ABILIFY® (aripiprazole) PRESCRIBING INFORMATION - SCHIZOPHRENIA TABLETS, ORODISPERSIBLE TABLETS, ORAL SOLUTION, MAINTENA®

Please refer to the full Summary of Product Characteristics (SmPC) before prescribing, particularly in relation to side effects, precautions and contra-indications.

PRESENTATION: Tablets: 5mg, 10mg, 15mg, 30mg aripiprazole; orodispersible tablets (ODT): 10mg, 15mg aripiprazole; Oral solution (OS): 1mg/ml aripiprazole; Prolonged-release suspension for injection: 400mg powder and solvent in vials; 400mg powder and solvent in pre-filled syringe. Tablets and orodispersible tablets contain lactose. Orodispersible tablets also contain aspartame. Oral solution contains fructose, sucrose, methyl and propyl parahydroxybenzoate.

INDICATIONS: Oral formulations: Adults: Schizophrenia. Paediatric patients: Schizophrenia in adolescents aged 15 years and older;

Prolonged-release suspension for injection: Maintenance treatment of schizophrenia in adult patients stabilised with oral aripiprazole.

Please refer to the SmPC for other indications.

DOSAGE AND ADMINISTRATION:

Oral formulations: Adults: Schizophrenia - Usual starting dose is 10 or 15mg once daily with or without food. Effective dose range is 10 to 30mg with a recommended maintenance dose of 15mg. Paediatric patients: Schizophrenia - Recommended dose is 10 mg/day once daily with or without food. Treatment to be initiated at 2 mg (using ABILIFY Oral Solution 1 mg/ml) for two days, titrated to 5 mg for two more days to reach recommended daily dose of 10 mg.

Maximum daily dose 30mg. No dosage adjustment required in renal or mild to moderate hepatic impairment. Elderly (> 65 years): Efficacy not established. Consider lower starting dose. Not recommended for use in patients below 13 years of age: Safety and efficacy not established.

Prolonged-release suspension for injection: For patients who have never taken aripiprazole, tolerability with oral aripiprazole must occur prior to initiation. The recommended starting and maintenance dose is 400mg once monthly. Titration of the dose of this medicinal product is not required. It should be administered once monthly as a single injection into the gluteal or deltoid muscle. After the first injection, treatment with 10mg to 20mg oral aripiprazole should be continued for 14 days. Consider reducing the dose to 300mg if there are adverse reactions. Dosage reductions are needed in patients who are taking concomitant strong CYP3A4 inhibitors and/or strong CYP2D6 inhibitors for more than 14 days. Refer to SmPC for instructions on use with these inhibitors, missed doses, reconstitution and injection procedure. Elderly (> 65 years): Safety and efficacy not established. Children and adolescents (<18 years): Not recommended, safety and efficacy not established. Renal impairment: No dosage adjustment required. Hepatic impairment: No dose adjustment required in mild or moderate hepatic impairment. In severely impaired hepatic function data available are insufficient to establish recommendations, and the oral formulation should be preferred.

WARNINGS AND PRECAUTIONS: Untill individual patient response is established, caution not to drive or operate machinery. All risk factors for venous thromboembolism (VTE) should be identified before and during treatment and preventive measures taken. Clinical improvement may take several days to some weeks: monitor patient throughout this period. Reduce dose or discontinue if signs of tardive dyskinesia appear. Discontinue if patient develops signs and symptoms indicative of neuroleptic malignant syndrome. Caution in patients with a history of seizure, cardiovascular disorders, conduction abnormalities, diabetes and elderly patients with dementia-related psychosis. Those at risk of aspiration pneumonia or history of pathological gambling may be at increased risk. Risk of akathisia and parkinsonism in paediatrics, and weight gain in adolescents. Caution in patients with family history of QT prolongation. Caution when co-administered with stimulants (see SmPC). Not indicated for the treatment of patients with dementia-related psychosis. Closely supervise high risk patients for risk of suicide.

FERTILITY, PREGNANCY AND LACTATION: Do not use during pregnancy unless potential benefit clearly outweighs potential risk to the foetus. Neonates exposed to antipsychotics during the third trimester of pregnancy are at risk of adverse reactions including withdrawal symptoms, and/or post- Natal withdrawal including somnolence, agitation, hypotonia, tremor, and/or convulsions. Neonates should be monitored carefully. Breastfeeding is not recommended.

DRUG INTERACTIONS: Increased hypotensive effect with certain antihypertensives. Caution is advised when combining with alcohol or other CNS medication with overlapping side effects such as sedation; and medicines known to cause QT prolongation or electrolyte imbalance. Cases of serotonin syndrome have been reported in patients taking aripiprazole. Reduce aripiprazole dose with concomitant use of potent CYP3A4 or CYP2D6 inhibitors, e.g. ketoconazole, fluoxetine, paroxetine. oral formulations: ABILIFY dose should be doubled when concomitant administration of ABILIFY occurs with carbamazepine. Other potent inducers of CYP3A4 (such as rifampicin, rifabutin, phenytoin, phenobarbital, primidone, efavirenz, nevirapine and St. John's Wort) may be expected to have similar effects and similar dose increases should therefore be applied. Upon discontinuation of potent CYP3A4 inducers, the dosage of ABILIFY should be reduced to the recommended dose. Prolonged release suspension for injection: Concomitant use with CYP3A4 inducers (e.g. carbamazepine, St. John’s Wort, rifampicin) should be avoided because blood aripiprazole levels may be below effective levels. See SmPC.

UNDESIRABLE EFFECTS: Oral formulations: In adult placebo-controlled trials, the following adverse drug reactions were reported: common (≥1/100 to <1/10): somnolence, dizziness, headache, akathisia, nausea, vomiting, restless, insomnia, anxiety, extrapyramidal disorder, tremor, sedation, blurred vision, dyspnea, constipation, salivary hypersecretion, fatigue; uncommon (≥1/1000 to <1/100): tachycardia, orthostatic hypotension, depression, hyperprolactinaemia. In adolescent (13-17 years) placebo-controlled trials, the adverse drug reactions reported were similar to those for adults; the following adverse drug reactions were reported more frequently than for adults: very common (≥1/10): somnolence, sedation, extrapyramidal disorder; common (≥1/100 to <1/10): dry mouth, increased appetite, orthostatic hypotension. Other adverse events from post-marketing surveillance include: allergic reaction (anaphylaxis & angioedema), hepatic failure, pancreatitis, priapism, pathological gambling, suicide, aggression, rhabdomyolysis, hyperglycaemia, diabetes, dysphagia, convulsions, cardiac disorders including arrhythmias & sudden unexplained death, serotonin syndrome, VTE (including pulmonary embolism and deep vein thrombosis), hypertension, hepatitis, leukopenia and thrombocytopenia, drug withdrawal syndrome neonatal. Symptoms of dystonia may occur in susceptible individuals during the first few days of treatment, with an elevated risk of acute dystonia observed in males and younger age groups. For other findings see SmPC.

Prolonged-release suspension for injection (vials and pre-filled syringe): Adverse drug reactions were reported during clinical trials and/or post-marketing use. Frequency of adverse reactions reported during post-marketing use cannot be derived as they are derived from spontaneous reports: Common (≥1/100 to <1/10): weight increased, weight decreased, diabetes mellitus, agitation, anxiety, restless, insomnia, extrapyramidal disorder, akathisia, tremor, dyskinesia, sedation, somnolence, dizziness, headache, dry mouth, musculoskeletald stiffness, erectile dysfunction, injection site pain, injection site induration, fatigue, blood creatinine phosphokinase increased; Uncommon (≥1/1000 to <1/100): hyperglycaemia, diabetes, angiospasm, convulsions, cardiac disorders including arrhythmias & sudden unexplained death, serotonin syndrome, VTE (including pulmonary embolism and deep vein thrombosis), hypertension, hepatitis, leukopenia and thrombocytopenia, drug withdrawal syndrome neonatal. Symptoms of dystonia may occur in susceptible individuals during the first few days of treatment, with an elevated risk of acute dystonia observed in males and younger age groups. For other findings see SmPC.

PRESCRIBING INJECTION (vials and pre-filled syringe): Adverse drug reactions were reported during clinical trials and/or post-marketing use. Frequency of adverse reactions reported during post-marketing use cannot be derived as they are derived from spontaneous reports: Common (≥1/100 to <1/10): weight increased, weight decreased, diabetes mellitus, agitation, anxiety, restless, insomnia, extrapyramidal disorder, akathisia, tremor, dyskinesia, sedation, somnolence, dizziness, headache, dry mouth, musculoskeletal stiffness, erectile dysfunction, injection site pain, injection site induration, fatigue, blood creatinine phosphokinase increased. Uncommon (≥1/1000 to <1/100): hypertonia, hypertonia, tremor, somnolence, respiratory distress, or feeding disorder in neonates have been reported. Newborns should be monitored carefully. Breastfeeding is not recommended.

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median onset on day 2 after the injection and a median duration of 4 days. Injection site related reactions were slightly more frequent with deltoid compared to gluteal administration in an open label bioavailability study. Leukopenia: Neutropenia has been reported in the clinical program with Abilify Maintena and typically starts around day 16 after first injection, and lasts a median of 18 days. Prescribers should consult the SmPC in relation to other adverse reactions.

OVERDOSE: Treatment should be symptomatic and supportive: adequate airway maintenance, cardiovascular monitoring and close medical supervision. Activated charcoal reduces serum concentrations. Prolonged-release suspension for injection: Care must be taken to avoid inadvertent injection into a blood vessel.

LEGAL CATEGORY: POM.

AUTHORISATION NUMBERS & BASIC NHS PRICE: 28 tablets; 5mg (EU/1/04/276/002) £96.04, 10mg (EU/1/04/276/007) £96.04, 15mg (EU/1/04/276/012) £96.04, 30mg (EU/1/04/276/017) £92.08, 28 orodispersible tablets; 10mg (EU/1/04/276/025) £96.04, 15mg (EU/1/04/276/028) £96.04. 150mL bottle 1mg/ml oral solution: (EU/1/04/276/034) £102.90. Prolonged-release suspension for injection: Single pack vial of 400mg powder, 2ml vial of solvent and syringes, (EU/1/13/882/002) £220.41. Single pack pre-filled syringe of 400mg, in 1.6ml (EU/1/13/882/006) £220.41.

MARKETING AUTHORISATION HOLDER: Otsuka Pharmaceutical Europe Ltd, Gallions – 1st Floor, Wexham Springs, Framewood Road, Wexham SL3 6PJ
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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 Otsuka Pharmaceuticals (U.K.) Ltd by email to OPUKSafety@otsuka.co.uk