ABILIFY MAINTENA 400 MG AND 300 MG LYOPHILISED POWDER FOR PROLONGED RELEASE SUSPENSION FOR INJECTION (IM)

SCHEDULING STATUS

S5

1. NAME OF THE MEDICINE

ABILIFY MAINTENA 400 mg

Lyophilised powder for prolonged release suspension for injection (IM)

ABILIFY MAINTENA 300 mg

Lyophilised powder for prolonged release suspension for injection (IM)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Abilify Maintena 300 mg powder and solvent for prolonged-release suspension for injection

Each vial contains 300 mg aripiprazole.

Abilify Maintena 400 mg powder and solvent for prolonged-release suspension for injection

Each vial contains 400 mg aripiprazole.

Abilify Maintena 400 mg powder and solvent for prolonged-release suspension for injection in pre-filled syringe

Each pre-filled syringe contains 400 mg aripiprazole.

After reconstitution each ml of suspension contains 200 mg aripiprazole.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Powder and solvent for prolonged-release suspension for injection

Powder: white to off-white Solvent: clear solution

4. CLINICAL PARTICULARS

4.1 Therapeutic indictions

Abilify Maintena is indicated for maintenance treatment of schizophrenia in adult patients stabilised with oral aripiprazole.

4.2 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.

If Abilify Maintena is to be discontinued, its prolonged release characteristics should be kept in mind.

The recommended starting and maintenance dose of Abilify Maintena is 400 mg.

Titration of the dose of Abilify Maintena is not required. It should be administered once monthly as a single injection (no sooner than 26 days after the previous injection).

After the first injection, treatment with 10 mg to 20 mg oral aripiprazole per day should be continued for 14 consecutive days to maintain therapeutic aripiprazole concentrations during initiation of therapy.

If there are adverse reactions with the 400 mg dosage, reduction of the dose to 300 mg once monthly should be considered.

Missed doses

Missed doses	
If 2nd or 3rd dose is missed and time since last injection is:	**Action**
> 4 weeks and < 5 weeks	The injection should be administered as soon as possible and then the monthly injection schedule should be resumed.
> 5 weeks	Concomitant oral aripiprazole should be restarted for 14 days with next administered injection.
If 4th or subsequent doses are missed (i.e., after attainment of steady state) and time since last injection is:	**Action**
> 4 weeks and < 6 weeks	The injection should be administered as soon as possible and then the monthly injection schedule should be resumed.
> 6 weeks	Concomitant oral aripiprazole should be restarted for 14 days with next administered injection and then resume monthly injection schedule.

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 (see section 4.4).

Renal impairment

No dosage adjustment is required for patients with renal impairment (see section 5.2).

Hepatic impairment

No dosage adjustment is required for patients with mild or moderate hepatic impairment. In patients with severe hepatic impairment (Child Pugh C), the data available are insufficient to establish recommendations. Oral formulation should be preferred (see section 5.2).

Known CYP2D6 poor metabolisers

In patients who are known to be CYP2D6 poor metabolisers, the starting and maintenance dose should be 300 mg. When used concomitantly with strong CYP3A4 inhibitors the dose should be reduced to 200 mg (see section 4.5).

Dose adjustments due to interactions with CYP2D6 and/or CYP3A4 inhibitors and/or CYP3A4 inducers

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 (see section 4.5). 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 (see section 4.5).

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

	Adjusted dose
Patients taking 400 mg of Abilify Maintena	

Strong CYP2D6 or strong CYP3A4 inhibitors	300 mg
Strong CYP2D6 and strong CYP3A4 inhibitors	200 mg*
CYP3A4 inducers	Avoid use
Patients taking 300 mg of Abilify Maintena	
Strong CYP2D6 or strong CYP3A4 inhibitors	200 mg*
Strong CYP2D6 and strong CYP3A4 inhibitors	160 mg*
CYP3A4 inducers	Avoid use

* 200 mg and 160 mg can be achieved via adjustment of the injection volume only by using Abilify Maintena powder and solvent for prolonged-release suspension for injection.

Paediatric population

The safety and efficacy of Abilify Maintena in children and adolescents aged < 18 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.

INSTRUCTIONS FOR HEALTH CARE PROFESSIONALS

Reconstitution of the Lyophilised ABILIFY MAINTENA 400 mg and ABILIFY MAINTENA 300 mg Powder. Packed together in a Vial Kit with a solvent vial

For deep intramuscular deltoid or gluteal injection: do not administer intravenously or subcutaneously. Inject immediately after reconstitution. Administer once monthly.

Step 1: Preparation Prior to Reconstitution

Lay out and confirm that components listed below are provided:

- ABILIFY MAINTENA package leaflet and instructions for healthcare professionals.
- Vial of powder.
- 2 ml vial of solvent.

Important: the solvent vial contains an overfill.

- One 3 ml luer lock syringe with pre-attached 38 mm (1.5 inch) 21 gauge hypodermic safety needle with needle protection device.
- One 3 ml disposable syringe with luer lock tip.
- One vial adapter.
- One 25 mm (1 inch) 23 gauge hypodermic safety needle with needle protection device.
- One 38 mm (1.5 inch) 22 gauge hypodermic safety needle with needle protection device.
- One 51 mm (2 inch) 21 gauge hypodermic safety needle with needle protection device.
- Syringe and needle instructions.
- Use appropriate aseptic techniques throughout reconstitution and reconstitute at room temperature

Step 2: Reconstitution of the powder

(a) Remove the solvent and powder vial caps and wipe the tops with a sterile alcohol swab.

(b) Using the syringe with pre-attached needle, withdraw the pre-determined solvent volume from the vial of the solvent into the syringe.

300 mg vial: Add 1.5 ml solvent to reconstitute the powder.

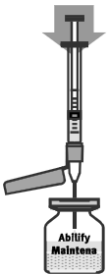
400 mg vial: Add 1.9 ml solvent to reconstitute the powder.

A small amount of residual solvent will remain in the vial following withdrawal. Any excess should be discarded.



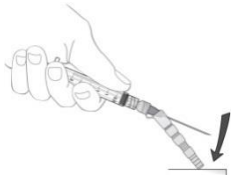
Water

(c) Slowly inject the solvent into the vial containing the powder.



d) Withdraw air to equalise the pressure in the vial by pulling back slightly on the plunger.

e) Subsequently, remove the needle from the vial. Engage the needle safety device by using the one-handed technique. Gently press the sheath against a flat surface until the needle is firmly engaged in the needle protection sheath. Visually confirm that the needle is fully engaged into the needle protection sheath, and discard.



Cover



Discard

f) Shake the vial vigorously for 30 seconds until the suspension appears uniform.



g) Visually inspect the reconstituted suspension for particulate matter and discolouration prior to administration. The reconstituted ABILIFY MAINTENA is a white to off-white, fluid suspension. Do not use if the reconstituted suspension contains particulate matter or any discolouration.

h) If the injection is not performed immediately after reconstitution, keep the vial below 25°C for up to 4 hours and shake the vial vigorously for at least 60 seconds to re-suspend prior to injection.

i) Do not store the reconstituted suspension in the syringe.

Step 3: Preparation Prior to Injection

Use appropriate aseptic techniques throughout injection of the reconstituted ABILIFY MAINTENA suspension.

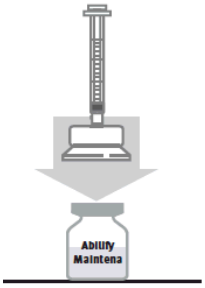
(a) Remove the cover but not the adapter from the package.



(b) Using the vial adapter package to handle the vial adapter, attach the pre-packaged Luer-Lok syringe to the vial adapter.



(c) Use the Luer-Lok syringe to remove the vial adapter from the package and discard the vial adapter package. Do not touch the spike tip of the adapter at any time.



(d) Determine the recommended volume for injection.

ABILIFY MAINTENA Reconstituted Suspension Volume to Inject

ABILIFY MAINTENA 400 mg Vial	
Dose	Volume to inject
400 mg	2,0 ml

300 mg	1,5 ml
200 mg	1,0 ml
160 mg	0,8 ml

ABILIFY MAINTENA 300 mg Vial	
Dose	Volume to inject
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300 mg	1,5 ml
200 mg	1,0 ml
160 mg	0,8 ml

(e) Wipe the top of the vial of the reconstituted ABILIFY MAINTENA suspension with a sterile alcohol swab.

(f) Place and hold the vial of the reconstituted ABILIFY MAINTENA suspension on a hard surface. Attach the adapter-syringe assembly to the vial by holding the outside of the adapter and pushing the adapter's spike firmly through the rubber stopper, until the adapter snaps in place.

(g) Slowly withdraw the recommended volume from the vial into the Luer-Lok syringe to allow for injection. A small amount of excess product will remain in the vial.



Step 4: Injection Procedure

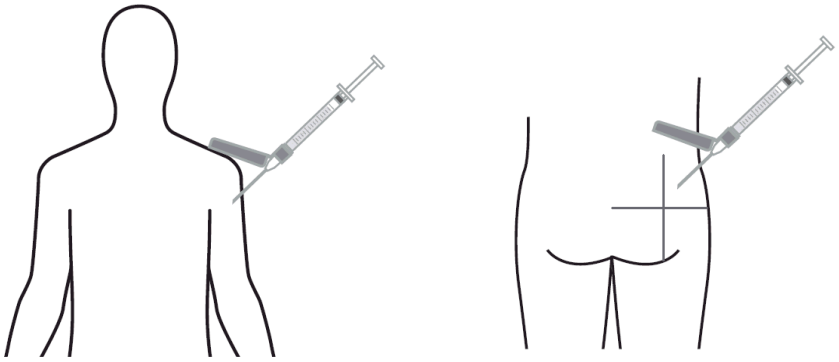
(a) Detach the Luer-Lok syringe containing the recommended volume of reconstituted ABILIFY MAINTENA suspension from the vial.

(b) Select one of the following hypodermic safety needles depending on the injection site and patient's weight and attach the needle to the luer lock syringe containing the suspension for injection. Ensure the needle is firmly seated on the needle protection device with a push and clockwise twist and then pull the needle cap straight away from the needle.

Body Type	Injection site	Needle size
Non-obese	Deltoid Gluteal	25 mm (1 inch) 23 gauge 38 mm (1.5 inch) 22 gauge
Obese	Deltoid Gluteal	38 mm (1.5 inch) 22 gauge 51 mm (2 inch) 21 gauge

c) Slowly inject the recommended volume as a single intramuscular injection into the gluteal or deltoid muscle. Do not massage the injection site. Care must be taken to avoid inadvertent injection into the blood vessel. Do not inject into an area with signs of inflammation, skin damage, lumps and/or bruises.

For deep intramuscular gluteal or deltoid injection only.

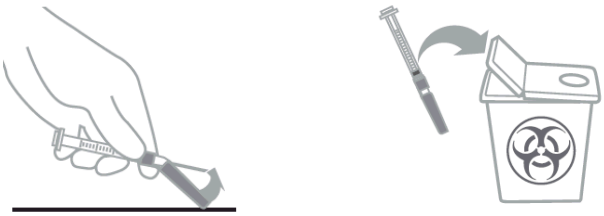


deltoid **gluteal**

Remember to rotate sites of injections between the two gluteal or deltoid muscles. Look for signs or symptoms of inadvertent intravenous administration.

Step 5: Procedures After Injection

Engage the needle safety device as described in Step 2 (e). Dispose of the vials, adapter, needles, and syringe appropriately after injection. **The sterile water for injection and ABILIFY MAINTENA vials are for single-use only.**



Cover **Discard**

Reconstitution of the ABILIFY MAINTENA 400 mg powder and solvent for prolonged-release suspension for injection in pre-filled syringe

For deep intramuscular deltoid or gluteal injection: do not administer intravenously or subcutaneously. Inject immediately after reconstitution. Administer once monthly.

Step 1: Preparation prior to reconstitution of the powder

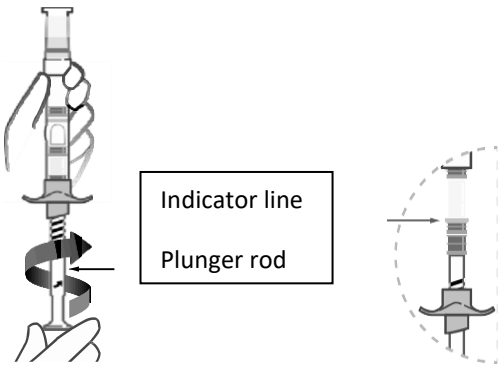
Lay out and confirm that components listed below are provided:

- **ABILIFY MAINTENA** package leaflet and instructions for healthcare professionals.
- One **ABILIFY MAINTENA** pre-filled syringe.
- One 25 mm (1 inch) 23 gauge hypodermic safety needle with needle protection device.
- One 38 mm (1.5 inch) 22 gauge hypodermic safety needle with needle protection device.
- One 50 mm (2 inch) 21 gauge hypodermic safety needle with needle protection device.
- Syringe and needle instructions.
- Use appropriate aseptic techniques throughout reconstitution and reconstitute at room temperature

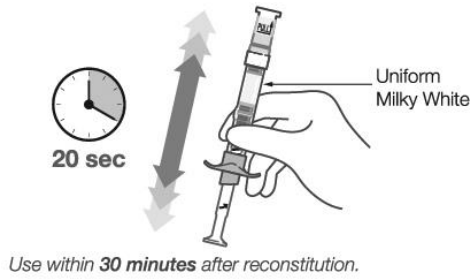
Step 2: Reconstitution of the powder

a) Push plunger rod slightly to engage threads. And then, rotate plunger rod until the rod stops

rotating to release diluent. After plunger rod is at complete stop, middle stopper will be at the indicator line.



b) Vertically shake the syringe vigorously for 20 seconds until the reconstituted suspension appears uniform. The suspension should be injected immediately after reconstitution.

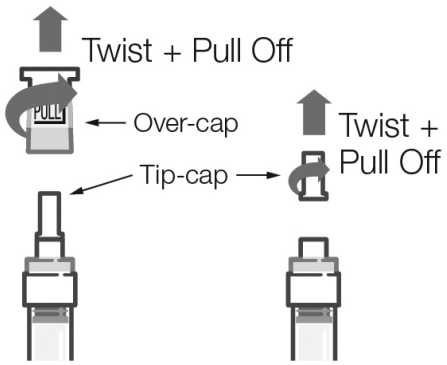


c) Visually inspect the syringe for particulate matter and discoloration prior to administration. The reconstituted **ABILIFY MAINTENA** suspension should appear to be a uniform, homogeneous suspension that is opaque and milky-white in color.

d) If the injection is not performed immediately after reconstitution, the syringe can be kept below 25 °C for up to 2 hours. Shake the syringe vigorously for at least 20 seconds to re-suspend prior to injection if the syringe has been left for more than 15 minutes.

Step 3: Injection procedure

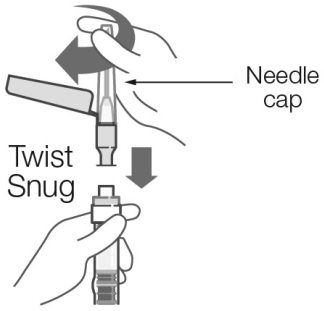
a) Twist and pull off Over-cap and Tip-cap.



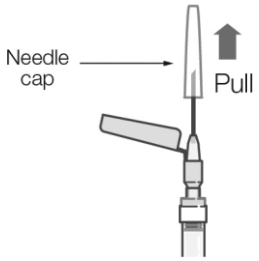
b) Select one of the following hypodermic safety needles depending on the injection site and patient's weight.

Body Type	Injection site	Needle size
Non-obese	Deltoid Gluteal	25 mm (1 inch) 23 gauge 38 mm (1.5 inch) 22 gauge
Obese	Deltoid Gluteal	38 mm (1.5 inch) 22 gauge 51 mm (2 inch) 21 gauge

c) While holding the needle cap, ensure the needle is firmly seated on the safety device with a push. Twist clockwise until snugly fitted.

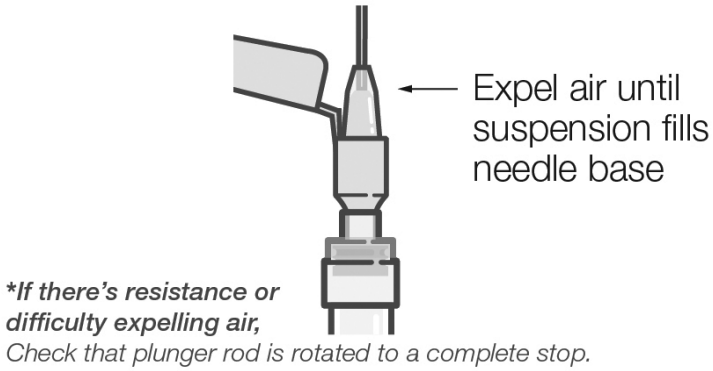


d) Then **pull** needle-cap straight up.



e) Hold syringe **upright and advance plunger rod slowly to expel the air**. If it's not possible to

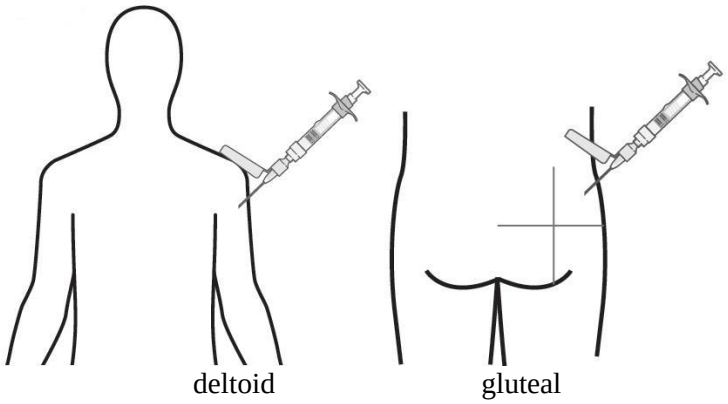
advance plunger rod to expel the air, check that plunger rod is rotated to a complete stop. It is not possible to re-suspend after the air in the syringe is expelled.



f) Slowly inject into the gluteal or deltoid muscle. Do not massage the injection site. Care must be taken to avoid inadvertent injection into the blood vessel. Do not inject into an area with signs

of inflammation, skin damage, lumps and/or bruises. For deep intramuscular gluteal or deltoid

injection only.

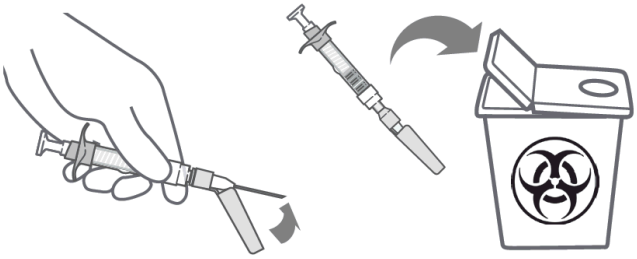


Remember to rotate sites of injections between the two gluteal or deltoid muscles. Look for signs or symptoms of inadvertent intravenous administration.

Step 4: Procedures after injection

Engage the needle safety device. Dispose of the needle and pre-filled syringe appropriately after

injection.



Cover Discard

For instructions on reconstitution of the medicine before administration, see section 6.6.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

During antipsychotic treatment, improvement in the patient's clinical condition may take several days to some weeks. Patients should be closely monitored throughout this period.

Use in patients who are in an acutely agitated or severely psychotic state

Abilify Maintena should not be used to manage acutely agitated or severely psychotic states when immediate symptom control is warranted.

Suicidality

The occurrence of suicidal behaviour is inherent in psychotic illnesses, and in some cases has been reported early after initiation or switch of antipsychotic treatment, including treatment with aripiprazole (see section 4.8).

Close supervision of high risk patients should accompany antipsychotic treatment.

Cardiovascular disorders

Abilify Maintena should be used with caution in patients with known cardiovascular disease (history of myocardial infarction or ischaemic heart disease, heart failure, or conduction abnormalities), cerebrovascular disease, conditions which would predispose patients to hypotension (dehydration, hypovolemia, and treatment with antihypertensive medicines) or hypertension, including accelerated or malignant.

Cases of venous thromboembolism (VTE) have been reported with antipsychotic medicines. Since patients treated with antipsychotics often present with acquired risk factors for VTE, all possible risk factors for VTE should be identified before and during treatment with Abilify Maintena and preventive measures undertaken (see section 4.8).

QT prolongation

Abilify Maintena should be used with caution in patients with a family history of QT prolongation (see section 4.8).

Tardive dyskinesia

Tardive dyskinesia has been reported with treatment with Abilify Maintena. If signs and symptoms of tardive dyskinesia appear in a patient on Abilify Maintena, dose reduction or discontinuation should

be considered (see section 4.8). These symptoms can temporally deteriorate or can even arise after discontinuation of treatment.

Body Temperature Regulation Disorder

Disruption of the body`s ability to regulate core temperature has been reported with antipsychotics such as aripiprazole, which may increase the risk of hyperthermia and/or hypothermia.

Neuroleptic Malignant Syndrome (NMS)

NMS is a potentially fatal symptom complex associated with the use of antipsychotics. Cases of NMS were reported during treatment with aripiprazole. Clinical manifestations of NMS are hyperpyrexia, muscle rigidity, altered mental status and evidence of autonomic instability (irregular pulse or blood pressure, tachycardia, diaphoresis and cardiac dysrhythmia). Additional signs may include elevated creatine phosphokinase, myoglobinuria (rhabdomyolysis), and acute renal failure. However, elevated creatine phosphokinase and rhabdomyolysis, not necessarily in association with NMS, have also been reported. If a patient develops signs and symptoms indicative of NMS, or presents with unexplained high fever without additional clinical manifestations of NMS, all antipsychotics, including Abilify Maintena, must be discontinued (see section 4.8).

Seizures

Seizures were reported during treatment with aripiprazole. Abilify Maintena should be used with caution in patients who have a history of seizure disorders or have conditions associated with seizures (see section 4.8).

Elderly patients with dementia-related psychosis

Increased mortality

In three placebo-controlled trials of oral aripiprazole in elderly patients with psychosis associated with Alzheimer's disease (n = 938; mean age: 82.4 years; range: 56-99 years), patients treated with aripiprazole were at an increased risk of death compared to placebo. The rate of death in oral aripiprazole-treated patients was 3.5 % compared to 1.7 % in placebo.

Although the causes of death were varied, most of the deaths appeared to be either cardiovascu;ar (e.g. heart failure, sudden deah) or infectious (e.g. pneumonia) in nature (see section 4.8).

Cerebrovascular adverse events

In the same trials with oral aripiprazole, cerebrovascular adverse reactions (e.g. stroke, transient ischaemic attack), including fatalities, were reported in patients (mean age: 84 years; range: 78-88 years). Overall, 1.3 % of oral aripiprazole-treated patients reported cerebrovascular adverse reactions compared with 0.6 % of placebo-treated patients in these trials. This difference was not statistically significant. However, in a fixed-dose trial, there was a significant dose- response relationship for cerebrovascular adverse reactions in patients treated with aripiprazole (see section 4.8).

Abilify Maintena **is not indicated for the treatment of patients with dementia-related psychosis**

Hyperglycaemia and diabetes mellitus

Hyperglycaemia, in some cases extreme and associated with ketoacidosis or hyperosmolar coma or death, has been reported in patients treated with aripiprazole. Risk factors that may predispose patients to severe complications include obesity and family history of diabetes. Patients treated with Abilify Maintena should be observed for signs and symptoms of hyperglycaemia (such as polydipsia, polyuria, polyphagia and weakness) and patients with diabetes mellitus or with risk factors for diabetes mellitus should be monitored regularly for worsening of glucose control (see section 4.8).

Hypersensitivity

Hypersensitivity reactions, characterised by allergic symptoms, may occur with Abilify Maintena (see section 4.8).

Weight gain

Weight gain is commonly seen in schizophrenic patients due to use of antipsychotics, including aripiprazole. Weight gain co-morbidities and poorly managed life-style might lead to severe complications. Weight gain has been reported in clinical trials with Abilify Maintena and post-marketing among patients prescribed oral aripiprazole. When seen, it is usually in those with significant risk factors such as history of diabetes, thyroid disorder or pituitary adenoma (see section 4.8).

Dysphagia

Oesophageal dysmotility and aspiration have been associated with the use of aripiprazole. Abilify Maintena should be used cautiously in patients at risk for aspiration pneumonia.

Pathological gambling and other impulse control disorders

Patients can experience increased urges, particularly for gambling, and the inability to control these urges while receiving Abilify Maintena. Other urges reported include: increased sexual urges, compulsive shopping, binge or compulsive eating, and other impulsive and compulsive behaviours.

It is important for prescribers to ask patients or their caregivers specifically about the development of new or increased gambling urges, sexual urges, compulsive shopping, binge or compulsive eating, or other urges while being treated with Abilify Maintena. It should be noted that impulse-control

symptoms can be associated with the underlying disorder; however, in some cases, urges were reported to have stopped when the dose was reduced or aripiprazole was discontinued. Impulse control disorders may result in harm to the patient and others if not recognised.

A dose reduction or stopping of Abilify Maintena should be considered if a patient develops such urges (see section 4.8*)*.

Falls

Abilify Maintena may cause somnolence, postural hypotension, motor and sensory instability, which may lead to falls. Caution should be taken when treating patients at higher risk, and a lower starting dose should be considered (e.g., elderly or debilitated patients; see section 4.2).

Sodium

Abilify Maintena contains less than 1 mmol of sodium (23 mg) per dose.

4.5 Interaction with other medicines and other forms of interaction

No interaction studies have been performed with Abilify Maintena. The information below is obtained from studies with oral aripiprazole.

Due to its α1-adrenergic receptor antagonism, Abilify Maintena has the potential to enhance the effect of certain antihypertensive medicines.

Given the primary central nervous system (CNS) effects of aripiprazole, caution should be used when Abilify Maintena is administered in combination with alcohol or other CNS medicines with overlapping adverse reactions such as sedation (see section 4.8).

If Abilify Maintena is administered concomitantly with medicines known to cause QT prolongation or electrolyte imbalance, caution should be used.

Potential for other medicines to affect Abilify Maintena

Quinidine and other strong CYP2D6 inhibitors

In a clinical trial of oral aripiprazole in healthy subjects, a strong inhibitor of CYP2D6 (quinidine) increased aripiprazole AUC by 107 %, while C_{max} was unchanged. The AUC and C_{max} of dehydro-aripiprazole, the active metabolite, decreased by 32 % and 47 %, respectively. Other strong inhibitors of CYP2D6, such as fluoxetine and paroxetine, may be expected to have similar effects and similar dose reduction should, therefore, be applied (see section 4.2).

Ketoconazole and other strong CYP3A4 inhibitors

In a clinical trial of oral aripiprazole in healthy subjects, a strong inhibitor of CYP3A4 (ketoconazole) increased aripiprazole AUC and C_{max} by 63 % and 37 %, respectively. The AUC and C_{max} of dehydro-aripiprazole increased by 77 % and 43 %, respectively. In CYP2D6 poor metabolisers, concomitant use of strong inhibitors of CYP3A4 may result in higher plasma concentrations of aripiprazole compared to that in CYP2D6 extensive metabolisers (see section 4.2). When considering concomitant administration of ketoconazole or other potent CYP3A4 inhibitors with aripiprazole, potential benefits should outweigh the potential risks to the patient. Other strong inhibitors of CYP3A4, such as itraconazole and HIV protease inhibitors may be expected to have similar effects and similar dose reductions should, therefore, be applied (see section 4.2). Upon discontinuation of the CYP2D6 or CYP3A4 inhibitor, the dosage of Abilify Maintena should be increased to the dose prior to the initiation of the concomitant therapy.

When weak inhibitors of CYP3A4 (e.g. diltiazem) or CYP2D6 (e.g. escitalopram) are used concomitantly with Abilify Maintena, modest increases in plasma aripiprazole concentrations may be expected.

Carbamazepine and other CYP3A4 inducers

Following concomitant administration of carbamazepine, a strong inducer of CYP3A4, and oral aripiprazole to patients with schizophrenia or schizoaffective disorder, the geometric means of C_{max} and AUC for aripiprazole were 68 % and 73 % lower, respectively, compared to when oral aripiprazole (30 mg) was administered alone. Similarly, for dehydro-aripiprazole the geometric means of C_{max} and AUC after carbamazepine co-administration were 69 % and 71 % lower, respectively, than those following treatment with oral aripiprazole alone.

Concomitant administration of Abilify Maintena and other inducers of CYP3A4 (such as rifampicin, rifabutin, phenytoin, phenobarbital, primidone, efavirenz, nevirapine and St. John's Wort) may be expected to have similar effects. The concomitant use of CYP3A4 inducers with Abilify Maintena should be avoided because the blood levels of aripiprazole are decreased and may be below the effective levels.

Serotonin syndrome

Cases of serotonin syndrome have been reported in patients taking aripiprazole, and possible signs and symptoms for this condition can occur especially in cases of concomitant use with other serotonergic medicinal products, such as SSRI/SNRI, or with medicinal products that are known to increase aripiprazole concentrations (see section 4.8).

4.6 Fertility, pregnancy and lactation

Pregnancy

Safety of Abilify Maintena has not been established in pregnancy.

Congenital anomalies have been reported; however, causal relationship with aripiprazole could not be established. Animal studies could not exclude potential developmental toxicity (see section 5.3).

Patients must be advised to notify their medical practitioner if they become pregnant or intend to become pregnant during treatment with Abilify Maintena.

Prescribers need to be aware of the long-acting properties of Abilify Maintena.

New-born infants exposed to antipsychotics (including aripiprazole) during the third trimester of pregnancy are at risk of adverse reactions including extrapyramidal and/or withdrawal symptoms that may vary in severity and duration following delivery. There have been reports of agitation, hypertonia, hypotonia, tremor, somnolence, respiratory distress, or feeding disorder. Consequently, new-born infants should be monitored carefully (see section 4.8).

Breastfeeding

Aripiprazole is excreted in human milk. Women using Abilify Maintena must not breastfeed their infants.

Fertility

Aripiprazole did not impair fertility based on data from reproductive toxicity studies in animals.

4.7 Effects on ability to drive and use machines

Abilify Maintena may affect the ability to drive and use machines. Patients should not drive and use machines until they know how treatment with Abilify Maintena affects them.

Abilify Maintena has potential nervous system and visual effects, such as dizziness**,** sedation, somnolence, syncope, vision blurred, diplopia and seizures (see section 4.8).

4.8 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 %).

Tabulated list of adverse reactions

The incidences of the ADRs associated with aripiprazole therapy are tabulated below. The table 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 " unknown".

	Reported in clinical studies Common	**Reported in clinical studies Uncommon**	**Post marketing reported adverse events. Frequencies are unknown**
Blood and lymphatic system disorders		Neutropenia Anaemia Thrombocytopenia Neutrophil count decreased White blood cell count decreased	Leukopenia
Immune system disorders		Hypersensitivity	Allergic reaction (e.g. anaphylactic reaction, angioedema including

	Reported in clinical studies Common	**Reported in clinical studies Uncommon**	**Post marketing reported adverse events. Frequencies are unknown**
			swollen tongue, tongue oedema, face oedema, pruritus, or urticaria)
Endocrine disorders		Blood prolactin decreased Hyperprolactinaemia	Diabetic hyperosmolar coma Diabetic ketoacidosis
Metabolism and nutrition disorders	Weight increased Diabetes mellitus Weight decreased	Hyperglycaemia Hypercholesterolaemia Hyperinsulinaemia Hyperlipidaemia Hypertriglyceridaemia Appetite disorder	Anorexia Hyponatraemia
Psychiatric disorders	Agitation Anxiety Restlessness Insomnia	Suicidal ideation Psychotic disorder Hallucination Delusion Hypersexuality Panic reaction Depression Affect lability Apathy Dysphoria Sleep disorder Bruxism Libido decreased Mood altered	Completed suicide Suicide attempt Pathological gambling Impulse-control disorders Binge eating Compulsive shopping Poriomania Nervousness Aggression
Nervous system disorders	Extrapyramidal disorder Akathisia Tremor Dyskinesia Sedation Somnolence Dizziness Headache	Dystonia Tardive dyskinesia Parkinsonism Movement disorder Psychomotor hyperactivity Restless legs syndrome Cogwheel rigidity Hypertonia Bradykinesia Drooling Dysgeusia Parosmia	Neuroleptic malignant syndrome Grand mal convulsion Serotonin syndrome Speech disorder
Eye disorders		Oculogyric crisis Vision blurred Eye pain Diplopia	
Cardiac disorders		Ventricular extrasystoles Bradycardia Tachycardia	Sudden unexplained death Cardiac arrest Torsades de pointes Ventricular dysrhythmias

	Reported in clinical studies Common	**Reported in clinical studies Uncommon**	**Post marketing reported adverse events. Frequencies are unknown**
		Electrocardiogram T wave amplitude decreased Electrocardiogram abnormal Electrocardiogram T wave inversion	QT prolongation
Vascular disorders		Hypertension Orthostatic hypotension Blood pressure increased	Syncope Venous thromboembolism (including pulmonary embolism and deep vein thrombosis)
Respiratory, thoracic and mediastinal disorders		Cough Hiccups	Oropharyngeal spasm Laryngospasm Aspiration pneumonia
Gastrointestinal disorders	Dry mouth	Gastrooesophageal reflux disease Dyspepsia Vomiting Diarrhoea Nausea Abdominal pain upper Abdominal discomfort Constipation Frequent bowel movement Salivary hypersecretion	Pancreatitis Dysphagia
Hepatobiliary disorders		Hepatic enzymes increased Alanine aminotransferase increased Gamma-glutamyl transferase increased Blood bilirubin increased Aspartate aminotransferase increased	Hepatic failure Jaundice Hepatitis Alkaline phosphatase increased
Skin and subcutaneous tissue disorders		Alopecia Acne Rosacea Eczema Skin induration	Rash Photosensitivity reaction Hyperhidrosis
Musculoskeletal and connective tissue disorders	Musculoskeletal stiffness	Muscle rigidity Muscle spasms Muscle twitching Muscle tightness Myalgia	Rhabdomyolysis

	Reported in clinical studies Common	**Reported in clinical studies Uncommon**	**Post marketing reported adverse events. Frequencies are unknown**
		Pain in extremity Arthralgia Back pain Joint range of motion decreased Nuchal rigidity Trismus	
Renal and urinary disorders		Nephrolithiasis Glycosuria	Urinary retention Urinary incontinence
Pregnancy, puerperium and perinatal conditions			Drug withdrawal syndrome neonatal (see section 4.6)
Reproductive system and breast disorders	Erectile dysfunction	Galactorrhoea Gynaecomastia Breast tenderness Vulvovaginal dryness	Priapism
General disorders and administration site conditions	Injection site pain Injection site induration, Fatigue	Pyrexia Asthenia Gait disturbance Chest discomfort Injection site reaction Injection site erythema Injection site swelling Injection site discomfort Injection site pruritus Thirst Sluggishness	Temperature regulation disorder (e.g. hypothermia, pyrexia) Chest pain Peripheral oedema
Investigations	Blood creatine phosphokinase increased	Blood glucose increased Blood glucose decreased Glycosylated haemoglobin increased Waist circumference increased Blood cholesterol decreased Blood triglycerides decreased	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

Leukopenia has been reported in the clinical program and post marketing setting with the use of Abilify Maintena.

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 (section 5.1).

Pathological gambling and other impulse control disorders

Pathological gambling, hypersexuality, compulsive shopping and binge or compulsive eating can occur in patients treated with aripiprazole (see section 4.4)

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare providers are asked to report any suspected adverse reactions *to SAHPRA via the '6.04 Adverse Drug Reactions Reporting Form found online under SAHPRA's publications:* http://www.sahpra.org.za/Publications/Index/8

4.9 Overdose

In overdose, adverse events can be presipitated and/or be of increased severity. See section 4.8. Care must be taken to avoid inadvertent injection of Abilify Maintena into a blood vessel. Following any confirmed or suspected accidental overdose/inadvertent intravenous administration, close observation of the patient is needed and if any potentially medically serious sign or symptom develops, monitoring, which should include continuous electrocardiographic monitoring, is required. Treatment is symptomatic and supportive. The medical supervision and monitoring should continue until the patient recovers.

Signs and symptoms after overdose with aripiprazole tablets as no information on overdose with Abilify Mantena is available:

Medically important signs and symptoms observed with overdose included lethargy, increased blood pressure, somnolence, tachycardia, nausea, vomiting and diarrhoea. Signs and symptoms reported in children included somnolence, transient loss of consciousness and extrapyramidal symptoms.

Management of overdose

Management of overdose should concentrate on symptomatic and supportive therapy, maintaining an adequate airway, oxygenation and ventilation, and management of symptoms. The possibility of multiple medicine involvement should be considered. Therefore, cardiovascular monitoring should be started immediately and should include continuous electrocardiographic monitoring to detect possible dysrhythmias. Following any confirmed or suspected overdose with Abilify Maintena, close medical supervision and monitoring should continue until the patient recovers.

Haemodialysis

Haemodialysis is unlikely to be useful in overdose management since aripiprazole is highly bound to plasma proteins.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Category and class

A 2.6.5 Tranquilizers – miscellaneous structures

Mechanism of action

Aripiprazole's efficacy in schizophrenia is probably mediated through a combination of partial agonism at dopamine D_2 and serotonin 5-HT_{1A} receptors and antagonism at serotonin 5-HT_{2A} receptors. Aripiprazole exhibited antagonist properties in animal models of dopaminergic hyperactivity and agonist properties of dopaminergic hypoactivity. Aripiprazole exhibits high binding affinity *in vitro* for dopamine D_2 and D_3, serotonin 5-HT_{1A} and 5-HT_{2A} receptors and has moderate

affinity for dopamine D_4, serotonin 5-HT_{2C} and 5-HT_7, alpha-1 adrenergic and histamine H_1 receptors. Aripiprazole also exhibited moderate binding affinity for the serotonin reuptake site and no appreciable affinity for cholinergic muscarinic receptors. Interaction with receptors other than dopamine and serotonin subtypes may explain some of the other clinical effects of aripiprazole. Aripiprazole oral doses ranging from 0,5 to 30 mg administered once a day to healthy subjects for 2 weeks produced a dose-dependent reduction in the binding of ^{11}C-raclopride, a D_2/D_3 receptor ligand, to the caudate and putamen detected by positron emission tomography.

Clinical efficacy and safety

Maintenance treatment of schizophrenia in adults

The efficacy of Abilify Maintena in the maintenance treatment of patients with schizophrenia was established in two randomised, double-blind, long-term trials.

The pivotal trial was a 38 week, randomised, double-blind, active-controlled trial designed to establish the efficacy, safety, and tolerability of Abilify Maintena administered as monthly injections compared to once daily oral aripiprazole tablets 10-30 mg as maintenance treatment in adult patients with schizophrenia. This trial consisted of a screening phase and 3 treatment phases: Conversion Phase, Oral Stabilisation Phase, and Double-blind, Active-controlled Phase.

Six-hundred and sixty two patients eligible for the 38-week Double-blind, Active-controlled Phase were randomly assigned in a 2:2:1 ratio to double-blind treatment to one of 3 treatment groups:

1) Abilify Maintena

2) the stabilisation dose of oral aripiprazole 10-30 mg, or

3) aripiprazole Long-Acting Injectable 50 mg/25 mg. The aripiprazole Long-Acting Injectable 50 mg/25 mg dose was included as a low dose aripiprazole to test assay sensitivity for the non-inferiority design.

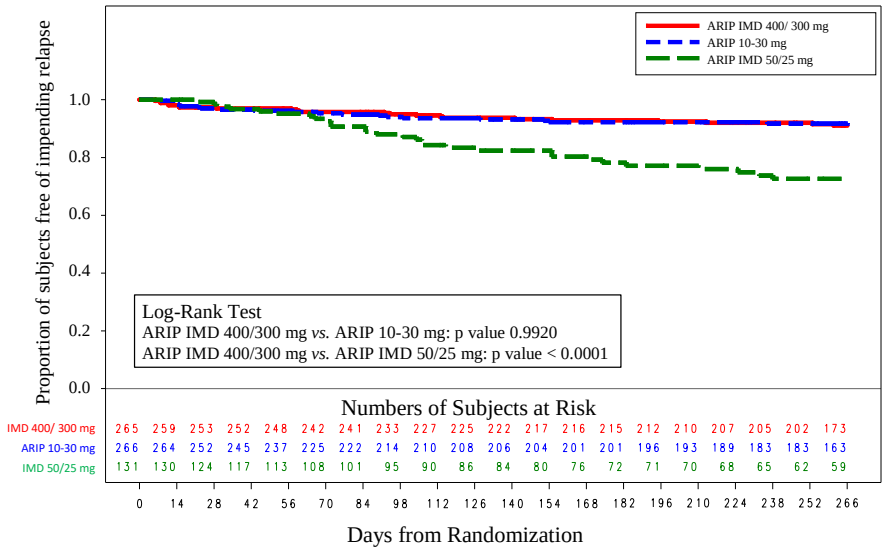
The results of analysis of the primary efficacy endpoint, the estimated proportion of patients experiencing impending relapse by end of Week 26 of the Double-blind, Active-controlled Phase, showed that Abilify Maintena 400 mg/300 mg is non-inferior to aripiprazole oral tablets 10-30 mg.

The estimated relapse rate by end of Week 26 was 7.12 % for Abilify Maintena, and 7.76 % for oral aripiprazole tablets 10-30 mg, a difference of -0.64 %.
The 95 % CI (-5.26, 3.99) for the difference in the estimated proportion of patients experiencing impending relapse by end of Week 26 excluded the predefined non-inferiority margin, 11.5 %. Therefore, Abilify Maintena is non-inferior to aripiprazole oral tablets 10-30 mg.

The estimated proportion of patients experiencing impending relapse by end of Week 26 for Abilify Maintena was 7.12 %, which was statistically significantly lower than in aripiprazole Long-Acting Injectable 50 mg/25 mg (21.80 %; p = 0.0006). Thus, superiority of Abilify Maintena over the aripiprazole Long-Acting Injectable 50 mg/25 mg was established and the validity of the trial design was confirmed.

The Kaplan-Meier curves of the time from randomisation to impending relapse during the 38-week, Double-blind, Active-controlled Phase for Abilify Maintena, oral aripiprazole 10-30 mg, and aripiprazole Long-Acting Injectable 50 mg/25 mg are shown in Figure 1

. **Figure 1 Kaplan-Meier Product Limit Plot for Time to Exacerbation of Psychotic Symptoms/Impending Relapse**



NOTE: ARIP IMD 400/300 mg = Abilify Maintena; ARIP 10-30 mg = oral aripiprazole; ARIP IMD 50/25 mg = Long-acting Injectable

Further, the non-inferiority of Abilify Maintena compared to oral aripiprazole 10-30 mg is supported by the results of the analysis of the Positive and Negative Syndrome Scale score (PANSS).

Table 1 PANSS Total Score – Change From Baseline to Week 38-LOCF:Randomised Efficacy Sample[a, b]

PANSS Total Score – Change From Baseline to Week 38-LOCF: Randomised Efficacy Sample[a, b]			
	Abilify Maintena 400 mg/300 mg (n = 263)	*Oral aripiprazole 10-30 mg/day (n = 266)*	*Aripiprazole Long-Acting Injectable 50 mg/25 mg (n = 131)*
Mean baseline (SD)	*57.9 (12.94)*	*56.6 (12.65)*	*56.1 (12.59)*
Mean change (SD)	*-1.8 (10.49)*	*0.7 (11.60)*	*3.2 (14.45)*
P-value	*NA*	*0.0272*	*0.0002*

a: Negative change in score indicates improvement.

b: Only patients having both baseline and at least one post baseline were included. P-values were derived from comparison for change from baseline within analysis of covariance model with treatment as term and baseline as covariate.

The second trial was a 52-week, randomised, withdrawal, double-blind, trial conducted in US adult patients with a current diagnosis of schizophrenia. This trial consisted of a screening phase and 4 treatment phases: Conversion, Oral Stabilisation, Abilify Maintena Stabilisation, and Double-blind Placebo- controlled. Patients fulfilling the oral stabilisation requirement in the Oral Stabilisation Phase were assigned to receive, in a single-blind fashion, Abilify Maintena and began an Abilify Maintena Stabilisation Phase for a minimum of 12 weeks and a maximum of 36 weeks. Patients eligible for the Double-blind, Placebo-controlled Phase were randomly assigned in a 2:1 ratio to double-blind treatment with Abilify Maintena or placebo, respectively.

The final efficacy analysis included 403 randomised patients and 80 exacerbations of psychotic symptoms/impending relapse events.

In the placebo group 39.6 % of the patients had progressed to impending relapse, whilst in the Abilify Maintena group impending relapse occurred in 10 % of the patients; thus patients in the placebo group had a 5.03-fold greater risk of experiencing impending relapse.

Prolactin

In the Double-blind, Active-controlled Phase of the 38-week trial, from baseline to last visit there was a mean decrease in prolactin levels in Abilify Maintena (−0.33 ng/ml) compared with a mean increase in oral aripiprazole tablets 10-30 mg (0.79 ng/ml; $p < 0.01$).

The incidence of Abilify Maintena patients with prolactin levels > 1 time the upper limit of normal range (ULN) at any assessment was 5.4 % compared with 3.5 % of the patients on oral aripiprazole tablets 10-30 mg.

Male patients generally had a higher incidence than female patients in each treatment group.

In the Double-blind Placebo-controlled Phase of the 52-week trial, from baseline to last visit there was a mean decrease in prolactin levels in Abilify Maintena (−0.38 ng/ml) compared with a mean increase in placebo (1.67 ng/ml). The incidences of Abilify Maintena patients with prolactin levels > 1 time the upper limit of normal range (ULN) was 1.9 % compared to 7.1 % for placebo patients.

Paediatric population

The safety and efficacy of Abilify Maintena in patients less than 18 years of age have not been established

5.2 Pharmacokinetic properties

Absorption

Aripiprazole absorption into the systemic circulation is slow and prolonged following Abilify Maintena administration due to low solubility of aripiprazole particles. The average absorption half-life of Abilify Maintena is 28 days. Absorption of aripiprazole from the IM depot formulation was complete relative to the IM standard (immediate-release) formulation. The dose adjusted C_{max} values for the depot formulation were approximately 5 % of C_{max} from IM standard formulation. Following a single dose administration of Abilify Maintena in the deltoid and gluteal muscle, the extent of absorption (AUC) was similar for both injection sites, but the rate of absorption (C_{max}) was higher following administration to the deltoid muscle. Following multiple intramuscular doses, the plasma concentrations of aripiprazole gradually rise to a maximum plasma concentration at a median t_{max} of 7 days for the gluteal muscle and 4 days for the deltoid muscle. Steady state concentrations for the typical subject were attained by the fourth dose for both sites of administration. Less than dose-proportional increases in aripiprazole and dehydro-aripiprazole concentrations and AUC parameters are observed after monthly Abilify Maintena injections of 300 mg to 400 mg.

Distribution

Based on results from trials with oral administration of aripiprazole, Aripiprazole is widely distributed throughout the body with an apparent volume of distribution of 4,9 l/kg, indicating extensive extravascular distribution. At therapeutic concentrations, aripiprazole and dehydro-aripiprazole are greater than 99 % bound to serum proteins, binding primarily to albumin.

Biotransformation

Aripiprazole is extensively metabolised by the liver primarily by three biotransformation pathways: dehydrogenation, hydroxylation, and N-dealkylation. Based on *in-vitro* studies, CYP3A4 and CYP2D6 enzymes are responsible for dehydrogenation and hydroxylation of aripiprazole, and N-dealkylation is catalysed by CYP3A4. Aripiprazole is the predominant active moiety in systemic circulation. After multiple dose administration of Abilify Maintena, dehydro-aripiprazole, the active metabolite, represents about 29 % of aripiprazole AUC in plasma.

Elimination

After administration of multiple dose of 400 mg or 300 mg of Abilify Maintena, the mean aripiprazole terminal elimination half-life is respectively 46.5 and 29.9 days presumably due to absorption rate-limited kinetics.

Following a single oral dose of [^{14}C]-labelled aripiprazole, approximately 27 % of the administered radioactivity was recovered in the urine and approximately 60 % in the faeces. Less than 1 % of unchanged aripiprazole was excreted in the urine and approximately 18 % was recovered unchanged in the faeces.

Pharmacokinetics in Special Patient Groups

CYP2D6 poor metabolisers

Based on population pharmacokinetic evaluation of **ABILIFY MAINTENA**, the total body clearance of aripiprazole was 3,71 l/h in extensive metabolisers of CYP2D6 and approximately 1,88 l/h (approximately 50 % lower) in poor metabolisers of CYP2D6 (for dose recommendation, see section 4.2).

Elderly

After oral administration of aripiprazole, there are no differences in the pharmacokinetics of aripiprazole between healthy elderly and younger adult subjects. Similarly, there was no detectable effect of age in a population pharmacokinetic analysis of **ABILIFY MAINTENA** in schizophrenia patients.

Gender

After oral administration of aripiprazole, there are no differences in the pharmacokinetics of aripiprazole between healthy male and female subjects. Similarly, there was no clinically relevant effect of gender in a population pharmacokinetic analysis of **ABILIFY MAINTENA** in schizophrenia patients.

Smoking

Population pharmacokinetic evaluation of oral aripiprazole has revealed no evidence of clinically relevant effects from smoking on the pharmacokinetics of aripiprazole.

Race

Population pharmacokinetic evaluation showed no evidence of race-related differences on the pharmacokinetics of aripiprazole.

Renal Impairment

In a single-dose study with oral administration of aripiprazole, the pharmacokinetic characteristics of aripiprazole and dehydro-aripiprazole were found to be similar in patients with severe renal disease compared to that in young healthy subjects.

Hepatic Impairment

A single-dose study with oral administration of aripiprazole to subjects with varying degrees of liver cirrhosis (Child-Pugh Classes A, B and C) did not reveal a significant effect of hepatic impairment on the pharmacokinetics of aripiprazole and dehydro-aripiprazole but the study included only 3 patients with Class C liver cirrhosis, which is insufficient to draw conclusions on their metabolic capacity.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Powder

Carmellose sodium

Mannitol

Sodium dihydrogen phosphate monohydrate

Sodium hydroxide

Solvent

Water for injections

6.2 Incompatibilities

Not applicable

6.3 Shelf life

3 years

Abilify Maintena powder and solvent for prolonged-release suspension for injection

The suspension should be injected immediately after reconstitution but can be stored below 25 °C for up to 4 hours in the vial.

Abilify Maintena powder and solvent for prolonged-release suspension for injection in pre-filled syringe

The suspension should be injected immediately after reconstitution but can be stored below 25 °C for up to 2 hours in the syringe.

After reconstitution

Abilify Maintena 300 mg powder and solvent for prolonged-release suspension for injection

Abilify Maintena 400 mg powder and solvent for prolonged-release suspension for injection

Chemical and physical in-use stability has been demonstrated for 4 hours at 25 °C. From a microbiological point of view, unless the method of opening/ reconstitution precludes the risk of microbial contamination, the product should be used immediately. If not used immediately, in-use storage times and conditions are the responsibility of user. Do not store the reconstituted suspension in the syringe.

Abilify Maintena 400 mg powder and solvent for prolonged-release suspension for injection in pre-filled syringe

If the injection is not performed immediately after reconstitution, the syringe can be kept below 25 °C for up to 2 hours.

6.4 Special precautions for storage

Do not freeze

Abilify Maintena 400 mg powder and solvent for prolonged-release suspension for injection in pre-filled syringe

Keep the syringe in the outer carton in order to protect from light.

For storage conditions after reconstitution of the medicinal product, see section 6.3.

6.5 Nature and contents of the container

Abilify Maintena 300 mg powder and solvent for prolonged-release suspension for injection

Abilify Maintena 400 mg powder and solvent for prolonged-release suspension for injection

Vial

Type-I glass vial stoppered with a laminated rubber stopper and sealed with a flip-off aluminium cap.

Solvent

2 ml Type-1 glass vial stoppered with a laminated rubber stopper and sealed with a flip-off aluminium cap.

Single pack

Each single pack containing one vial of powder, 2 ml vial of solvent, one 3 ml luer lock syringe with pre-attached 38 mm (1.5 inch) 21 gauge, hypodermic safety needle with needle protection device, one 3 ml disposable syringe with luer lock tip, one vial adapter and three hypodermic safety needles: one 25 mm (1 inch) 23 gauge, one 38 mm (1.5 inch) 22 gauge and one 51 mm (2 inch) 21 gauge.

Multipack

Bundle pack of 3 single packs.

Abilify Maintena 400 mg powder and solvent for prolonged-release suspension for injection in pre-filled syringe

Clear glass pre-filled syringe (type-I glass) with grey chlorobutyl stoppers (front-, middle- and end stopper), polypropylene front assembly, polypropylene finger grip, plunger rod, and silicone over-cap. The front chamber between front stopper and middle stopper contains the powder and the rear chamber between middle stopper and end stopper the solvent.

Single pack

Each single pack containing one pre-filled syringe, and three hypodermic safety needles: one 25 mm (1 inch) 23 gauge, one 38 mm (1.5 inch) 22 gauge and one 51 mm (2 inch) 21 gauge.

Multipack

Bundle pack of 3 single packs

6.6 Special precautions for disposal and other handling

Abilify Maintena 300 mg powder and solvent for prolonged-release suspension for injection

Abilify Maintena 400 mg powder and solvent for prolonged-release suspension for injection

Shake the vial vigorously for at least 30 seconds until the suspension appears uniform.

If the injection is not performed immediately after reconstitution shake it vigorously for at least 60 seconds to re-suspend prior to injection.

Abilify Maintena 400 mg powder and solvent for prolonged-release suspension for injection in pre-filled syringe

Vertically shake the syringe vigorously for 20 seconds until medicine is uniformly milky-white and use immediately. If the injection is not performed immediately after reconstitution, the syringe can be

kept below 25 °C for up to 2 hours. Shake the syringe vigorously for at least 20 seconds to re-suspend prior to injection if the syringe has been left for more than 15 minutes.

Gluteal muscle administration

The recommended needle for gluteal administration is a 38 mm (1.5 inch), 22 gauge hypodermic safety needle; for obese patients (Body mass index > 28 kg/m^2), a 51 mm (2 inch), 21 gauge hypodermic safety needle should be used. Gluteal injections should be alternated between the two gluteal muscles.

Deltoid muscle administration

The recommended needle for deltoid administration is a 25 mm (1 inch), 23 gauge hypodermic safety needle; for obese patients, a 38 mm (1.5 inch), 22 gauge hypodermic safety needle should be used.

Deltoid injections should be alternated between the two deltoid muscles.

The powder and solvent vials and the pre-filled syringe are for single-use only.

Discard vial, adapter, syringe, needles, unused suspension and water for injections appropriately.

Any unused medicine or waste material should be disposed of in accordance with local requirements.

7. HOLDER OF CERTIFICATE OF REGISTRATION

H. Lundbeck (Pty) Ltd

Unit 9 Blueberry Office Park

Apple Street

Randpark Ridge Ext 114

2156

South Africa

8. REGISTRATION NUMBER(S)

ABILIFY MAINTENA 400 mg 48/2.6.5/0531

ABILIFY MAINTENA 300 mg 48/2.6.5/0530

9. DATE OF FIRST AUTHORISATION/ RENEWAL OF THE AUTHORISATION

10 November 2020

10. DATE OF REVISION OF THE TEXT