

SCHEDULING STATUS

S5

1 NAME OF THE MEDICINE

INIR 10, capsule

INIR 18, capsule

INIR 25, capsule

INIR 40, capsule

INIR 60, capsule

WARNING:

SUICIDAL IDEATION IN CHILDREN AND ADOLESCENTS

Atomoxetine increased the risk of suicidal ideation in short-term studies in children or adolescents with Attention-Deficit/Hyperactivity Disorder (ADHD). Anyone considering the use of INIR in a child or adolescent must balance this risk with the clinical need. Co-morbidities occurring with ADHD may be associated with an increase in the risk of suicidal ideation and/or behaviour. Patients who are started on therapy should be monitored closely for suicidality (suicidal thinking and behaviour), clinical worsening, or unusual changes in behaviour. Families and caregivers should be advised of the need for close observation and communication with the prescriber. INIR is approved for ADHD in paediatric and adult patients. INIR is not approved for major depressive disorder.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

INIR 10: Each capsule contains atomoxetine hydrochloride equivalent to 10 mg atomoxetine.

INIR 18: Each capsule contains atomoxetine hydrochloride equivalent to 18 mg atomoxetine.

INIR 25: Each capsule contains atomoxetine hydrochloride equivalent to 25 mg atomoxetine.

INIR 40: Each capsule contains atomoxetine hydrochloride equivalent to 40 mg atomoxetine.

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INIR 60: Each capsule contains atomoxetine hydrochloride equivalent to 60 mg atomoxetine.

Sugar-free.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Capsule.

INIR 10: White to off- white powder filled in size '4' hard gelatin capsules with opaque white coloured cap and opaque white coloured body imprinted "RDY" on cap and "519" on body with black ink.

INIR 18: White to off-white powder filled in size '3' hard gelatin capsules with opaque dark gold coloured cap and opaque white coloured body imprinted 'RDY' on cap and '520' on body with black ink.

INIR 25: White to off-white powder filled in size '3' hard gelatin capsules with opaque dark blue coloured cap and opaque white coloured body imprinted 'RDY' on cap and '528' on body with black ink.

INIR 40: White to off-white powder filled in size '1' hard gelatin capsules with opaque dark blue coloured cap and opaque dark blue coloured body imprinted 'RDY' on cap and '521' on body with black ink.

INIR 60: White to off-white powder filled in size '1' hard gelatin capsules with opaque dark blue coloured cap and opaque dark gold coloured body imprinted 'RDY' on cap and '522' on body with black ink.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

INIR is indicated for the treatment of Attention-Deficit/Hyperactivity Disorder (ADHD) in children 6 years of age or older, adolescents and adults.

4.2 Posology and method of administration

Treatment must be initiated by or under the supervision of a medical practitioner with appropriate knowledge and experience of childhood and/or adolescent behavioural disorders (for example, paediatrician or child/adolescent psychiatrist) (see section 4.4).

Do not exceed the recommended daily dose and subsequent increases, as potentially serious side effects

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could result with overdosing.

INIR capsules should not be opened. In the event of the capsule contents coming into contact with the eye, the eyes should be immediately flushed with water and medical advice obtained. Hands and any contaminated surfaces should be washed as soon as possible.

Dosing of children and adolescents up to 70 kg body weight

INIR should be initiated at a total dose of approximately 0,5 mg/kg. The initial dose should be maintained for a minimum of 7 days prior to upward dose titration according to clinical response and tolerability. The recommended maintenance dose is approximately 1,2 mg/kg/day (depending on the patient's weight and available dosage strengths of INIR). No additional benefit has been demonstrated for doses higher than 1,2 mg/kg/day.

Dosing of children and adolescents over 70 kg body weight and adults

INIR should be initiated at a total daily dose of 40 mg. The initial dose should be maintained for a minimum of 7 days prior to upward dose titration according to clinical response and tolerability. The recommended maintenance dose is 80 mg. No additional benefit has been demonstrated for doses higher than 80 mg.

General dosing information

For those ADHD patients who have hepatic insufficiency or end-stage renal disease, cautious titration of INIR to the desired clinical response is recommended. Atomoxetine clearance may be reduced in patients with hepatic insufficiency. INIR may exacerbate hypertension in patients with end-stage renal disease. INIR may be discontinued without tapering the dose.

Long-term use

No fixed dose-response studies have been conducted in adults. The recommended daily dose of 80 mg reflects the optimal daily dose of 1,2 mg/kg/day demonstrated in children and adolescents.

No controlled long-term studies have been conducted in adults. Open-label study data from 384 patients with up to 97 weeks of treatment with atomoxetine are consistent with maintenance of efficacy in long-term treatment.

Missing a dose

If patients miss a dose, they should take it as soon as possible; however, they should not take more than

the prescribed total daily amount of INIR in a 24-hour period.

Method of administration

INIR may be taken with or without food.

4.3 Contraindications

INIR should not be used in:

- Patients with a hypersensitivity to atomoxetine or to any of the excipients of INIR listed in section 6.1.
- Patients with uncontrolled hypertension or impairment of liver function.
- Combination with monoamine oxidase inhibitors (MAOIs) including linezolid. INIR should not be used within a minimum of 2 weeks after discontinuing therapy with MAOIs. Treatment with MAOIs should not be initiated within 2 weeks after discontinuing INIR.
- Narrow angle glaucoma: In clinical studies, the use of atomoxetine, which is an active excipient in INIR, was associated with an increased risk of mydriasis and therefore its use is not recommended in patients with narrow angle glaucoma.
- Severe Cardiovascular Disorders: INIR should not be used in patients with severe cardiovascular disorders whose condition would be expected to deteriorate if they experienced increases in blood pressure or in heart rate that could be clinically important (for example 15 to 20 mm Hg in blood pressure or 20 beats per minute in heart rate) (see section 4.4 – Cardiovascular Effects).
- Pheochromocytoma: INIR should not be used in patients with pheochromocytoma or a history of pheochromocytoma (see section 4.4 – Cardiovascular Effects).

4.4 Special warnings and precautions for use

Treatment must only be initiated by or under the supervision of a medical practitioner with appropriate knowledge and experience of childhood and adolescent behaviour disorders (e.g., paediatrician or child/adolescent psychiatrist).

Possible allergic events

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Allergic reactions including anaphylactic reactions, rash, angioedema and urticaria, have been reported in patients taking atomoxetine.

Suicidal behaviour, hostility

Suicidal behaviour, suicidal ideation, hostility (predominantly aggression, oppositional behaviour and anger) and emotional lability were more frequently observed in clinical trials among patients treated with atomoxetine compared to those treated with placebo but the differences were not statistically significant.

Patients beginning treatment for ADHD should be carefully monitored for the appearance or worsening of suicide-related behaviour, hostility and emotional lability.

Severe cases have been reported concerning paediatric patients, including reports of physical assault, or threatening behaviour and thoughts of harming others. Families and caregivers of paediatric patients treated with atomoxetine should be counselled to alert a healthcare professional immediately if significant changes in mood or patterns of behaviour are noted, particularly after starting treatment or changing the dose. Health care professionals should evaluate the need for dose adjustment or treatment discontinuation in patients experiencing behavioural changes.

The possibility of serious psychiatric adverse events cannot be excluded.

There is evidence that the risk of psychiatric adverse events is increased in children with a personal history of mood disorders, or who have a family history of mood disorders.

Serotonin syndrome

Serotonin syndrome has been reported following concomitant use of atomoxetine with other serotonergic medicines (e.g., serotonin-norepinephrine reuptake inhibitors [SNRIs], selective serotonin reuptake inhibitors [SSRIs], other SNRIs, triptans, opioids, and tricyclic and tetracyclic antidepressants). If concomitant use of atomoxetine with a serotonergic medicine is warranted, prompt recognition of the symptoms of serotonin syndrome is important. These symptoms 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.

Psychotic or manic symptoms

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Treatment emergent psychotic or manic symptoms, e.g., hallucinations, delusional thinking, mania or agitation in patients without a prior history of psychotic illness or mania can be caused by atomoxetine at usual doses. If such symptoms occur, consideration should be given to a possible causal role of atomoxetine, and discontinuation of treatment should be considered. The possibility that INIR will cause the exacerbation of pre-existing psychotic or manic symptoms cannot be excluded.

Depression

INIR lacks efficacy as treatment modality in depression and should not be used for the treatment of depression.

Hepatic effects

INIR should be discontinued in patients with jaundice or laboratory evidence of liver injury and should not be restarted. Spontaneous reports of liver injury manifested by elevated hepatic enzymes and bilirubin with jaundice, have been reported, in some cases associated with, severe liver injury and acute liver failure. Signs and symptoms likely to indicate liver involvement include, pruritus, dark urine, jaundice, right upper quadrant tenderness or unexplained "flu-like" symptoms. Laboratory testing to determine liver enzyme levels and bilirubin should be done upon the first sign or symptom of possible liver involvement. Due to the seemingly idiosyncratic nature of the liver injury, routine monitoring of liver function is unlikely to be helpful in minimising the risk of such reactions.

Growth

Weight gain and longitudinal growth should be monitored during treatment with INIR. Paediatric patients treated with atomoxetine in ADHD clinical trials had a mean initial decrease in weight and height gain. Subsequently, over the long-term period, patients recovered to the mean weight and height predicted by group baseline data.

Sudden death and pre-existing cardiac abnormalities

Sudden death has been reported in patients with structural cardiac abnormalities who were taking atomoxetine at usual doses. Although some serious structural cardiac abnormalities alone carry an increased risk of sudden death, atomoxetine should only be used with caution in patients with known serious structural cardiac abnormalities and in consultation with a cardiac specialist.

Cardiovascular effects

INIR can significantly increase heart rate and blood pressure. It is recommended that the heart rate and blood pressure be measured before treatment is started and periodically during treatment to detect possible clinically important increases.

Most patients taking INIR experience a modest increase in heart rate (mean <10 bpm) and/or increase in blood pressure (mean <5 mm Hg) (see section 4.8).

However, data from ADHD clinical trials show that some patients (approximately 5 to 10 % of children and adults) do experience clinically important changes in heart rate (20 beats per minute or greater) or blood pressure (15 to 20 mm Hg or greater).

INIR should be used with caution in patients whose underlying medical conditions could be worsened by increases in blood pressure or heart rate, such patients with hypertension, tachycardia, cardiovascular or cerebrovascular disease. It should not be used in patients with severe cardiovascular disorders whose condition would be expected to deteriorate if they experienced increases in blood pressure or heart rate that could be clinically important (see section 4.3 – Severe Cardiovascular Disorders).

In addition, INIR should be used with caution in patients with congenital long QT syndrome, acquired long QT syndrome (for example, due to concomitant use of a medicine that prolongs the QT), or a family history of QT prolongation. Orthostatic hypotension has also been reported. Use with caution in any condition that may predispose patients to hypotension, or conditions associated with abrupt heart rate or blood pressure changes.

INIR should not be used in patients with Raynaud's phenomenon.

Cerebrovascular effects

Patients with additional risk factors for cerebrovascular conditions (such as a history of cardiovascular disease, concomitant medications that elevate blood pressure) should be assessed at every visit for neurological signs and symptoms after initiating treatment with atomoxetine.

Seizures

Seizures are a potential risk with atomoxetine. Atomoxetine should be introduced with caution in patients with a history of seizure. Discontinuation of atomoxetine should be considered in any patient developing a

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seizure or if there is an increase in seizure frequency where no other cause is identified.

Effects on micturition

In adult ADHD controlled trials, the rates of urinary retention and urinary hesitation were increased among the subjects taking atomoxetine compared with placebo subjects. A complaint of urinary retention or urinary hesitancy should be considered potentially related to INIR.

Paediatric use

The safety and efficacy of INIR in paediatric patients less than 6 years of age have not been established. The efficacy of atomoxetine beyond 18 months of treatment and safety of INIR beyond 2 years of treatment have not been systematically evaluated.

Geriatric use

The safety and efficacy of INIR in geriatric patients have not been established.

Special Populations

INIR has been used in patients with ADHD without deterioration of conditions of motor tics, Tourette syndrome (children), co-morbid major depressive disorder (adolescents) and anxiety disorders (adults and children).

4.5 Interaction with other medicines and other forms of interaction

Monoamine oxidase inhibitors (MAOIs): INIR should not be used with MAOIs (see section 4.3).

Interactions with other medicines and other forms of interaction:

Beta-adrenergic receptor agonists: INIR should be administered with caution to patients being treated with systemically administered (oral, inhaled or intravenous) salbutamol or other β_2 agonists, because the action of salbutamol on the cardiovascular system can be potentiated.

Cytochrome P450 enzyme: Atomoxetine did not cause clinically significant inhibition of induction of cytochrome P450 enzymes, including CYP1A2, CYP3A, CYP2D6 and CYP2C9. Atomoxetine is principally metabolised by the CYP2D6 pathway. In CYP2D6 extensive metabolisers, inhibitors of CYP2D6 increase atomoxetine steady-state plasma concentrations to exposures similar to those observed in CYP2D6 poor metabolisers.

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In vitro studies suggest that co-administration of cytochrome P450 inhibitors to CYP2D6 poor metabolisers will not increase the plasma concentrations of atomoxetine.

Slower titration of atomoxetine may be necessary. No dosage adjustment of INIR is required when co-administered with CYP2D6 inhibitors.

Medicines that affect norepinephrine (noradrenaline): Medicines that affect norepinephrine (noradrenaline) should be used cautiously when co-administered with INIR because of the potential for additive or synergistic pharmacological effects.

Methylphenidate: Co-administration of methylphenidate with INIR did not increase cardiovascular effects beyond those seen with methylphenidate administration alone.

Pressor medicines: Because of possible effects on blood pressure, INIR should be used cautiously with anti-hypertensive medicines and pressor medicines or other medicines that increase blood pressure.

Medicines that affect gastric pH: Medicines that elevate gastric pH (magnesium hydroxide/aluminium hydroxide, omeprazole) had no effect on atomoxetine bioavailability.

Alcohol: Consumption of ethanol with INIR did not change the intoxicating effects of ethanol.

Midazolam: Co-administration of INIR (60 mg BID for 12 days) with midazolam, a model compound for CYP3A4 metabolised medicines (single dose of 5 mg), resulted in 15 % increase in AUC of midazolam. No dose adjustment is recommended for medicines metabolized by CYP3A.

Medicines highly bound to plasma protein: *In vitro* medicine-displacement studies were conducted with INIR and other highly bound medicines at therapeutic concentrations. INIR did not affect the binding of warfarin, acetylsalicylic acid, phenytoin or diazepam to human albumin. Similarly, these compounds did not affect the binding of INIR to human albumin.

Serotonergic medicines: Atomoxetine should be used with caution in combination with serotonergic medicines, selective serotonin re-uptake inhibitors (SSRIs), serotonin norepinephrine re-uptake inhibitors (SNRIs), opioids such as tramadol, and tetracyclic or tricyclic antidepressants as the risk of serotonin syndrome, a potentially life-threatening condition, is increased (see section 4.4).

4.6 Pregnancy and lactation

Pregnancy

No adequate and well-controlled studies have been conducted with INIR in pregnant women.

Breastfeeding

INIR and/or its metabolites were excreted in the milk of rats. It is not known if INIR is excreted in human milk. Because of the lack of data, atomoxetine should be avoided during breastfeeding.

4.7 Effects on ability to drive and use machines

Patients should be advised to use caution when driving a car or operating hazardous machinery until they are reasonably certain that their performance is not affected by INIR.

4.8 Undesirable effects

Table 1: Side effects in child and adolescent patients

System Organ Class/Adverse Event	Frequent	Less frequent	Frequency unknown
Infections and infestations			
Influenza	x		
Metabolism and nutritional disorders			
Anorexia (loss of appetite)	x		
Decreased appetite	x		
Psychiatric disorders			
Suicidal ideation*		x	
Suicidal behaviour		x	
Aggression/hostility*	x		
Anger*		x	
Early morning awakening		x	
Irritability	x		

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Mood swings	X		
Agitation	X		
Anxiety	X		
Depression and depressed mood	X		
Tics	X		
Emotional lability		X	
Psychosis (including hallucinations)		X	
Bruxism			X
Nervous system disorders			
Dizziness	X		
Headache	X		
Somnolence ²	X		
Syncope		X	
Tremor		X	
Migraine		X	
Paraesthesia		X	
Hypoaesthesia		X	
Seizure		X	
Eye disorders			
Mydriasis		X	
Blurred vision		X	
Cardiac disorders			
Palpitations		X	
Sinus tachycardia		X	
QT interval prolongation		X	
Vascular disorders			
Raynaud's phenomenon		X	

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Respiratory, thoracic and mediastinal disorders			
Dyspnoea	X		
Gastrointestinal disorders			
Abdominal pain ¹	X		
Constipation	X		
Dyspepsia	X		
Nausea	X		
Vomiting	X		
Hepatobiliary disorders			
Increased blood bilirubin		X	
Abnormal/increased liver function tests		X	
Jaundice		X	
Hepatitis		X	
Liver injury		X	
Acute hepatic failure		X	
Skin and subcutaneous tissue disorders			
Dermatitis	X		
Pruritus		X	
Rash	X		
Hyperhidrosis		X	
Allergic reactions		X	
Renal and urinary disorders			
Urinary hesitation		X	
Urinary retention		X	
Reproductive system and breast disorders			
Priapism		X	

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Male genital pain		X	
General Disorders and administration site conditions			
Asthenia		X	
Fatigue	X		
Lethargy	X		
Chest pain	X		
Investigations			
Decreased weight	X		
Increased heart rate	X		
Increased blood pressure	X		

¹ Also includes upper abdominal pain, stomach and epigastric discomfort

² Also includes sedation

Table 2: Side effects in adult patients

System Organ Class/Adverse Event	Frequent	Less frequent
Metabolism and nutritional disorders		
Decreased appetite	X	
Psychiatric disorders		
Early morning awakening	X	
Agitation	X	
Aggression and hostility		X
Decreased libido	X	
Sleep disorder	X	
Insomnia	X	
Suicide-related events		X
Anxiety	X	
Depression and depressed mood	X	

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Tics		X
Emotional lability		X
Restlessness		X
Psychosis (including hallucinations)		X
Nervous system disorders		
Dizziness	X	
Insomnia ²	X	
Paraesthesia	X	
Sinus headache	X	
Headache	X	
Dysgeusia	X	
Somnolence (including sedation)	X	
Tremor	X	
Syncope		X
Migraine		X
Hypoaesthesia		X
Seizure		X
Eye disorders		
Blurred vision		X
Cardiac disorders		
Palpitations	X	
Tachycardia	X	
QT interval prolongation		X
Vascular disorders		
Hot flushes	X	
Flushing	X	
Peripheral coldness		X

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Raynaud's phenomenon		X
Respiratory, thoracic and mediastinal disorders		
Dyspnoea		X
Gastrointestinal disorders		
Abdominal pain ¹	X	
Constipation	X	
Dry mouth	X	
Dyspepsia	X	
Flatulence	X	
Nausea	X	
Hepatobiliary disorders		
Abnormal/increased liver function tests		X
Jaundice		X
Hepatitis		X
Liver injury		X
Acute hepatic failure		X
Increased blood bilirubin		X
Skin and subcutaneous tissue disorders		
Rash	X	
Hyperhidrosis	X	
Dermatitis	X	
Allergic reactions		X
Pruritis		X
Urticaria		X
Musculoskeletal and connective tissue disorders		
Muscle spasms		X
Renal and urinary disorders		

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Difficulty in micturition	X	
Urinary hesitation	X	
Urinary retention	X	
Dysuria	X	
Pollakiuria	X	
Micturition urgency		X
Reproductive system and breast disorders		
Dysmenorrhoea	X	
Ejaculation disorder	X	
Ejaculation failure	X	
Erectile disturbance	X	
Menstruation irregular	X	
Prostatitis	X	
Male genital pain	X	
Abnormal orgasm		X
Priapism		X
General Disorders and administration site conditions		
Fatigue	X	
Chills	X	
Asthenia	X	
Lethargy	X	
Feeling jittery	X	
Irritability	X	
Thirst	X	
Feeling cold		X
Chest pain		X
Investigations		

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Increased blood pressure	X	
Increased heart rate	X	
Decreased weight		X

¹ Also includes upper abdominal pain, stomach and epigastric discomfort

² Also includes sedation

***Post-marketing experience:**

The following events have been reported: aggression, hostility, suicidal ideation, anger, suicidal behaviour, abnormal liver function tests, jaundice and hepatitis* (see section 4.4).

Investigations: increased blood pressure.

Vascular disorders: peripheral vascular instability and/or Raynaud's phenomenon, potential to worsen pre-existing Raynaud's phenomenon.

Urogenital system: painful or prolonged penile erection, male genital pain, urinary hesitation and urinary retention in children and adolescents.

Nervous system disorders: syncope, paraesthesia in children and adolescents, hypoaesthesia.

Psychiatric disorders: sensory disturbances including hallucinations.

General disorders and administration site conditions: lethargy.

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Health care providers are requested to report any suspected adverse drug reactions to SAHPRA via Med Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found on SAHPRA website.

For any information about this medicine, please contact the local representative of the Holder of Certificate of Registration: Dr. Reddy's Laboratories (Pty) Ltd. Tel: +27 11 324 2100

4.9 Overdose

Human experience

The most commonly reported symptoms accompanying acute and chronic overdoses were somnolence,

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agitation, hyperactivity, abnormal behaviour and gastrointestinal symptoms. Signs and symptoms consistent with mild to moderate sympathetic nervous system activation (e.g., mydriasis, tachycardia, blood pressure increased, dry mouth) have also been observed. In some cases of overdose, seizures and very rarely QT prolongation and serotonin syndrome have been reported. There have also been reports of fatal acute overdose involving a mixed ingestion of INIR and at least one other medicine.

Management of overdose

An airway should be established. Monitoring of cardiac and vital signs is recommended, along with appropriate symptomatic and supportive measures. Gastric lavage may be indicated if performed soon after ingestion. Activated charcoal may be useful in limiting absorption. Because INIR is highly protein-bound, dialysis is not likely to be useful in the treatment of overdose.

5 PHARMACOLOGICAL PROPERTIES

Pharmacological classification: A1.2 Psychoanaleptics

Pharmacotherapeutic group: Psychoanaleptics, centrally acting sympathomimetics

ATC code: N06BA09

5.1 Pharmacodynamic properties

Atomoxetine is a selective inhibitor of the presynaptic norepinephrine transporter, without directly affecting the serotonin or dopamine transporters. Atomoxetine has minimal affinity for other noradrenergic receptors or for other neurotransmitter transporters or receptors.

5.2 Pharmacokinetic properties

The pharmacokinetics of atomoxetine in children and adolescents are similar to those in adults. The pharmacokinetics of atomoxetine have not been evaluated in children under the age of 6 years.

Absorption

Atomoxetine is well absorbed after oral administration and reaches a mean maximal observed plasma concentration (C_{max}) approximately 1 to 2 hours after dosing.

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Atomoxetine can be administered with or without food.

Distribution

Atomoxetine is widely distributed. Atomoxetine is extensively bound to plasma proteins, primarily albumin.

Metabolism

Atomoxetine undergoes biotransformation primarily through the cytochrome P450 2D6 (CYP2D6) enzymatic pathway.

4-hydroxyatomoxetine is the major oxidative metabolite formed, that is glucuronidated.

4-hydroxyatomoxetine is equipotent to atomoxetine but circulates in plasma at much lower concentrations.

As 4-hydroxyatomoxetine is primarily formed by CYP2D6, in individuals that lack CYP2D6 activity, 4-hydroxyatomoxetine is still formed by several other cytochrome P450 enzymes, but at a slower rate.

The CYP2D6 pathway is not inhibited or induced by atomoxetine.

Elimination

In extensive metabolisers the mean elimination half-life of atomoxetine after oral administration is 3,6 hours and in poor metabolisers it is 21 hours. Atomoxetine is excreted primarily as 4-hydroxyatomoxetine-O-glucuronide, mainly in the urine.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

The other ingredients are dimethicone and pregelatinised starch.

6.2 Incompatibilities

Not applicable

6.3 Shelf-life

4 years

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6.4 Special precautions for storage

Store at or below 25 °C.

Store protected from light and moisture.

Store in the original blister packs.

Keep the blisters in the carton until required for use.

Keep the HDPE containers tightly closed.

KEEP OUT OF REACH OF CHILDREN.

6.5 Nature and contents of container

HDPE containers: The capsules will be packaged in white plastic containers with white plastic caps containing 30 or 500 capsules.

PVC-PVdC/Alu pack: The capsules are packed in blister strips of clear transparent PVC film coated with PVdC on one side and paper backed aluminium foil with heat seal coating on the other side. The blister strips will be packaged in a cardboard box containing 7, 10, or 14 capsules.

6.6 Special precautions for disposal and other handling

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

7 HOLDER OF CERTIFICATE OF REGISTRATION

Dr. Reddy's Laboratories (Pty) Ltd.

Block C, Woodmead North Office Park,

54 Maxwell Drive,

Woodmead, Sandton,

Gauteng,

2191

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8 REGISTRATION NUMBERS

INIR 10: 43/1.2/0809

INIR 18: 43/1.2/0810

INIR 25: 43/1.2/0811

INIR 40: 43/1.2/0812

INIR 60: 43/1.2/0813

9 DATE OF FIRST AUTHORISATION

25 November 2016

10 DATE OF REVISION OF THE TEXT

31 July 2025