adaflex ava (melatonin) Prescribing Information

Please refer to the Summary of Product Characteristics (SmPC) before prescribing.

adaflex ava 1 mg, 2 mg, 3 mg, 4 mg and 5 mg tablets

ACTIVE INGREDIENT: Each tablet contains 1 mg, 2 mg, 3 mg, 4 mg or 5 mg melatonin.

INDICATIONS: Insomnia in children and adolescents aged 6–17 years and adults with attention deficit hyperactivity disorder (ADHD), where sleep hygiene measures have been insufficient. Insomnia (prolonged sleep onset) in children and adolescents aged 2–17 years with autism spectrum disorder (ASD), where sleep hygiene measures have been insufficient. Delayed sleep-wake phase disorder (DSWPD) in children and adolescents aged 6–17 years and adults up to 25 years of age, where sleep hygiene measures have been insufficient.

DOSAGE AND ADMINISTRATION: For all indications, the dose should be adjusted individually until sufficient effect is attained; the lowest effective dose should be sought. Maximum dose 5 mg once a day. Limited data are available for up to 3 years of treatment.

Insomnia with ADHD (6–17 years and adults): Treatment should be initiated by, or on the advice of, a healthcare professional experienced in ADHD and/or sleep medicine in the relevant patient population (paediatric or adult). Recommended starting dose, independent of age, is 0.5–2 mg once a day, 30–60 minutes before the desired bedtime. After at least 3 months of treatment, evaluate the treatment effect and consider stopping if no clinically relevant effect is seen. Monitor at regular intervals (at least every 6 months) to check that adaflex ava is still the most appropriate treatment. During ongoing treatment, especially if the treatment effect is uncertain, discontinuation attempts should be made regularly, e.g. once a year. If the sleep disorder started during treatment with medicinal products for ADHD, dose adjustment or switching to another product should be considered.

Insomnia (prolonged sleep onset) with ASD (2–17 years): Treatment should be initiated by, or on the advice of, a healthcare professional experienced in paediatric ASD and/or sleep medicine. Recommended starting dose, independent of age, is 1–2 mg once a day, 30–60 minutes before the desired bedtime; a 0.5 mg starting dose may be sufficient in some patients and may be considered for gradual dose titration. After at least 3 months of treatment, evaluate the treatment effect and consider stopping if no clinically relevant effect is seen. Monitor at regular intervals (at least every 6 months); during ongoing treatment, especially if the treatment effect is uncertain, discontinuation attempts should be made regularly, e.g. once a year.

DSWPD (6–17 years and adults up to 25 years): Treatment should be initiated by, or on the advice of, a healthcare professional experienced in paediatric DSWPD and/or sleep medicine. Recommended starting dose, independent of age, is 1–2 mg once a day, 1–2 hours before the desired bedtime; a 0.5 mg starting dose may be sufficient in some patients and may be considered for gradual dose titration. The lowest effective dose should be taken for the shortest period. After 6 weeks of treatment, evaluate the treatment effect and consider stopping if no clinically relevant effect is seen. After an advanced sleep-wake phase has been achieved for 6 weeks, stop treatment to evaluate whether the patient can independently maintain an advanced sleep-wake schedule; if withdrawal results in clinical relapse, treatment can be resumed and continued. Adults over 25 years: in adults whose symptoms persist past the age of 25 and who have shown clear benefit from treatment, it may be appropriate to continue treatment.

Administration: Oral use. The tablet can be crushed and dispersed in water directly before administration. It is recommended that food is not consumed 2 hours before or after intake. Intake with carbohydrate-rich meals may impair blood glucose control for several hours.

Special populations: Elderly: no specific dosage recommendations; caution in significantly older patients and individualised dosing recommended. Renal impairment: caution recommended; not recommended in severe renal impairment. Hepatic impairment: not recommended in moderate or severe hepatic impairment. Paediatric population: efficacy and safety have not been established in children with ADHD or DSWPD aged 0–6 years; there is no relevant use in children aged 0–2 years for the treatment of insomnia.

CONTRAINDICATIONS: Hypersensitivity to the active substance or to any of the excipients (microcrystalline cellulose, mannitol, colloidal anhydrous silica, croscarmellose sodium, magnesium stearate).

SPECIAL WARNINGS AND PRECAUTIONS FOR USE: Melatonin may cause drowsiness; use with caution if the effects of drowsiness are likely to be associated with a risk to patient safety. Elderly: caution in significantly older patients; individualised dosing recommended. Autoimmune diseases: occasional case reports of exacerbation; not recommended in patients with autoimmune diseases. Epilepsy: melatonin has been reported to increase, decrease or have no effect on seizure frequency; some caution should be exercised. Impaired glucose tolerance: take at least 2 hours before and after a meal; ideally at least 3 hours after a meal in patients with significantly impaired glucose tolerance or diabetes. Contains less than 1 mmol sodium (23 mg) per tablet (essentially ‘sodium-free’).

INTERACTIONS: Melatonin is mainly metabolised by CYP1A enzymes. Concomitant use should be avoided with the CYP1A2 inhibitor fluvoxamine (melatonin exposure increased 17-fold), warfarin and other vitamin K antagonists (may alter prothrombin levels; anticoagulant dose adjustment may be required) and benzodiazepine-related hypnotics such as zolpidem (enhanced sedation). Use with caution with the CYP1A2 inhibitors ciprofloxacin, norfloxacin and verapamil, other quinolones, 5- or 8-methoxypsoralen, cimetidine and caffeine, which may increase melatonin levels. Oestrogens, including combined hormonal contraceptives containing ethinylestradiol and gestagen, markedly increase melatonin concentration – the melatonin dose may need to be reduced. CYP1A2 inducers (carbamazepine, phenytoin, rifampicin, omeprazole and cigarette smoking) may decrease melatonin levels – melatonin dose adjustment may be needed. Alcohol should not be used concomitantly as it may reduce the effect of melatonin on sleep. Melatonin may reduce the hypotensive effect of nifedipine – use with caution; nifedipine dose adjustment may be needed; caution with other calcium antagonists. NSAIDs (e.g. acetylsalicylic acid, ibuprofen) taken in the evening may suppress endogenous melatonin – avoid evening administration where possible. Beta-blockers

may suppress endogenous melatonin and should be administered in the morning.

PREGNANCY, LACTATION AND FERTILITY: Not recommended during pregnancy or in women of childbearing potential not using contraceptives. Should not be used during breastfeeding. High doses of melatonin impaired male and female fertility in animals; the relevance of these data for human fertility is unknown.

DRIVING AND USE OF MACHINES: Moderate influence on the ability to drive and use machines. Melatonin may cause drowsiness; use with caution if drowsiness is likely to be associated with a safety risk.

UNDESIRABLE EFFECTS: Adults: Common: headache, somnolence. **Uncommon:** irritability, nervousness, restlessness, insomnia, abnormal dreams, nightmares, anxiety, migraine, lethargy, psychomotor hyperactivity, dizziness, hypertension, abdominal pain, abdominal pain upper, dyspepsia, mouth ulceration, dry mouth, nausea, hyperbilirubinaemia, dermatitis, night sweats, pruritus, rash, pruritus generalised, dry skin, pain in extremity, glycosuria, proteinuria, menopausal symptoms, asthenia, chest pain, liver function test abnormal, weight increased. **Rare:** herpes zoster, leukopenia, thrombocytopenia, hypertriglyceridaemia, hypocalcaemia, hyponatraemia, mood altered, aggression, agitation, crying, stress symptoms, disorientation, early morning awakening, libido increased, depressed mood, depression, syncope, memory impairment, disturbance in attention, dreamy state, restless legs syndrome, poor quality sleep, paraesthesia, visual acuity reduced, vision blurred, lacrimation increased, vertigo positional, vertigo, angina pectoris, palpitations, hot flush, gastro-oesophageal reflux disease, gastrointestinal disorder, oral mucosal blistering, tongue ulceration, gastrointestinal upset, vomiting, bowel sounds abnormal, flatulence, salivary hypersecretion, halitosis, abdominal discomfort, gastric disorder, gastritis, eczema, erythema, hand dermatitis, psoriasis, rash generalised, rash pruritic, nail disorder, arthritis, muscle spasms, neck pain, night cramps, polyuria, haematuria, nocturia, priapism, prostatitis, fatigue, pain, thirst, hepatic enzyme increased, blood electrolytes abnormal, laboratory test abnormal. **Not known:** hypersensitivity reaction, hyperglycaemia, hallucinations, drowsiness, sedation, angioedema, oedema of mouth, tongue oedema, galactorrhoea.

Paediatric population: a low frequency of generally mild adverse reactions has been reported, not differing significantly from placebo. The most common were headache, hyperactivity, dizziness and abdominal pain. No serious adverse reactions have been observed. Prescribers should consult the SmPC in relation to other adverse reactions.

LEGAL CATEGORY: POM.

PRESENTATION AND BASIC NHS PRICE: adaflex ava 1 mg, 2 mg, 3 mg, 4 mg and 5 mg tablets, 30 tablets: £10.89.

MARKETING AUTHORISATION NUMBERS:
PL 52497/0007–0011.

MARKETING AUTHORISATION HOLDER: AGB-Pharma AB, Scheeletorget 1, Medicon Village, 223 81 Lund, Sweden. Marketed in the UK by AGB-Pharma AB.

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 AGB-Pharma AB at pharmacovigilance@agb-pharma.com

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