SCHEDULING STATUS: S5

1. NAME OF THE MEDICINE

MIRTAZAPINE 15 VIATRIS (film-coated tablets)

MIRTAZAPINE 30 VIATRIS (film-coated tablets)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each **MIRTAZAPINE 15 VIATRIS** film-coated tablet contains 15 mg mirtazapine.

Each **MIRTAZAPINE 30 VIATRIS** film-coated tablet contains 30 mg mirtazapine.

Excipient with known effect

MIRTAZAPINE 15 VIATRIS contains sugar (Lactose anhydrous 113,25 mg).

MIRTAZAPINE 30 VIATRIS contains sugar (Lactose anhydrous 226,50mg).

For full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Film-coated tablets.

MIRTAZAPINE 15 VIATRIS: A normal convex, yellow film-coated tablet debossed “MR scoreline 15” on one side and “G” on the other.

MIRTAZAPINE 30 VIATRIS: A normal convex, buff film-coated tablet debossed “MR scoreline 30” on one side and “G” on the other.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Treatment of major depressive illness in adults.

4.2 Posology and method of administration

Posology

MIRTAZAPINE VIATRIS should be given in an initial daily dose of 15 mg which may be increased gradually according to clinical response.

The usual effective dose lies within the range of 15 to 45 mg.

Mirtazapine begins to exert its effect in general after 1 - 2 weeks of treatment.

For treatment of acute depressive episodes, treatment should be continued for at least 6 months.

MIRTAZAPINE VIATRIS should be withdrawn gradually to reduce the risk of withdrawal symptoms (see section 4.4).

Special populations

Elderly

The recommended dose is the same as that for adults. In elderly patients an increase in dosing should be done under close supervision to elicit a satisfactory and safe response.

Renal impairment

The clearance of mirtazapine may be decreased in patients with renal impairment. This should be taken into account when prescribing **MIRTAZAPINE VIATRIS** to this category of patients.

Hepatic impairment

The clearance of mirtazapine may be decreased in patients with hepatic impairment. This should be taken into account when prescribing **MIRTAZAPINE VIATRIS** to this category of patients.

Paediatric population

MIRTAZAPINE VIATRIS should not be used in children and adolescents under the age of 18 years as efficacy was not demonstrated in two short-term clinical trials (see section 5.1) and because of safety concerns (see sections 4.4, 4.8 and 5.1).

Method of administration

MIRTAZAPINE VIATRIS should be taken preferably as a single night-time dose before going to bed. It may also be given in 2 divided doses (once in the morning and once at night-time).
Tablets should be taken orally, with fluid, and swallowed without chewing.

4.3 Contraindications

Hypersensitivity to Mirtazapine or to any of the excipients listed in section 6.1.
Pregnancy and lactation, as there is insufficient clinical data available.
Children and adolescents under the age of 18 years (see section 4.4).
Concomitant monoamine oxidase inhibitors or within 14 days of discontinuation thereof (see section 4.5).

4.4 Special warnings and precautions for use

Use in children and adolescents under 18 years of age

MIRTAZAPINE VIATRIS should not be used in the treatment of children and adolescents under the age of 18 years (see section 4.3). Suicide-related behaviours (suicide attempt and suicidal thoughts), and hostility (predominantly aggression, oppositional behaviour and anger) were more frequently observed in clinical trials among children and adolescents treated with antidepressants, such as **MIRTAZAPINE VIATRIS**, compared to those treated with placebo.

Bone marrow depression

Bone marrow depression, usually presenting as granulocytopenia or agranulocytosis, has been reported during treatment with **MIRTAZAPINE VIATRIS**. Patients should be advised to report any of the following symptoms during treatment: fever, sore throat, stomatitis, or other signs of infection. These may be signs of bone marrow depression (neutropenia, agranulocytosis). Treatment should be stopped, and a blood count performed.

Jaundice

Treatment should be stopped if jaundice develops.

Suicide/suicidal thoughts or clinical worsening

Depression is associated with an increased risk of suicidal thoughts, self-harm and suicide (suicide-related events). This risk may persist until significant remission occurs. As improvement may not occur during the first few weeks or more of treatment, patients should be closely monitored until such improvement occurs. It is general clinical experience that the risk of suicide may increase in the early stages of recovery.

Patients with a history of suicide-related events or those exhibiting a significant degree of suicidal ideation prior to commencement of treatment are known to be at greater risk of suicidal thoughts or suicide attempts and should receive careful monitoring during treatment with **MIRTAZAPINE VIATRIS**.

Clinical trials of antidepressants, such as **MIRTAZAPINE VIATRIS** , in adult patients with psychiatric disorders showed an increased risk of suicidal behaviour with antidepressants, such as **MIRTAZAPINE VIATRIS**, compared to placebo in patients less than 25 years old.
Close supervision of patients, in particular those at high risk, should accompany therapy with antidepressants, such as **MIRTAZAPINE VIATRIS**, especially in early treatment and following dose changes. Patients (and caregivers of patients) should be alerted about the need to monitor for any clinical worsening, suicidal behaviour or thoughts and unusual changes in behaviour and to seek medical advice immediately if these symptoms present.
With regards to the change of suicide, in particular at the beginning of treatment, only a limited number of **MIRTAZAPINE VIATRIS** tablets should be given to a patient consistent with good patient management, in order to reduce the risk of overdose.

Severe cutaneous adverse reactions
Severe cutaneous adverse reactions (SCARs) including Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), drug reaction with eosinophilia and systemic symptoms (DRESS), bullous dermatitis and erythema multiforme, which can be life-threatening or fatal, have been reported in association with **MIRTAZAPINE VIATRIS** treatment. If signs and symptoms suggestive of these reactions appear, **MIRTAZAPINE VIATRIS** should be withdrawn immediately. If the patient has developed one of these reactions with the use of **MIRTAZAPINE**

VIATRIS, treatment with **MIRTAZAPINE VIATRIS** must not be restarted in this patient at any time.

Careful dosing as well as regular and close monitoring is necessary in patients with:

Epilepsy and organic brain syndrome: MIRTAZAPINE VIATRIS should be introduced cautiously in patients who have a history of seizures. Treatment should be discontinued in any patient who develops seizures, or where there is an increase in seizure frequency.

Cardiac diseases like conduction disturbances, angina pectoris and recent myocardial infarction, where normal precautions should be taken, and concomitant medicines carefully administered.

Low blood pressure.

Diabetes mellitus: In patients with diabetes, antidepressants such as **MIRTAZAPINE VIATRIS** may alter glycaemic control. Insulin and/or oral hypoglycaemic dosage may need to be adjusted and close monitoring is recommended.

The following should be taken into account:

Worsening psychotic symptoms can occur when **MIRTAZAPINE VIATRIS** is administered to patients with schizophrenia or other psychotic disturbances; paranoid thoughts can be intensified.

When the depressive phase of bipolar disorder is being treated, it can transform into the manic phase. Patients with a history of mania/hypomania should be closely monitored. **MIRTAZAPINE VIATRIS** should be discontinued in any patient entering a manic phase.

Post-marketing experience with mirtazapine as contained in **MIRTAZAPINE VIATRIS** shows that abrupt termination of treatment after long term administration of **MIRTAZAPINE VIATRIS** may result in withdrawal symptoms. The majority of withdrawal reactions are mild and self-limiting. Among the various reported withdrawal symptoms, dizziness, agitation, anxiety, headache and nausea were the most frequently reported. Even though they have been reported as withdrawal symptoms, it should be realised that these symptoms may be related to the underlying disease. As advised in section 4.2 it is recommended to discontinue treatment with **MIRTAZAPINE VIATRIS** gradually.

MIRTAZAPINE VIATRIS has weak antimuscarinic activity, therefore caution should be exercised in patients with micturition disturbances like prostate hypertrophy and in patients with eye disorders such as closed-angle glaucoma and raised intra-ocular pressure.
Akathisia/psychomotor restlessness: The use of **MIRTAZAPINE VIATRIS** has been associated with the development of akathisia, characterised by a subjectively unpleasant or distressing restlessness and a need to move often, accompanied by an inability to sit or stand still. This is most likely to occur within the first few weeks of treatment. In patients who develop these symptoms, increasing the dose may be detrimental.

The effect of mirtazapine, such as contained in **MIRTAZAPINE VIATRIS**, on QTc interval was assessed. The QTc interval was not affected to a clinically meaningful extent.

During the post-marketing use of mirtazapine, cases of QT prolongation, Torsades de Pointes, ventricular tachycardia and sudden death, have been reported. The majority of reports occurred in association with overdose or in patients with other risk factors for QT prolongation, including concomitant use of QTc prolonging medicines (see section 4.5). Caution should be exercised when **MIRTAZAPINE VIATRIS** is prescribed in patients with known cardiovascular disease or family history of QT prolongation, and in concomitant use with other medicines thought to prolong the QTc interval.

Hyponatraemia: Hyponatraemia, probably due to inappropriate antidiuretic hormone secretion (SIADH), has been reported with the use of **MIRTAZAPINE VIATRIS**. Caution should be exercised in patients at risk, such as elderly patients or patients concomitantly treated with medicines known to cause hyponatraemia.

Serotonin syndrome: Interaction with serotonergic active substances: Serotonin syndrome may occur when **MIRTAZAPINE VIATRIS** is used concomitantly with other serotonergic active substances (see section 4.5). Symptoms of serotonin syndrome may be hyperthermia, rigidity, myoclonus, autonomic instability with possible rapid fluctuations of vital signs, mental status changes that include confusion, irritability and extreme agitation progressing to delirium and coma.

Caution should be advised and a closer clinical monitoring is required when these active substances are combined with **MIRTAZAPINE VIATRIS**. Treatment with **MIRTAZAPINE VIATRIS** should be discontinued if such events occur and supportive symptomatic treatment initiated.

Concomitant administration of serotonergic medicines, such as MAO inhibitors, selective serotonin re-uptake inhibitors (SSRIs), serotonin norepinephrine re-uptake inhibitors (SNRIs) or

tricyclic antidepressants, and buprenorphine-containing medicines may result in serotonin syndrome, a potentially life-threatening condition (see section 4.5).

If concomitant treatment with buprenorphine-containing medicines is clinically warranted, careful observation of the patient is advised, particularly during treatment initiation and dose increases.

Symptoms of serotonin syndrome may include mental-status changes, autonomic instability, neuromuscular abnormalities, and/or gastrointestinal symptoms.
If serotonin syndrome is suspected, a dose reduction or discontinuation of therapy should be considered depending on the severity of the symptoms.

MAO-Inhibitors

In patients receiving **MIRTAZAPINE VIATRIS** in combination with a monoamine oxidase inhibitor (MAOI) and in patients who have recently discontinued **MIRTAZAPINE VIATRIS** and then are started on an MAOI, there have been reports of serious and sometimes fatal reactions e.g. including nausea, vomiting, flushing, dizziness, tremor, myoclonus, rigidity, diaphoresis, hyperthermia, autonomic instability with rapid fluctuations of vital signs, seizures and mental status changes ranging from agitation to coma. **MIRTAZAPINE VIATRIS** should not be used in combination with an MAOI, or within 14 days of initiating or discontinuing therapy with an MAOI including linezolid (see sections 4.3 and 4.5).

Elderly patients

Elderly patients are often more sensitive, especially with regards to the undesirable effects of antidepressants, including **MIRTAZAPINE VIATRIS**. During clinical research with mirtazapine

as contained in **MIRTAZAPINE VIATRIS**, undesirable effects have not been reported more often in elderly patients than in other age groups.

Excipient information

Lactose

MIRTAZAPINE VIATRIS contains lactose. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take **MIRTAZAPINE VIATRIS**.

4.5 Interaction with other medicines and other forms of interaction

Pharmacodynamic interactions

MAOI: **MIRTAZAPINE VIATRIS** should not be used concomitantly with MAO Inhibitors, or within 2 weeks of discontinuing a MAOI.

In the opposite way about 2 weeks should pass before patients treated with **MIRTAZAPINE VIATRIS** should be treated with MAO inhibitors (see section 4.3).

Alcohol: **MIRTAZAPINE VIATRIS** may potentiate the central nervous depressant action of alcohol and patients should therefore be advised to avoid alcohol.

Anxiolytics or Hypnotics: Use of **MIRTAZAPINE VIATRIS** may potentiate the sedative effects of benzodiazepines and other sedatives (including antipsychotics, antihistamine H_1 antagonists, opioids). Caution should be taken when these medicines are prescribed together with **MIRTAZAPINE VIATRIS.**

Co-administration with other serotonergic active substances (L-tryptophan, triptans, tramadol, linezolid, methylene blue, SSRI's, venlafaxine, lithium and St. John's Wort - *Hypericum perforatum*) may lead to an incidence of serotonin associated effects (serotonin syndrome: see section 4.4). Caution should be advised, and a closer clinical monitoring is required when these active substances are combined with **MIRTAZAPINE VIATRIS**.

Mirtazapine such as contained in **MIRTAZAPINE VIATRIS** dosed at 30 mg once daily caused a small, but statistically significant increase in the international normalised ratio (INR) in subjects treated with warfarin. As at a higher dose of **MIRTAZAPINE VIATRIS** a more pronounced effect cannot be excluded. It is advisable to monitor the INR in case of concomitant treatment of warfarin with **MIRTAZAPINE VIATRIS**.

The risk of QT prolongation and/or ventricular dysrhythmias (e.g. Torsades de Pointes) may be increased with concomitant use of medicines which prolong the QTc interval (e.g. some antipsychotics and antibiotics) and in case of **MIRTAZAPINE VIATRIS** overdose.

Pharmacokinetic interactions

Carbamazepine and phenytoin, CYP3A4 inducers, increased mirtazapine, as contained in **MIRTAZAPINE VIATRIS**, clearance about two-fold, resulting in a decrease in average plasma mirtazapine concentration of 60 % and 45 %, respectively. When carbamazepine or any other inducer of hepatic metabolism (such as rifampicin) is added to **MIRTAZAPINE VIATRIS** therapy, the **MIRTAZAPINE VIATRIS** dose may have to be increased. If treatment with such medicines is discontinued, it may be necessary to reduce the **MIRTAZAPINE VIATRIS** dose.

Co-administration of the potent CYP3A4 inhibitor ketoconazole increased the peak plasma levels and the AUC of mirtazapine, as contained in **MIRTAZAPINE VIATRIS**, by approximately 40 % and 50 % respectively.

When cimetidine (weak inhibitor of CYP1A2, CYP2D6 and CYP3A4) is administered with **MIRTAZAPINE VIATRIS**, the mean plasma concentration of mirtazapine may increase more than 50 %. Caution should be exercised, and the dose may have to be decreased when co-administering **MIRTAZAPINE VIATRIS** with potent CYP3A4 inhibitors, HIV protease inhibitors, azole antifungals, erythromycin, cimetidine or nefazodone.

Interaction studies did not indicate any relevant pharmacokinetic effects on concurrent treatment of **MIRTAZAPINE VIATRIS** with paroxetine, amitriptyline, risperidone or lithium.
Buprenorphine-containing medicines: **MIRTAZAPINE VIATRIS** should be used cautiously when co-administered with Buprenorphine-containing medicines as the risk of serotonin syndrome, a potentially life-threatening condition, is increased (see section 4.4).

Paediatric population:
Interaction studies have only been performed in adults.

4.6 Fertility, pregnancy and lactation

MIRTAZAPINE VIATRIS is contraindicated in pregnancy and lactation (see section 4.3).

4.7 Effects on ability to drive and use machines

MIRTAZAPINE VIATRIS has minor or moderate influence on the ability to drive and use machines. It may decrease alertness, judgment, thinking and concentration. Patients should avoid the performance of potentially dangerous tasks, which require alertness and good concentration, such as driving a motor vehicle or operating machinery, at any time when affected.

4.8 Undesirable effects

Depressed patients display a number of symptoms that are associated with the illness itself. It is therefore sometimes difficult to ascertain which symptoms are a result of the illness itself and which are a result of treatment with **MIRTAZAPINE VIATRIS**.

Summary of the safety profile

The most commonly reported adverse reactions, occurring in more than 5 % of patients are somnolence, sedation, dry mouth, weight increase, increase in appetite, dizziness and fatigue.

Severe cutaneous adverse reactions (SCARs), including Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), drug reaction with eosinophilia and systemic symptoms (DRESS), bullous dermatitis and erythema multiforme have been reported in association with Mirtazapine treatment (see section 4.4).

Cases of suicidal ideation and suicidal behaviours have been reported during **MIRTAZAPINE VIATRIS** therapy or early after treatment discontinuation.

Tabulated list of adverse reactions

Blood and lymphatic system disorders	
Frequent:	Reversible agranulocytosis.
Frequency unknown:	Leucopoenia and granulocytopenia.
Metabolism and nutrition disorders	
Frequent:	An increase in appetite and

	weight gain.
Psychiatric disorders	
Frequent:	Abnormal dreams, confusion, anxiety, insomnia.
Less frequent:	Nightmares, psychomotor restlessness (incl. akathisia, hyperkinesia), aggression.
Nervous system disorders	
Frequent:	Drowsiness or sedation, dizziness, somnolence, headache, tremor, lethargy, amnesia.
Less frequent:	Mania, hallucinations, convulsions, epileptic seizures, vertigo, agitation, paraesthesia, restless legs syndrome, myoclonus, syncope.
Vascular disorders	
Frequent:	Orthostatic hypotension.
Less frequent:	Oedema, peripheral oedema, hypotension.
Gastrointestinal disorders	

Frequent:	Dry mouth, constipation, nausea, vomiting, diarrhoea.
Less frequent:	Thirst, oral hypoaesthesia, pancreatitis.
Frequency unknown:	Bitter taste in mouth.
Hepato-biliary disorders	
Frequent:	Elevations in serum transaminase activities.
Frequency unknown:	Jaundice may occur.
Skin and subcutaneous tissue disorders	
Frequent:	Exanthema.
Musculoskeletal, connective tissue and bone disorders	
Frequent:	Arthralgia and myalgia, back pain.
General disorders and administration site conditions	
Less frequent:	Asthenia, flu like syndrome, increased sweating, fatigue.
Investigations	
Frequency unknown:	Increases in liver enzyme levels have been reported.

Post-marketing side effects

The reported post-marketing adverse reactions of which the frequency is not known:

Blood and lymphatic system disorders:
Bone marrow depression (granulocytopenia, agranulocytosis, aplastic anaemia and thrombocytopenia), eosinophilia.
Endocrine disorders:
Inappropriate antidiuretic hormone secretion, hyperprolactinemia (and related symptoms galactorrhoea and gynaecomastia).
Metabolism and nutrition disorders:
Hyponatraemia.
Psychiatric disorders:
Suicidal ideation, suicidal behaviour, somnambulism.
Nervous system disorders:
Convulsions (insults), serotonin syndrome, oral paraesthesia, dysarthria.
Gastrointestinal disorders:
Mouth oedema, increased salivation.
Skin and subcutaneous tissue disorders:
Stevens-Johnson syndrome, dermatitis bullous, erythema multiforme, toxic epidermal necrolysis (TEN), drug reaction with eosinophilia and systemic symptoms (DRESS).
Musculoskeletal, connective tissue and bone disorders:

Rhabdomyolysis.
Renal and urinary disorders:
Urinary retention.
Reproductive system and breast disorders
Priapism
General disorders and administration site conditions:
Generalised oedema, localised oedema.
Investigations:
Increased creatinine kinase.

Paediatric population:

The following adverse events were observed commonly in clinical trials in children: weight gain, urticaria and hypertriglyceridaemia (see also section 5.1).

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 requested to report any suspected adverse drug reactions to SAHPRA via the Med Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found on SAHPRA website.

4.9 Overdose

There is no specific antidote for **MIRTAZAPINE VIATRIS.**

Present experience concerning overdose with **MIRTAZAPINE VIATRIS** alone indicates that symptoms are usually mild. Depression of the central nervous system with disorientation and prolonged sedation have been reported, together with tachycardia and mild hyper- or hypotension. However, there is a possibility of more serious outcomes (including fatalities) at dosages much higher than the therapeutic dose, especially with mixed overdoses. In these cases, QT prolongation and Torsade de Pointes have also been reported.

Cases of overdose should receive appropriate symptomatic and supportive therapy for vital functions. ECG monitoring should be undertaken. Activated charcoal should also be considered.

Paediatric population

The appropriate actions as described for adults should be taken in case of an overdose in paediatrics.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

A 1.2 Psychoanaleptics (antidepressants)

Pharmacotherapeutic group: other antidepressants, ATC code: N06AX11

Mechanism of action/pharmacodynamic effects

Mirtazapine is a centrally active presynaptic α2-antagonist, which increases central noradrenergic and serotonergic neurotransmission. The enhancement of serotonergic neurotransmission is specifically mediated via 5-HT1 receptors, because 5-HT2 and 5-HT3 receptors are blocked by mirtazapine. Both enantiomers of mirtazapine are presumed to contribute to the antidepressant activity, the S(+) enantiomer by blocking α2 and 5-HT2 receptors and the R(-) enantiomer by blocking 5-HT3 receptors.

Clinical efficacy and safety

The histamine H_1-antagonistic activity of mirtazapine is associated with its sedative properties. It has practically no anticholinergic activity and, at therapeutic doses, has only limited effects (e.g. orthostatic hypotension) on the cardiovascular system.

The effect of mirtazapine on QTc interval was assessed in a randomised, placebo and moxifloxacin controlled clinical trial involving 54 healthy volunteers using a regular dose of 45 mg and a supra-therapeutic dose of 75 mg. Linear e-max modelling suggested that prolongation of QTc intervals remained below the threshold for clinically meaningful prolongation.

Paediatric population:

Two randomised, double-blind, placebo-controlled trials in children aged between 7 and 18 years with major depressive disorder (n = 259) using a flexible dose for the first 4 weeks (15 - 45 mg mirtazapine) followed by a fixed dose (15, 30 or 45 mg mirtazapine) for another 4 weeks failed to demonstrate significant differences between mirtazapine and placebo on the primary and all secondary endpoints. Significant weight gain (≥ 7 %) was observed in 48,8 % of the mirtazapine treated subjects compared to 5,7 % in the placebo arm. Urticaria (11,8 % vs 6,8 %) and hypertriglyceridaemia (2,9 % vs 0 %) were also commonly observed.

5.2 Pharmacokinetic properties

Absorption

After oral administration of Mirtazapine, the active substance mirtazapine is rapidly and well absorbed (bioavailability ≈ 50 %), reaching peak plasma levels after approximately 2 hours. Food intake has no influence on the pharmacokinetics of mirtazapine.

Distribution

Plasma protein binding is approximately 85 %.

Biotransformation

Mirtazapine is extensively metabolised in the liver and the major biotransformation pathways are demethylation and oxidation followed by glucuronide conjugation; cytochrome P450 isoenzymes involved are CYP2D6, CYP1A2, and CYP3A4. The N-desmethyl metabolite is pharmacologically active and appears to have the same pharmacokinetic profile as the parent compound.

Elimination

Mirtazapine is extensively metabolised and eliminated via the urine (75 %) and faeces (15 %) within a few days.

The mean plasma elimination half-life is 20 – 40 hours; longer half-lives, up to 65 hours, have occasionally been recorded and shorter half-lives have been seen in young men. The half-life of elimination is sufficient to justify once-a-day dosing. Steady state is reached after 3 - 4 days, after which there is no further accumulation.

Linearity/non-linearity

Mirtazapine displays linear pharmacokinetics within the recommended dose range.

Special populations

Hepatic impairment: Following a single 15 mg oral dose of mirtazapine as contained in **MIRTAZAPINE 15 VIATRIS**, the clearance of mirtazapine was approximately 35 % decreased

in mild to moderate hepatically impaired patients, compared to subjects with normal hepatic function. The average plasma concentration of mirtazapine as contained in **MIRTAZAPINE 15 VIATRIS** was about 55 % increased. The clearance of mirtazapine may be decreased as a result of hepatic impairment.

Renal impairment: Following a 15 mg oral dose of mirtazapine as contained in **MIRTAZAPINE 15 VIATRIS**, in patients with moderate (creatinine clearance < 40 ml/min) and severe (creatinine clearance < 10 ml/min) renal impairment the clearance of mirtazapine was about 30 % and 50 % decreased respectively, compared to normal subjects. The average plasma concentration of mirtazapine was about 55 % and 115 % increased, respectively. No significant differences were found in patients with mild renal impairment (creatinine clearance < 80 ml/min) as compared to the control group. The clearance of mirtazapine may be decreased as a result of renal impairment.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Colloidal Anhydrous Silica

Hydroxypropylcellulose

Lactose Anhydrous

Magnesium Stearate

Maize Starch

Film-coating:

MIRTAZAPINE 15 VIATRIS:

Opadry Yellow 39F52901 consisting of:

Hypromellose

Lactose monohydrate

Macrogol 4000

Titanium dioxide

Quinoline yellow CI 47005

Iron oxide yellow CI 77492

MIRTAZAPINE 30 VIATRIS:

Opadry Buff OY-LS-37200 consisting of:

Hypromellose

Lactose monohydrate

Macrogol 4000

Titanium dioxide

Iron oxide yellow CI 77492

Iron oxide red CI 77491

Iron oxide black CI 77499

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

36 months

6.4 Special precautions for storage

Store at or below 25 ºC.

Protect from light and moisture.

Keep medicine in original container until needed for use.

6.5 Nature and contents of container

Aluminium/Clear PVC/PVDC blister strips in packs of – 10, 14, 20, 28, 30, 50, 100, 250 & 500 tablets.

White or grey polypropylene securitainers with polyethylene caps containing – 10, 14, 20, 28, 30, 50, 100, 250 & 500 tablets.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements.

7. HOLDER OF CERTIFICATE OF REGISTRATION

Viatris South Africa (Pty) Ltd

4 Brewery Street

Isando

Kempton Park

Gauteng, 1601

Tel.: +2711 451 1300

8. REGISTRATION NUMBERS

MIRTAZAPINE 15 VIATRIS: 41/1.2/0367

MIRTAZAPINE 30 VIATRIS: 41/1.2/0368

9. DATE OF FIRST AUTHORISATION/RENEWAL OF AUTHORISATION

10 August 2007

10. DATE OF REVISION OF THE TEXT

22 October 2025