopressin-related products. This medicinal product should only be prescribed by a healthcare professional with expertise in the management of persistent enuresis. **Dosage and administration:** Oral use. When stopping therapy the drug should be gradually withdrawn over several weeks. *Major depressive disorder:* Dosage should be initiated at a low level and increased gradually, carefully noting the clinical response and any evidence of intolerability. An electrocardiogram (ECG) should be performed prior to initiating therapy with amitriptyline to exclude long QT syndrome. *Adults:* Initially 25mg 2 times daily (50mg daily). If necessary, the dose can be increased by 25mg every other day up to 150mg daily divided into two doses. The maintenance dose is the lowest effective dose. *Elderly patients over 65 years of age and patients with cardiovascular disease:* Initially 10mg - 25mg daily. The daily dose may be increased up to 100mg – 150mg, depending on individual patient response and tolerability. Daily doses above 100mg should be used with caution. The maintenance dose is the lowest effective dose. *Children and Adolescents (aged <18 years)*: Not recommended for use. *Neuropathic pain, prophylactic treatment of chronic tension type headache and prophylactic treatment of migraine in adult:* Patients should be individually titrated to the dose that provides adequate analgesia with tolerable adverse drug reactions. Generally, the lowest effective dose should be used for the shortest duration required to treat the symptoms. *Adults:* Recommended doses are 25mg - 75mg daily in the evening. Doses above 100mg should be used with caution. *Elderly patients over 65 years of age and patients with cardiovascular disease:* 10mg - 25mg in the evening is recommended. Doses above 75mg should be used with caution. *Children and Adolescents (aged <18 years)*: Not recommended for use. *Prophylactic treatment of chronic tension type headache and prophylactic treatment of migraine in adults:* Treatment must be continued for an appropriate length of time. Regular reassessment is recommended to confirm that continuation of the treatment remains appropriate for the patient. *Nocturnal enuresis*: *Children (aged 6 to 10 years)*: 10mg - 20mg. *Children (aged 11 and above)*: 25mg – 50mg daily. *Renal Impairment*: No dose adjustment. *Hepatic Impairment:* Careful dosing and a serum level determination is advisable. **Contraindications:** Hypersensitivity to the active substance or to any of the excipients. Recent myocardial infarction (any degree of heart block or disorders of cardiac rhythm and coronary artery insufficiency). Concomitant treatment with MAOIs (monoamine oxidase inhibitors), as this may cause serotonin syndrome. Severe liver disease. Children under 6 years of age. **Precautions and warnings:** Cardiac arrhythmias and severe hypotension are likely to occur with high dosage. They may also occur in patients with pre-existing heart disease taking normal dosage. QT interval prolongation: Cases of QT interval prolongation and arrhythmia have been reported during the postmarketing period. Caution is advised in patients with significant bradycardia, in patients with uncompensated heart failure, or in patients concurrently taking QT-prolonging drugs. Anaesthetics given during tri/tetracyclic antidepressant therapy may increase the risk of arrhythmias and hypotension. If possible, discontinue this medicinal product several days before surgery. Great care is necessary if amitriptyline is administered to hyperthyroid patients, those receiving thyroid medication, and the elderly. This medical product should be used with caution in patients with convulsive disorders, urinary retention, prostatic hypertrophy, hyperthyroidism, paranoid symptomatology and advanced hepatic or cardiovascular disease, pylorus stenosis and paralytic ileus. In patients with the rare condition of shallow anterior chamber and narrow chamber angle, attacks of acute glaucoma due to dilation of the pupil may be provoked. Depression is associated with an increased risk of suicidal thoughts, self-harm and suicide (suicide-related events). This risk persists until significant remission occurs. As improvement may not occur during the first few weeks or more of treatment, patients should be closely monitored until such improvement occurs. Patients with a history of suicide-related events, or those exhibiting a significant degree of suicidal ideation prior to commencement of treatment, are known to be at greater risk of suicidal thoughts or suicide attempts, and should receive careful monitoring during treatment. In manic-depressives, a shift towards the manic phase may occur; should the patient enter a manic phase amitriptyline should be discontinued. Amitriptyline may modify insulin and glucose responses calling for adjustment of the antidiabetic therapy in diabetic patients; in addition the depressive illness itself may affect patients' glucose balance. Hyperpyrexia has been reported with tricyclic antidepressants (TCAs) when administered with anticholinergic or with neuroleptic medications, especially in hot weather. After prolonged administration, abrupt cessation of therapy

may produce withdrawal symptoms such as headache, malaise, insomnia and irritability. Amitriptyline should be used with caution in patients receiving SSRIs. Amitriptyline for enuresis should not be combined with an anticholinergic drug. Suicidal thoughts and behaviours may also develop during early treatment with antidepressants for disorders other than depression; the same precautions observed when treating patients with depression should therefore be followed when treating patients with enuresis. Long-term safety data in children and adolescents concerning growth, maturation and cognitive and behavioural development are not available. The tablets contain lactose. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not receive this medicine. **Interactions:** Use with MAOIs (non-selective as well as selective A (moclobemide) and B (selegiline)) is contraindicated due to a risk of serotonin syndrome. Amitriptyline may potentiate the cardiovascular effects of sympathomimetics (e.g. adrenaline, ephedrine, isoprenaline) and anticholinergic agents affecting the eye, central nervous system, bowel and bladder. TCAs may counteract the antihypertensive effects of centrally acting antihypertensives (e.g. guanethidine, betanidine). Drugs which prolong the QT-interval including antiarrhythmics (e.g. quinidine), antihistamines (e.g. astemizole and terfenadine), antipsychotics (e.g. pimozide and sertindole), cisapride, halofantrine, and sotalol, may increase the likelihood of ventricular arrhythmias when taken with TCAs. Amitriptyline may inhibit the metabolism of thioridazine, leading to increased risk of cardiac side effects. Amitriptyline may inhibit tramadol metabolism causing, seizures, serotonin syndrome and opioid toxicity. Antifungals (e.g. fluconazole and terbinafine) increase serum concentrations of TCAs causing syncope and torsade de pointes. Amitriptyline may enhance the sedative effects of alcohol, barbiturates, and other CNS depressants. Concomitant administration of amitriptyline and buprenorphine may result in serotonin syndrome, a potentially life-threatening condition. If concomitant treatment with buprenorphine containing medicinal products is clinically warranted, careful observation of the patient is advised, particularly during treatment initiation and dose increases. Symptoms of serotonin syndrome may include mental-status changes, autonomic instability, neuromuscular abnormalities, and/or gastrointestinal symptoms. If serotonin syndrome is suspected, a dose reduction or discontinuation of therapy should be considered depending on the severity of the symptoms. TCAs including amitriptyline are primarily metabolised by CYP2D6 and CYP2C19. Caution when administered with CYP2D6 inhibitors like serotonin reuptake inhibitors, beta blockers, and antiarrhythmics (e.g. bupropion, fluoxetine, paroxetine and quinidine) which may reduce TCA metabolism. Cimetidine, methylphenidate, calcium-channel blockers and antifungals may increase plasma levels of TCAs. Fluvoxamine (strong CYP1A2 inhibitor) was shown to increase amitriptyline plasma concentrations and this combination should be avoided. TCAs and neuroleptics mutually inhibit the metabolism of each other which may lead to seizures. Oral contraceptives, rifampicin, phenytoin, barbiturates, carbamazepine and St. John's Wort may increase the metabolism of TCAs and result in lowered plasma levels of TCAs and reduced antidepressant response. Ethanol, sodium valproate and valpromide may increase amitriptyline free plasma concentrations. **Pregnancy and lactation:** Not recommended during pregnancy unless clearly necessary and only after careful consideration of the risk/benefit. During chronic use and after administration in the final weeks of pregnancy, neonatal withdrawal symptoms can occur. Amitriptyline and its metabolites are excreted into breast milk . A decision must be made whether to discontinue breast-feeding or to discontinue/abstain from the therapy of this medicinal product taking into account the benefit of breast feeding for the child and the benefit of therapy for the woman. **Effects on ability to drive and use machines:** Amitriptyline is a sedative drug. Patients who are prescribed psychotropic medication may be expected to have some impairment in general attention and concentration and should be cautioned about their ability to drive or operate machinery. These adverse effects can be potentiated by the concomitant intake of alcohol. **Adverse reactions:** Anaphylaxis, angioedema, agranulocytosis, leucopenia, thrombocytopenia, delirium, hallucination, suicidal thoughts or behaviour, convulsion, polyneuropathy, acute glaucoma; arrhythmia; cardiomyopathies, Torsades de Pointes, hypersensitivity myocarditis, ileus paralytic, jaundice, hepatitis, urinary retention, erectile dysfunction, ECG abnormal, ECG QT prolonged, ECG, QRS complex prolonged. *Very Common***:** aggression, somnolence, tremor, dizziness, headache, drowsiness, speech disorder (dysarthria), accommodation disorder, palpitations, tachycardia, orthostatic hypotension, congested nose, dry mouth, constipation, nausea, hyperhidrosis, weight increased. *Common:* confusional state, libido decreased, agitation, disturbance in attention, dysgeusia, paresthesia, ataxia, mydriasis, atrioventricular block, bundle branch block, micturition disorders, fatigue, feeling thirst. Consult the Summary of Product Characteristics in relation to other side effects. **Overdose:** Symptoms include anticholinergic symptoms and cardiac symptoms. Ingestion of 750mg or more by an adult may result in severe toxicity. The effects in overdose will be potentiated by simultaneous ingestion of alcohol and other psychotropic. Consult the Summary of Product Characteristics in relation to in-depth overdose symptoms & treatment. **List Price:** 10mg Tablets, Pack of 28: £0.59. 25mg Tablets, Pack of 28: £0.64; 50mg Tablets, Pack of 28: £1.31. **Legal category:** POM. **Marketing Authorisation Number:** PL 00289/0178-0180. **Marketing Authorisation Holder:** Teva UK Limited, Ridings Point, Whistler Drive, Castleford, WF10 5HX. **Job Code:** MED-GB-00432. **Date of Preparation:** April 2025