ABILIFY® (**aripiprazole**) PRESCRIBING INFORMATION – ABILIFY® TABLETS, ABILIFY® ORODISPERSIBLE TABLETS, ABILIFY® ORAL SOLUTION, ABILIFY® SOLUTION FOR INJECTION (INTRAMUSCULAR (IM)), ABILIFY MAINTENA® POWDER AND SOLVENT FOR PROLONGED-RELEASE SUSPENSION FOR INJECTION, ABILIFY MAINTENA® POWDER AND SOLVENT FOR PROLONGED-RELEASE SUSPENSION FOR INJECTION IN PRE-FILLED SYRINGE.

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

PRESENTATIONS: Tablets: 5mg, 10mg, 15mg, 30mg; Orodispersible tablets: 10mg, 15mg, 30mg; Oral solution: 1mg/ml; Solution for injection (IM): Vial with 9.75mg aripiprazole (7.5mg/ml); Powder and solvent for prolonged-release suspension for injection: Vial with 300mg or 400mg aripiprazole; Pre-filled syringe with 300mg or 400mg aripiprazole. **INDICATIONS: Oral formulations:** Treatment of schizophrenia in adults and adolescents aged 15 years and older; **7.5mg/ml solution for injection (IM):** Rapid control of agitation and disturbed behaviours in adults with schizophrenia, when oral therapy is not appropriate. Treatment with aripiprazole solution for injection should be discontinued as soon as clinically appropriate and use of oral aripiprazole should be initiated; **Prolonged-release suspension for injection:** Maintenance treatment of schizophrenia in adults stabilised with oral aripiprazole. **DOSAGE: Oral formulations:** Adults: Recommended starting dose 10 or 15mg once a day, maintenance dose 15mg once a day without regard to meals. Aripiprazole is effective in a dose range of 10 to 30mg once a day. Enhanced efficacy at doses higher than 15mg daily has not been demonstrated although individual patients may benefit from higher dose. Maximum daily dose should not exceed 30mg. Adolescents (≥15 years old): Initiate at 2mg (using oral 1mg/ml solution) for 2 days, titrate to 5mg for 2 further days to reach recommended daily dose of 10mg. If needed, dose can be increased in 5mg increments, maximum daily dose 30mg. Enhanced efficacy at doses higher than 10mg daily has not been demonstrated although individual patients may benefit from higher dose. **7.5mg/ml solution for injection (IM):** Recommended initial dose 9.75mg (1.3ml), administered as single IM injection into deltoid or deep into gluteus maximus muscle (should not be administered intravenously or subcutaneously). Effective dose range 5.25mg-15mg as a single injection. Lower dose of 5.25mg (0.7ml) may be given on basis of clinical status – which should include consideration of medicines already given either for maintenance or acute treatment. A second injection may be administered 2 hours after the first injection, based on clinical status. No more than 3 injections should be given in 24 hours. Maximum daily dose of aripiprazole is 30mg (including all Abilify® formulations). If continued treatment indicated with oral aripiprazole, see SmPCs for oral aripiprazole preparations. **Prolonged-release suspension for injection:** For patients who have never taken aripiprazole, tolerability with oral aripiprazole must occur prior to initiation. Abilify Maintena® is only intended for IM use and should not be administered intravenously or subcutaneously. Starting dose can be administered as one injection start or as two injection start. **One injection start:** On the day of initiation, administer one injection of 400mg Abilify Maintena® and continue treatment with 10mg to 20mg oral aripiprazole per day for 14 consecutive days to maintain therapeutic aripiprazole concentration during initiation of therapy. Suspension should be injected slowly as a single injection (doses must not be divided) into gluteal or deltoid muscle (care should be taken to avoid inadvertent injection into a blood vessel). **Two injection start:** On the day of initiation, administer two separate injections of 400mg Abilify Maintena® at separate injection sites (see SmPCs for method of administration), along with one 20mg dose of oral aripiprazole. If initiating with the two injection start, inject into two different sites in two different muscles. DO NOT inject both injections concomitantly into the same deltoid or gluteal muscle. For known CYP2D6 poor metabolisers administer in either two separate deltoid muscles or one deltoid and one gluteal muscle. DO NOT inject into two gluteal muscles. After either the one or the two injection start, the recommended maintenance dose of Abilify Maintena® is 400mg once monthly as a single injection (no sooner than 26 days after the previous injection). Consider reducing dose to 300mg once monthly if adverse reactions experienced. **SPECIAL POPULATIONS:** Hepatic impairment: No dose adjustment required for mild-moderate hepatic impairment. Manage dose cautiously in severe hepatic impairment. **Oral formulations and 7.5mg/ml solution for injection (IM):** Maximum daily dose of 30mg should be used with caution in patients with severe hepatic impairment. **Prolonged-release suspension for injection:** Oral formulation preferred in severe hepatic impairment. Renal impairment: No dose adjustment required. Elderly: Safety and efficacy not established in patients ≥ 65 years old. Consider a lower starting dose (oral formulations and 7.5 mg/ml solution for injection (IM)). Paediatrics: **Oral formulations:** Safety and efficacy below 15 years of age not established and use in <15 years not recommended. **7.5mg/ml solution for injection (IM) and prolonged-release suspension for injection:** Safety and efficacy in children and adolescents aged 0-17 not established. **All formulations**: For advice on use with CYP2D6 inhibitors or CYP3A4 inhibitors or inducers see SmPCs. For Abilify Maintena®, see SmPC for instructions on missed doses, reconstitution and injection procedure. **CONTRAINDICATIONS:** Hypersensitivity to active substance or excipients. **WARNINGS AND PRECAUTIONS: All formulations:** During antipsychotic treatment, improvement in clinical condition may take days to weeks – monitor closely. Suicidal behaviour has been reported early after initiation or switch of antipsychotic treatment – closely supervise high risk patients. Use with caution in patients with known cardiovascular disease, cerebrovascular disease conditions predisposing to hypotension or hypertension, family history of QT prolongation, history of seizure disorder or have conditions associated with seizures. Extreme caution should be taken when concomitantly administering aripiprazole and stimulants. Oesophageal dysmotility and aspiration have been associated with aripiprazole and aripiprazole should be used cautiously in patients at risk for aspiration pneumonia. Cases of venous thromboembolism (VTE) have been reported with antipsychotics. All possible VTE risk factors should be identified before and during treatment and preventive measures taken. There were uncommon reports of treatment emergent dyskinesia during aripiprazole treatment. If signs and symptoms of tardive dyskinesia appear during treatment, reduce dose or discontinue. Symptoms can temporally deteriorate or even arise after treatment discontinuation. If signs and symptoms of other extra pyramidal symptoms appear e.g. akathisia or Parkinsonism, reduce the dose and monitor closely (except Abilify Maintena®). Rare cases of neuroleptic malignant syndrome (NMS) were reported in aripiprazole clinical trials. If patient develops signs and symptoms indicative of NMS or unexplained high fever without additional clinical manifestations of NMS, all antipsychotics, including aripiprazole, must be discontinued. May cause somnolence, postural hypotension, motor and sensory instability which may lead to falls. Caution when treating patients at higher risk e.g. elderly or debilitated patients – consider a lower starting dose. Not indicated for treatment of patients with dementia-related psychosis. Hyperglycaemia has been reported with aripiprazole. Observe for signs and symptoms of hyperglycaemia and monitor diabetes mellitus patients or those at risk of diabetes mellitus regularly for worsening glucose control. Weight gain has been reported post-marketing with oral aripiprazole, usually in those with significant risk factors. If weight gain is clinically significant, consider reducing dose. Increased urges can be experienced while taking aripiprazole and inability to control urges e.g. gambling, sexual urges, compulsive shopping, binge or compulsive eating. Patients or caregivers should be asked about development of new or increased urges. If urges develop during treatment, consider dose reduction or treatment cessation. Caution driving vehicles or using machines as sedation, somnolence, syncope, blurred vision or diplopia may occur. **Oral formulations:** Tablets and orodispersible tablets contain lactose. Should not be taken by patients with galactose intolerance, total lactase deficiency or glucose-galactose malabsorption. Orodispersible tablets contain aspartame, a source of phenylalanine which may be harmful to those with phenylketonuria. Orodispersible tablets contain sodium (< 1mmol/tablet). Oral solution and 7.5ml/ml solution for injection contain sodium (both contain <1mmol/dosage unit). Oral solution contains fructose and sucrose. Should not be taken by patients with fructose intolerance, glucose- galactose malabsorption or sucrase-isomaltase insufficiency. Oral solution contains methyl/propyl parahydroxybenzoate, which may cause allergic reactions. **7.5mg/ml solution for injection (IM):** Observe and monitor for orthostatic hypotension. Simultaneous administration with parenteral benzodiazepine may be associated with excessive sedation and cardiorespiratory depression. If given with parenteral benzodiazepine, monitor for excessive sedation and orthostatic hypotension. Safety and efficacy not evaluated in those with alcohol or medicinal product intoxication. **Prolonged-release suspension for injection:** Abilify Maintena® should not be used for acutely agitated or severely psychotic states when immediate symptom control needed. Abilify Maintena contains sodium (<1 mmol/dose). **INTERACTIONS: All formulations:** Aripiprazole has potential to enhance effect of certain antihypertensives. Caution when administering with alcohol or CNS medicines with overlapping effects such as sedation. Caution if administered with medicines known to cause QT prolongation or electrolyte imbalance. Monitor for serotonin syndrome if aripiprazole is used concomitantly with serotonergic medicines such as Selective Serotonin Reuptake Inhibitor (SSRI)/ Serotonin-Norepinephrine Reuptake Inhibitor (SNRI) or medicines known to increase aripiprazole concentrations. **All formulations**: For advice on use with CYP2D6 inhibitors or CYP3A4 inhibitors or inducers see SmPCs. **FERTILITY, PREGNANCY AND LACTATION:** Should not be used in pregnancy unless expected benefit clearly justifies potential risk to foetus. Neonates exposed to antipsychotics during third trimester of pregnancy at risk of reactions including extrapyramidal and/or withdrawal symptoms: monitor carefully. Aripiprazole/metabolites are excreted in human milk. Make a benefit-risk decision whether to discontinue breastfeeding or discontinue/abstain aripiprazole therapy. **UNDESIRABLE EFFECTS:** For further details on adverse events, consult SmPC. **Oral formulations and 7.5mg/ml solution for injection (IM):** Common (≥1/100 to <1/10): Diabetes mellitus, insomnia, anxiety, restlessness, akathisia, extrapyramidal disorder, tremor, headache, sedation, somnolence, dizziness, vision blurred, constipation, dyspepsia, nausea, salivary hypersecretion, vomiting, fatigue. Uncommon: (≥1/1000 to <1/100):Hyperprolactinaemia, hyperglycaemia, depression, hypersexuality, tardive dyskinesia, dystonia, diplopia, photophobia, tachycardia, orthostatic hypotension, hiccups, restless legs syndrome. For 7.5mg/ml solution for injection (IM) only: mouth dry, diastolic blood pressure increased. Frequency not known (cannot be estimated from the available data): Leukopenia, neutropenia, thrombocytopenia, allergic reaction (e.g. anaphylactic reaction, angioedema including swollen tongue, tongue oedema, face oedema, pruritus allergic, or urticaria), diabetic hyperosmolar coma, diabetic ketoacidosis, hyponatraemia, anorexia, suicide attempt, ideation or completed, pathological gambling, impulse-control disorder, binge eating, compulsive shopping, poriomania, aggression, agitation, nervousness, neuroleptic malignant syndrome, grand mal convulsion, serotonin syndrome, speech disorder, oculogyric crisis, sudden death unexplained, torsades de pointes, ventricular arrhythmia, cardiac arrest, bradycardia, venous thromboembolism (including pulmonary embolism and deep vein thrombosis), hypertension, syncope, aspiration pneumonia, laryngospasm, oropharyngeal spasm, pancreatitis, dysphagia, diarrhoea, abdominal discomfort, stomach discomfort, hepatic failure, hepatitis, jaundice, rash, photosensitivity reaction, alopecia, hyperhidrosis, rhabdomyolysis, myalgia, stiffness, urinary incontinence, urinary retention, drug withdrawal syndrome neonatal, priapism, temperature regulation disorder (e.g. hypothermia, pyrexia), chest pain, peripheral oedema, weight decreased, weight gain, alanine aminotransferase increased, aspartate aminotransferase increased, gamma-glutamyltransferase increased, alkaline phosphatase increased, QT prolonged, blood glucose increased, glycosylated haemoglobin increased, blood glucose fluctuation, creatine phosphokinase increased, drug reaction with eosinophilia and systemic symptoms (DRESS). **Prolonged-release suspension for injection:** Common (≥1/100 to <1/10): Weight increased, diabetes mellitus, weight decreased, agitation, anxiety, restlessness, insomnia, extrapyramidal disorder, akathisia, tremor, dyskinesia, sedation, somnolence, dizziness, headache, dry mouth, musculoskeletal stiffness, erectile dysfunction, injection site pain, injection site induration, fatigue, blood creatine phosphokinase increased. Uncommon (≥1/1000 to <1/100): Neutropenia, anaemia, thrombocytopenia, neutrophil count decreased, white blood cell count decreased, hypersensitivity, blood prolactin decreased, hyperprolactinaemia, hyperglycaemia, hypercholesterolaemia, hyperinsulinaemia, hyperlipidaemia, hypertriglyceridaemia, appetite disorder, suicidal ideation, psychotic disorder, hallucination, delusion, hypersexuality, panic reaction, depression, affect lability, apathy, dysphoria, sleep disorder, bruxism, libido decreased, mood altered, dystonia, tardive dyskinesia, Parkinsonism, movement disorder, psychomotor hyperactivity, restless legs syndrome, cogwheel rigidity, hypertonia, bradykinesia, drooling, dysgeusia, parosmia, oculogyric crisis, vision blurred, eye pain, diplopia, photophobia, ventricular extrasystoles, bradycardia, tachycardia, electrocardiogram (ECG) T wave amplitude decreased, ECG abnormal, ECG T wave inversion, hypertension, orthostatic hypotension, blood pressure increased, cough, hiccups, gastrooesophageal reflux disease, dyspepsia, vomiting, diarrhoea, nausea, abdominal pain upper, abdominal discomfort, constipation, frequent bowel movement, salivary hypersecretion, liver function test abnormal, hepatic enzymes increased, alanine aminotransferase increased, gamma-glutamyl transferase increased, blood bilirubin increased, aspartate aminotransferase increased, alopecia, acne, rosacea, eczema, skin induration, muscle rigidity, muscle spasms, muscle twitching, muscle tightness, myalgia, pain in extremity, arthralgia, back pain, joint range of motion decreased, nuchal rigidity, trismus, nephrolithiasis, glycosuria, galactorrhoea, gynaecomastia, breast tenderness, vulvovaginal dryness, pyrexia, asthenia, gait disturbance, chest discomfort, injection site reaction, injection site erythema, injection site swelling, injection site discomfort, injection site pruritis, thirst, sluggishness, blood glucose increased or decreased, glycosylated haemoglobin increased, waist circumference increased, blood cholesterol or triglycerides decreased. Frequency not known (cannot be estimated from the available data): Leukopenia, allergic reaction (e.g. anaphylactic reaction, angioedema including swollen tongue, tongue oedema, face oedema, pruritis, or urticaria), diabetic hyperosmolar coma, diabetic ketoacidosis, anorexia, hyponatraemia, completed suicide, suicide attempt, pathological gambling, impulse-control disorders, binge eating, compulsive shopping, poriomania, nervousness, aggression, neuroleptic malignant syndrome, grand mal convulsion, serotonin syndrome, speech disorder, sudden unexplained death, cardiac arrest, torsades de pointes, ventricular arrhythmias, QT prolongation, syncope, venous thromboembolism (including pulmonary embolism and deep vein thrombosis), oropharyngeal spasm, laryngospasm, aspiration pneumonia, pancreatitis, dysphagia, hepatic failure, jaundice, hepatitis, alkaline phosphatase increased, rash, photosensitivity reaction, hyperhidrosis, rhabdomyolysis, urinary retention, urinary incontinence, drug withdrawal syndrome neonatal, priapism, temperature regulation disorder (e.g. hypothermia, pyrexia), chest pain, peripheral oedema, blood glucose fluctuation, drug reaction with eosinophilia and systemic symptoms (DRESS). **OVERDOSE: All formulations:** Supportive therapy, maintaining an adequate airway, oxygenation and ventilation, management of symptoms with cardiovascular monitoring, including continuous electrocardiographic monitoring with close medical supervision and monitoring. For oral formulations, activated charcoal administered may be effective in treatment of overdose.

LEGAL CATEGORY: Prescription Only Medicine (POM).

MARKETING AUTHORISATION (MA) NUMBER: Abilify® tablets: EU/1/04/276/001-020; Abilify® orodispersible tablets: EU/1/04/276/024-032; Abilify® 1 mg/ml oral solution: EU/1/04/276/033-035; Abilify® 7.5 mg/ml solution for injection (IM): EU/1/04/276/036; Abilify Maintena® powder and solvent for prolonged release suspension for injection: vial: EU/1/13/882/ 001-004, pre-filled syringe: EU/1/13/882/005-008.

MA HOLDER: Otsuka Pharmaceutical Netherlands B.V, Herikerbergweg 292, 1101 CT, Amsterdam, The Netherlands.

PRESCRIBING INFORMATION DATE: August 2021

Adverse events should be reported to the relevant regulatory authorities. A list of the relevant regulatory authorities is available on request from Otsuka Pharmaceutical Europe Ltd.

Adverse events should also be reported to Otsuka Pharmaceutical Europe Ltd. by email to vigilance@otsuka-europe.com

Example Price, UK: Abilify® tablets: 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) £192.08; Abilify® orodispersible tablets: 28 tablets: 10mg (EU/1/04/276/025) £96.04, 15mg (EU/1/04/276/028) £96.04; Abilify® 1 mg/ml oral solution: 150ml (EU/1/04/276/034) £102.90; Abilify® 7.5 mg/ml solution for injection 1.3ml vial (EU/1/04/276/036) £3.43; Abilify Maintena® prolonged release suspension for injection 400mg: powder and solvent: (EU/1/13/882/ 002) £220.41; pre-filled syringe: (EU/1/13/882/006) £220.41.

For reference in Denmark:

PACK SIZES: Tablets: 5 mg: 28 tabs, 56 tabs; 10 mg: 28 tabs, 56 tabs; 15 mg: 28 tabs, 56 tabs; 30 mg: 28 tabs, 56 tabs. Orodispersible Tablets: 10 mg 28 tabs, 15 mg 28 tabs. Oral solution: 1 mg/ml 150 ml. Solution for Injection: 7,5 mg/ml. 400 mg powder and solvent for prolonged-release suspension for injection, suspension in vial (single pack) and in pre-filled syringe (single pack, multipack).

REFERENCE TO CURRENT PRICE: www.medicinpriser.dk

DISPENSING GROUP: B

REIMBURSEMENT STATUS: general reimbursement (tablets), conditional reimbursement (orodispersible tablets, oral solution, powder and solvent for prolonged-release suspension for injection), non-reimbursement on Solution for Injection.

OPE-AM-2100104; DOP: August 2021

ABILIFY MAINTENA essential information compliant with SmPC of 10/2020

Abilify Maintena 400 mg powder and solvent for prolonged-release suspension for injection. **QUALITATIVE AND QUANTITATIVE COMPOSITION:** Each vial contains 400 mg aripiprazole. After reconstitution each ml of suspension contains 200 mg aripiprazole. **PHARMACEUTICAL FORM:** Powder and solvent for prolonged-release suspension for injection. Powder: white to off-white Solvent: clear solution. **CLINICAL PARTICULARS: Therapeutic indications:** Abilify Maintena is indicated for maintenance treatment of schizophrenia in adult patients stabilisedwith oral aripiprazole. **Posology and method of administration:** Posology: For patients who have never taken aripiprazole, tolerability with oral aripiprazole must occur prior to initiating treatment with Abilify Maintena. Titration of the dose for Abilify Maintena is not required. The starting dose can be administered by following one of two regimens; *One injection start:* On the day of initiation, administer one injection of 400 mg Abilify Maintena and continue treatment with 10 mg to 20 mg oral aripiprazole per day for 14 consecutive days to maintain therapeutic aripiprazole concentrations during initiation of therapy; *Two injection start:* On the day of initiation, administer two separate injections of 400 mg Abilify Maintena at separate injection sites (see method of administration), along with one 20 mg dose of oral aripiprazole. After the injection start, the recommended maintenance dose of Abilify Maintena is 400 mg. Abilify Maintena should be administered once monthly as a single injection (no sooner than 26 days after the previous injection). If there are adverse reactions with the 400 mg dosage, reduction of the dose to 300 mg once monthly should be considered (for details regarding "Missing doses" please consult Summary of Product Characteristics). Special populations: *Elderly:* The safety and efficacy of Abilify Maintena in the treatment of schizophrenia in patients 65 years of age or older has not been established. *Renal impairment:* No dosage adjustment is required for patients with renal impairment. *Hepatic impairment:* No dosage adjustment is required for patients with mild or moderate hepatic impairment. In patients with severe hepatic impairment, the data available are insufficient to establish recommendations. In these patients dosing should be managed cautiously. Oral formulation should be preferred. *Known CYP2D6 poor metabolisers:* In patients who are known to be CYP2D6 poor metabolisers: *One injection start:* The starting dose should be 300 mg Abilify Maintena and continue treatment with prescribed dose of oral aripiprazole per day for 14 consecutive days. *Two injection start:* The starting dose should be 2 separate injections of 300 mg Abilify Maintena along with one single dose of the previous prescribed dose of oral aripiprazole. In patients who are known to be CYP2D6 poor metabolisers and concomitantly use a strong CYP3A4 inhibitor: *The one injection start:* The starting dose should be reduced to 200 mg and continue treatment with the prescribed dose of oral aripiprazole per day for 14 consecutive days. Two injection start is not to be used in patients who are known to be CYP2D6 poor metabolisers and concomitantly use a strong CYP3A4 inhibitor. Abilify Maintena should be administered once monthly as a single injection (no sooner than 26 days after the previous injection). Maintenance dose adjustments due to interactions with CYP2D6 and/or CYP3A4 inhibitors and/or CYP3A4 inducers Maintenance dosage adjustments should be made in patients taking concomitant strong CYP3A4 inhibitors or strong CYP2D6 inhibitors for more than 14 days. If the CYP3A4 inhibitor or CYP2D6 inhibitor is withdrawn, the dosage may need to be increased to the previous dose. In case of adverse reactions despite dose adjustments of Abilify Maintena, the necessity of concomitant use of CYP2D6 or CYP3A4 inhibitor should be reassessed. Concomitant use of CYP3A4 inducers with Abilify Maintena should be avoided for more than 14 days because the blood levels of aripiprazole are decreased and may be below the effective levels (for details regarding "Maintenance dose adjustments of Abilify Maintena in patients who are taking concomitant strong CYP2D6 inhibitors, strong CYP3A4 inhibitors, and/or CYP3A4 inducers for more than 14 days" please consult Summary of Prodcut Characteristics): *Paediatric population*: The safety and efficacy of Abilify Maintena in children and adolescents aged 0-17 years have not been established. No data are available. Method of administration: Abilify Maintena is only intended for intramuscular use and should not be administered intravenously or subcutaneously. It should only be administered by a healthcare professional. The suspension should be injected slowly as a single injection (doses must not be divided) into the gluteal or deltoid muscle. Care should be taken to avoid inadvertent injection into a blood vessel. If initiating with the two injection start, inject into two different sites in two different muscles. DO NOT inject both injections concomitantly into the same deltoid or gluteal muscle. For known CYP2D6 poor metabolisers administer in either two separate deltoid muscles or one deltoid and one gluteal muscle. DO NOT inject into two gluteal muscles. Full instructions for use and handling of Abilify Maintena are provided in the package leaflet (information intended for healthcare professionals) (for instructions on reconstitution of the medicinal product before administration, please consult Summary of Prodcut Characteristics). **Contraindications:** Hypersensitivity to the active substance or to any of the excipients. **Undesirable effects:** Summary of the safety profile: The most frequently observed adverse drug reactions (ADRs) reported in ≥ 5 % of patients in two double-blind, long-term trials of Abilify Maintena were weight increased (9.0 %), akathisia (7.9 %), insomnia (5.8 %), and injection site pain (5.1 %). List of adverse reactions: The incidences of the ADRs associated with aripiprazole therapy are mentioned below. This information is based on adverse reactions reported during clinical trials and/or post-marketing use. All ADRs are listed by system organ class and frequency; very common (≥ 1/10), common (≥ 1/100 to < 1/10), uncommon (≥ 1/1,000 to < 1/100), rare (≥ 1/10,000 to < 1/1,000), very rare (< 1/10,000) and not known (cannot be estimated from the available data). Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness. The frequency of adverse reactions reported during post-marketing use cannot be determined as they are derived from spontaneous reports. Consequently, the frequency of these adverse events is qualified as "not known". **Blood and lymphatic system disorders:** Uncommon**:** Neutropenia; Anaemia; Thrombocytopenia; Neutrophil count decreased; White blood cell count decreased. Not known: Leukopenia. **Immune system disorders:** Uncommon: Hypersensitivity. Not known: Allergic reaction (e.g. anaphylactic reaction, angioedema including swollen tongue, tongue oedema, face oedema, pruritus, or urticaria). **Endocrine disorders:** Uncommon: Blood prolactin decreased Hyperprolactinaemia. Not known: Diabetic hyperosmolar coma; Diabetic ketoacidosis. **Metabolism and nutrition disorders:** Common: Weight increased; Diabetes mellitus; Weight decreased. Uncommon: Hyperglycaemia; Hypercholesterolaemia; Hyperinsulinaemia; Hyperlipidaemia; Hypertriglyceridaemia; Appetite disorder. Not known: Anorexia; Hyponatraemia. **Psychiatric disorders:** Common: Agitation; Anxiety; Restlessness; Insomnia. Uncommon: Suicidal ideation; Psychotic disorder; Hallucination; Delusion Hypersexuality; Panic reaction; Depression; Affect lability; Apathy Dysphoria; Sleep disorder; Bruxism; Libido decreased; Mood altered. Not known: Completed suicide; Suicide attempt; Pathological gambling; Impulse-control disorders; Binge eating; Compulsive shopping; Poriomania; Nervousness Aggression. **Nervous system disorders:** Common: Extrapyramidal disorder; Akathisia; Tremor; Dyskinesia; Sedation; Somnolence; Dizziness; Headache Uncommon: Dystonia; Tardive dyskinesia; Parkinsonism; Movement disorder; Psychomotor hyperactivity; Restless legs syndrome; Cogwheel rigidity; Hypertonia; Bradykinesia; Drooling; Dysgeusia; Parosmia. Not known: Neuroleptic malignant syndrome; Grand mal convulsion; Serotonin syndrome; Speech disorder. **Eye disorders** Uncommon: Oculogyric crisis; Vision blurred; Eye pain; Diplopia; Photophobia. **Cardiac disorders** Uncommon: Ventricular extrasystoles; Bradycardia; Tachycardia; Electrocardiogram T wave amplitude decreased; Electrocardiogram abnormal; Electrocardiogram T wave inversion. Not known**:** Sudden unexplained death; Cardiac arrest; Torsades de pointes; Ventricular arrhythmias QT prolongation. **Vascular disorders:** Uncommon: Hypertension; Orthostatic hypotension; Blood pressure increased. Not known: Syncope; Venous thromboembolism (including pulmonary embolism and deep vein thrombosis). **Respiratory, thoracic and mediastinal disorders:** Uncommon: Cough; Hiccups. Not known: Oropharyngeal spasm; Laryngospasm; Aspiration pneumonia. **Gastrointestinal disorders:** Common: Dry mouth. Uncommon: Gastrooesophageal reflux disease; Dyspepsia; Vomiting; Diarrhoea; Abdominal pain upper; Abdominal discomfort; Constipation; Frequent bowel movement; Salivary hypersecretion. Not known: Pancreatitis; Dysphagia. **Hepatobiliary disorders** Uncommon: Liver function test abnormal; Hepatic enzyme increased; Alanine aminotransferase increased; Gamma-glutamyl transferase increased; Blood bilirubin increased; Aspartate aminotransferase increased. Not known: Hepatic failure; Jaundice; Hepatitis; Alkaline phosphatase increased. **Skin and**

subcutaneous tissue disorders: Uncommon: Alopecia; Acne; Rosacea; Eczema; Skin induration. Not known: Rash; Photosensitivity reaction; Hyperhidrosis; Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS). **Musculoskele tal and connective tissue disorders:** Common: Musculoskeletal stiffness. Uncommon: Muscle rigidity; Muscle spasms; Muscle twitching; Muscle tightness; Myalgia; Pain in extremity; Arthralgia; Back pain; Joint range of motion decreased; Nuchal rigidity; Trismus. Not known: Rhabdomyolysis. **Renal and urinary disorders:** Uncommon: Nephrolithiasis; Glycosuria. Not known: Urinary retention; Urinary incontinence. **Pregnancy, puerperium and perinatal conditions:** Not known: Drug withdrawal syndrome neonatal. **Reproductive system and breast disorders:** Common: Erectile dysfunction. Uncommon: Galactorrhoea Gynaecomastia; Breast tenderness; Vulvovaginal dryness. Not known: Priapism. **General disorders and administration site conditions:** Common: Injection site pain; Injection site induration; Fatigue. Uncommon: Pyrexia; Asthenia; Gait disturbance; Chest discomfort; Injection site reaction; Injection site erythema; Injection site swelling; Injection site discomfort; Injection site pruritus; Thirst Sluggishness. Not known: Temperature regulation disorder (e.g. hypothermia, pyrexia); Chest pain; Peripheral oedema. **Investigations:** Common: Blood creatine phosphokinase increased. Uncommon: Blood glucose increased; Blood glucose decreased; Glycosylated haemoglobin increased; Waist circumference increased; Blood cholesterol decreased; Blood triglycerides decreased. Not known: Blood glucose fluctuation. Description of selected adverse reactions: Injection site reactions: During the double-blind, controlled phases of the two long-term trials, injection site reactions were observed; those seen were generally mild to moderate in severity, and resolved over time. Injection site pain (incidence 5.1 %), had a median onset on day 2 after the injection and a median duration of 4 days. In an open label study comparing bioavailability of Abilify Maintena administered in the deltoid or gluteal muscle, injection site related reactions were slightly more frequent in the deltoid muscle. The majority were mild and improved on subsequent injections. When compared to studies where Abilify Maintena was injected in the gluteal muscle, repeated occurrence of injection site pain was more frequent in the deltoid muscle. Leukopenia Neutropenia has been reported in the clinical program with Abilify Maintena and typically started around day 16 after first injection, and lasted a median of 18 days. Extrapyramidal Symptoms (EPS) In trials in stable patients with schizophrenia, Abilify Maintena was associated with a higher frequency of EPS symptoms (18.4 %) than oral aripiprazole treatment (11.7 %). Akathisia was the most frequently observed symptom (8.2 %) and typically started around day 10 after first injection, and lasted a median of 56 days. Subjects with akathisia typically received anti-cholinergic medicines as treatment, primarily benzatropine mesilate and trihexyphenidyl. Less often substances such as propranolol and benzodiazepines (clonazepam and diazepam) were administered to control akathisia. Parkinsonism events followed in frequency of 6.9 % for Abilify Maintena, 4.15 % for oral aripiprazole 10-30 mg tablets and 3.0 % for placebo, respectively. Dystonia Class effect: Symptoms of dystonia, prolonged abnormal contractions of muscle groups, may occur in susceptible individuals during the first few days of treatment. Dystonic symptoms include spasm of the neck muscles, sometimes progressing to tightness of the throat, swallowing difficulty, difficulty breathing, and/or protrusion of the tongue. While these symptoms can occur at low doses, they occur more frequently and with greater severity with high potency and at higher doses of first generation antipsychotic medicinal products. An elevated risk of acute dystonia is observed in males and younger age groups. Weight During the Double-blind, Active-controlled Phase of the 38-week long-term trial, the incidence of weight gain of ≥ 7 % from baseline to last visit was 9.5 % for Abilify Maintena and 11.7 % for the oral aripiprazole tablets 10-30 mg. The incidence of weight loss of ≥ 7 % from baseline to last visit was 10.2 % for Abilify Maintena and 4.5 % for oral aripiprazole tablets 10-30 mg. During the Double-blind, Placebo-controlled Phase of the 52-week long-term trial, the incidence of weight gain of ≥ 7 % from baseline to last visit was 6.4 % for Abilify Maintena and 5.2 % for placebo. The incidence of weight loss of ≥ 7 % from baseline to last visit was 6.4 % for Abilify Maintena and 6.7 % for placebo. During double-blind treatment, mean change in body weight from baseline to last visit was -0.2 kg for Abilify Maintena and -0.4 kg for placebo (p = 0.812). Prolactin In clinical trials for the approved indications and post-marketing, both increase and decrease in serum prolactin as compared to baseline was observed with aripiprazole. Pathological gambling and other impulse control disorders Pathological gambling, hypersexuality, compulsive shopping and binge or compulsive eating can occur in patients treated with aripiprazole. Reporting of suspected adverse reactions Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via INFARMED I.P.: Direção de Gestão do Risco de Medicamentos, Parque da Saúde de Lisboa, Av. Brasil 53, 1749-004 Lisboa, Phone: +351 21 798 73 73, Medicine line: 800 222 444 (free of charge). Website: http://www.infarmed.pt/web/infarmed/submissaoram. E-mail: farmacovigilancia@infarmed.pt. **MARKETING AUTHORISATION HOLDER:** Otsuka Pharmaceutical Netherlands B.V. Herikerbergweg 292 1101 CT, Amsterdam Netherlands **DATE OF REVISION OF THE TEXT:** 10/2020. Detailed information on this medicinal product is available on the website of the European Medicines Agency http://www.ema.europa.eu. Medicinal product subject to medical prescription. Level A reimbursed medicine (general regímen 90% and special regimen 95%). For further information please contact the Marketing Authorisation Holder. **LOCAL REPRESENTATIVE:** Lundbeck Portugal. Quinta da Fonte | Rua Quinta da Fonte, Nº 13, Edifício Q34 Forum, Piso 1, Fração F, 2770-192 Paço De Arcos, Portugal. NIF: 503573922.