Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Tranylcypromine Eignapharma 20 mg Film-coated Tablet

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Tranylcypromine Eignapharma 20 mg Film-coated Tablet

Each film-coated tablet contains 27.36 mg tranylcypromine sulphate, corresponding to 20 mg tranylcypromine.

Excipient with known effect:

Tranylcypromine Eignapharma 20 mg Film-coated Tablet

Each film-coated tablet contains 108.78 mg lactose.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Film-coated tablet
Tranylcypromine Eignapharma 20 mg Film-coated Tablet
White to off-white, round-shaped film-coated tablet with a score line on one side and a score line on the other side.
Diameter: 9.03 – 9.13 mm
Thickness: 4.39 – 4.56 mm
The tablet can be divided into equal doses.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

For the treatment of depressive episodes (episodes of major depression) in adults. Tranylcypromine Eignapharma should be used as a reserve antidepressant, i.e.

- if appropriate treatment with 2 standard antidepressant agents (including tricyclic antidepressants) has not brought sufficient success, or
- if such standard agents are contraindicated or not tolerated by the patient.

4.2 Posology and method of administration

Posology

The treatment should be started with 10 mg tranylcypromine once daily in the morning. The mood-elevating and antidepressant effect normally occurs after 1 to 3 weeks only. The initial daily dose can be increased by 10 mg/day tranylcypromine per week, depending on the effect and tolerability, up to a therapeutic dose corresponding to the individual reaction.
The usual effective dose is 20 to 40 mg/day. The individual dose is always adjusted to the response and to the severity of disease.

Resistance to treatment: If the therapeutic response is insufficient, the dose can be increased further, under inpatient conditions, in increments of 10 mg/day every 1 to 3 weeks up to a maximum daily dose of 60 mg/day.

The total daily dose can be divided into 1 to 3 doses. The last dose of the day should be taken no later than 3 p.m., to avoid sleep disturbances.

As a maintenance dose,10mg to 20 mg/day tranylcypromine is sufficient in many cases.

It generally takes at least 4 - 6 weeks of treatment for the symptoms to subside. After the depressive symptoms have resolved, treatment with tranylcypromine should be continued, if possible at a reduced dose, for 4 to 6 months.

Sudden discontinuation of a long-term therapy with tranylcypromine should be avoided as withdrawal symptoms such as anxiety, restlessness, sleep disturbances, drowsiness or delirium may occur. The treatment should be withdrawn, if necessary, by gradual reduction of the dose.

When a patient is switched from another antidepressant to tranylcypromine, there should be a break in treatment of at least 7 days, and only 10 mg/day should be prescribed for at least for the first week.

Elderly patients

In elderly patients the dose should be increased more slowly with regular blood pressure monitoring (see section 4.4).

Renal impairment

There are insufficient clinical data for tranylcypromine in the treatment of patients with impaired kidney function. Therefore, patients withs severe renal impairment should not be treated with tranylcypromine (see section 4.3). Other patients with impaired renal function should be carefully monitored (see section 4.4).

Hepatic impairment

Tranylcypromine is contraindicated in patients with impaired liver function (see section 4.3).

Paediatric population

Tranylcypromine is contraindicated in children and adolescents (see section 4.3).

Method of administration

For oral use.
The tablets should be swallowed with plenty of liquid (preferably a glass of water).

4.3 Contraindications

Tranylcypromine must not be used in case of:

- Hypersensitivity to the active substance or to any of the excipients listed in section 6.1
- pheochromocytoma
- carcinoid
- Cerebrovascular disorders
- Blood vessel malformations such as aneurysms
- severe forms of hypertension or cardiovascular disorders
- hepatic dysfunction or liver disease, severe renal impairment or kidney disease
- porphyria
- diabetes insipidus
- malignant hyperthermia including a previous history of the same
- acute delirium
- acute intoxication with CNS depressants e.g. hypnotics, analgesics and psychotropic drugs such as neuroleptics, antidepressants, lithium and alcohol
- Children and young people

Tranylcypromine must not be given to patients who are concomitantly receiving the following:

- medicinal products with pronounced serotonin reuptake inhibition, such as all selective serotonin reuptake inhibitors, clomipramine, venlafaxine, duloxetine, milnacipran, sibutramine, vortioxetine
- L-tryptophan
- serotonin agonists such as triptans for the treatment of migraine
- buspirone
- imipramine
- indirect sympathomimetics (contained, for example, in medicines that increase blood pressure and in certain nasal, cough or flu medicines)
- amphetamines ("uppers" or appetite suppressants)
- pethidine, tramadol, dextrometorphan (dextromethorphan contained in cough suppressants)
- disulfiram
- levodopa, unless combined with decarboxylase inhibitors (such as benserazide or carbidopa) (also see section 4.5).

4.4 Special warnings and precautions for use

Tyramine-rich foods must not be consumed in the period from one day before to 14 days after treatment with tranylcypromine (also see section 4.5).

Patients with elevated or low blood pressure and patients with an increased risk of hypertensive reactions (e.g. hyperthyroidism) should take tranylcypromine only if their blood pressure is checked regularly.

Tranylcypromine is characterised by a significant acute toxicity. This should also be considered when prescribing to suicidal patients.

If a manic episode occurs discontinue tranylcypromine immediately (also see section 4.8). The same applies to acute productive symptoms during treatment of depressive syndromes in schizophrenia.

Particular caution is required if the patient has a previous history of substance abuse.

Tranylcypromine can lower the seizure threshold, therefore epileptic patients' susceptibility to seizures may increase. Therefore, tranylcypromine should only be used with caution in patients with known epilepsy.

Suspected cases of interactions of frequently prescribed antidepressants (e.g. citalopram, paroxetine, venlafaxine, duloxetine, amitriptyline) with buprenorphine indicate that a potentially life-threatening excitatory interaction syndrome (serotonin syndrome) cannot be ruled out even with co-medication of tranylcypromine with buprenorphine. If concomitant treatment with buprenorphine is clinically necessary, care should be taken to monitor patients carefully, especially at the start of therapy and when increasing the dose. Symptoms of serotonin syndrome may include changes in psyche, autonomic nervous system instability, neuromuscular changes and/or gastrointestinal symptoms. If serotonin syndrome is suspected, a dose reduction or discontinuation of therapy should be considered, depending on the severity of symptoms.

Treatment with tranylcypromine can influence blood glucose in patients with diabetes. The dosage of insulin and/or oral antidiabetics may need to be adjusted (also see section 4.5).

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 persists until significant remission occurs. As improvement may not occur during the first weeks or more of treatment, patients should be closely monitored until such improvement occurs. Clinical experience to date suggests that the risk of suicide may be 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 the treatment are known to be at greater risk of suicidal thoughts or suicide attempts and should carefully monitoring during treatment. A meta-analysis of placebo-controlled clinical trials of antidepressants in adult patients with

psychiatric disorders showed an increased risk of suicidal behaviour with antidepressants compared to placebo in patients less than 25 years old.

Close supervision of patients and in particular those at high risk should accompany therapy, 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.

Patients with renal impairment

There is insufficient clinical data for tranylcypromine in the treatment of patients with impaired kidney function. Therefore, patients with severe renal impairment should not be treated with tranylcypromine (see Section 4.3). Other patients with impaired renal function should be carefully monitored (see Section 4.2).

Elderly patients

In the treatment of elderly patients, the daily dose should be increased more slowly, with regular monitoring of blood pressure. The daily dose administered should be kept as low as possible (also see section 4.2).

This medicinal product contains lactose

Patients with rare hereditary galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicinal product.

4.5 Interaction with other medicinal products and other forms of interaction

Interactions with other medicinal products
It should be noted that when patients are switched from certain medicinal product to tranylcypromine and vice versa, there must be a break in treatment. When switching from a drug that cannot be combined with tranylcypromine, a washout period of approximately 5 times the half-life of the drug and its active metabolites is recommended before starting the treatment with tranylcypromine. Conversely, after stopping tranylcypromine, a 14 day treatment break is recommended before starting treatment with a drug that is incompatible with tranylcypromine.

Medicinal products affecting tranylcypromine
Tranylcypromine must not be taken concomitantly with the following active substances (also see section 4.3):

- medicinal products with pronounced serotonin reuptake inhibition such as all selective serotonin reuptake inhibitors, clomipramine, venlafaxine, duloxetine, milnacipran, sibutramine and vortioxetine (risk of triggering a serotonin syndrome [see section 4.4] with sometimes severe and life-threatening symptoms)
- L-tryptophane (symptoms of delirium can occur)
- serotonin agonists such as triptans for the treatment of migraine (risk of a serotonin syndrome, see first item on list)
- buspirone (a steep rise in blood pressure has been reported)
- imipramine (serious adverse effects such as irritability, coma, hyperthermia, seizures and sharp fluctuations in blood pressure, in particular blood pressure increases can occur)
- indirect sympathomimetics (contained e.g. in medicines that increase blood pressure, as well as in certain nasal, cough or flu medicines) (risk of severe hypertensive crises)
- amphetamines ("uppers" or appetite suppressants) (risk of serious hypertensive crises)
- pethidine, tramadol, dextromethorphan (dextromethorphan contained in cough suppressants) (life-threatening adverse effects on the CNS and life-threatening effects on respiratory and cardiovascular function are possible)
- disulfiram (delirium possible)
- levodopa unless combined with decarboxylase inhibitors (such as benserazide or carbidopa) (risk of an uncontrolled rise of blood pressure)

Combination with direct-acting sympathomimetics (e.g. in cardiovascular agents for raising blood pressure or to treat bronchospasm, or in nasal drops) should be avoided. The usually low concentrations of adrenaline or noradrenaline in local

anaesthetics or eye drops do not present any particular risk to patients treated with tranylcypromine as an alternative catabolic pathway is possible via catechol-O-methyltransferase. Similarly, combination with selective β_2-sympathomimetics for inhalation is not associated with any particular risk.

In treatment-resistant cases of depression, tranylcypromine may in exceptional cases be administered in addition to existing treatment with tricyclic antidepressants (however, not including clomipramine or parenterally administered antidepressants), provided that all necessary precautions are taken and the dose is increased slowly. The most clinical data is available for the combination tranylcypromine/amitriptyline.

Tranylcypromine affecting other medicinal products

The blood pressure lowering effect of antihypertensive agents (e.g. guanethidine, methyldopa) can be potentiated by tranylcypromine; in isolated cases, a rise in blood pressure (with states of agitation) can be triggered.

The effect of insulin and oral antidiabetics can be increased (also see section 4.4).

Undesirable effects of bupropione (or amfebutamone- an agent for smoking cessation), such as seizures and state of agitation can be potentiated by co-administration of tranylcypromine. This combination should therefore be avoided.

The effect of CNS depressants (neuroleptics, antidepressants, analgesics, benzodiazepines) may be potentiated when tranylcypromine is co-administered.

Suspected cases of interactions of commonly prescribed antidepressants (e.g. citalopram, paroxetine, venlafaxine, duloxetine, amitriptyline) with buprenorphine indicate that a potentially life-threatening excitatory interaction syndrome (serotonin syndrome) may also occur with co-medication of tranylcypromine with buprenorphine (see section 4.4).

Interaction during surgery and dental treatment

Withdrawal of tranylcypromine should be considered 14 days before elective surgery with use of anaesthetics or certain analgesics, as interactions have been reported between irreversible MAO inhibitors (such as tranylcypromine) and anaesthetics, and these were in some cases serious (cardiovascular instability, comatose states). Pethidine, a strong analgesic used for post-operative pain therapy, must never be administered to patients treated with tranylcypromine (also see section 4.3).
The possibility of over-excitation of the sympathetic nervous system always exists in patients treated with tranylcypromine. Inhalation narcotics, with the exception of ether, which should not be used, do not pose any additional risk beyond that of inhalation narcotics per se.
The usually low concentrations of adrenaline or noradrenaline in local anaesthetics (e.g. for dental procedures) or eye drops, do not present any particular risk for patients treated with tranylcypromine.
These interactions apply even in the case that the above medicinal products are used only for a short time.

Interaction with food (also see section 4.4)

Biogenic amines are physiological substances in microorganisms, plants, animals and humans that play a role in nerve functions and as hormones. They can also accumulate in foodstuffs through metabolic processes: in normal fermentation processes in production but also as a result of excessively warm storage or spoiling.
If biogenic amines are consumed in excess (approx. 800 to 2,000 mg per meal, without MAO inhibitors) toxic phenomena can occur, especially in the form of changes in the blood pressure and even a hypertensive crisis.
During the treatment with MAO inhibitors unpleasant effects are already possible from a tyramine content of 6 mg and a phenylethylamine content of 1mg per meal. Severe reactions must be expected from a content of 25 mg tyramine per meal.

A decisive factor in possible intolerance is not only the tyramine content per gram or millilitre of a particular foodstuff but also the amount of this food consumed. On the other hand, the absorbed proportion of tyramine is higher in small meals and also if alcohol is consumed at the same time.

Tranylcypromine causes inhibition (MAO inhibition) of an enzyme system that is necessary for detoxification of biogenic amines. Therefore, 1 day before, during and up to 14 days after treatment with tranylcypromine, special dietary instructions must be followed (low-tyramine diet) to prevent health disorders in the form of nausea, headaches and high blood pressure.

Patients should eat a balanced diet with full calorie content. All foodstuffs should be used as fresh as possible, and uncooked or partially cooked dishes must be eaten on the day of preparation. Semi-preserved tinned/bottled goods and frozen vegetables or fruit must be used immediately after opening or thawing. Opened tinned/bottled goods or completely cooked meals can be stored in the refrigerator at 4°C for a maximum of 48 hours before consumption.

Irrespective of the dose of the MAO inhibitor the following foods are prohibited or permitted only in small quantities 1 day before, during and for 14 days after treatment with tranylcypromine:

Please note: A maximum of only one foodstuff that is in a small amount is advisable per meal.

Prohibited:

- Brine hard cheese (e.g. Emmental, Bergkäse, Parmesan and similar cheeses made from raw milk which can be sliced or grated)
- Cheese containing edible moulds e.g. Roquefort, Camembert and similar varieties
- Smear-ripened cheese, e.g. Limburger, Butterkäse (butter cheese), red smear cheese, Harzer cheese, Handkäse (sour milk cheese)
- Chocolate ice-cream and nougat ice-cream
- Beef and poultry liver
- Kidneys of all farmed animals and game
- Stock and bouillon cubes
- Game meat and other meat products with strong ageing and a strong odour,
- Matured hard salami and similar raw sausages, particularly with edible mould casing
- Salted herring, soused herring, salted sardines, anchovies, caviar and similar salt-cured raw products
- Cold smoked fish (e.g. cold smoked kipper, cold smoked mackerel, etc.)
- Dried fish, stock fish, dried salted fish
- Cod liver
- Squid (octopus)
- Fish sauces, Asian sauces, soya sauces, matured tofu products, etc.
- Pickled eggs
- Marmite and other concentrated yeast extracts
- fermented drinks made with yeast (beer, wine, champagne, sparkling wine including non-alcoholic brands) and drinks with a high alcohol content (liqueur, brandies, whiskey, rum etc.)
- Sprouted Barley seedlings (malt)
- Ripe brown beans (e.g. kidney beans), broad beans (also known as fava beans or field beans), haricot beans
- Bean sprouts
- Large bars of dark chocolate or dark chocolate figures (see "Permitted in small quantities")
- Cognoc chocolate liqueurs, liqueur pralines, cocoa liqueur
- Walnut nougat or nougat with undeclared ingredients
- Very ripe bananas, pears and avocados, red plums, figs (see "Permitted in small quantities")
- Fruit preserved in rum
- Raw sauerkraut
- Raw gherkins, barrel gherkins
- Mixed pickles, pickled mushrooms
- Walnuts
- Juices with a high pear, banana or plum content
- Commercial grapefruit juice
- Juices from citrus fruit concentrates

Permitted in small quantities:

- Semi-hard cheese for sliced (stored cold and for a short time, little odour) made from pasteurised milk (e.g. Gouda, Cheshire, Edam): 1 x 20 g slice
- Mozzarella or Feta-type cheese each made from pasteurised milk with cow's milk content up to 20 g
- Yoghurt, kefir and their preparations approx. 250ml
- Vanilla and fruit-flavoured ice-cream: 1 scoop
- Pig's liver: maximum 100 g
- Fresh knackwurst (similar to frankfurters), maximum 100 g (still soft!)

- Air-dried and cured ham up to 20 g
- Teewurst (similar to Bologna sausage), mettwurst (pork and beef paté), fine Braunschweiger (finely minced pork and beef sausage): up to 50 g
- Pickled herring, rollmops: up to 100 g
- Herring pieces in mayonnaise or jelly: up to 100 g
- Tinned tuna: up to 50 g
- Commercial ready-made sauces and sauces from industrial kitchens etc. up to 100 ml sauce
- Commercially available powders for the preparation of sauces up to 100ml sauce
- Commercially available ready meals with up to 100ml sauce
- Chocolates with cream, fruit, or marzipan filling: up to 20 g
- Hazelnut nougat: up to 20 g
- Marzipan: up to 20 g
- Milk chocolate: up to 20 g and chocolate bars with milk, cream or marzipan filling: up to 50 g (also as white chocolate)
- Muesli bars with chocolate coating: up to 20 g
- Chocolate containing whole hazelnuts, cashew nuts or almonds: up to 20 g
- Commercial orange juice: up to 100 ml
- Blackcurrants: up to 50 g, red grapes up to 250 g, ½ a not too ripe banana, pear or avocado
- Dried fruits: up to 20 g
- Pasteurised wine sauerkraut: up to 100 g
- Pasteurised pickled gherkins: up to 100 g
- Carrots (i.e. young carrots, usually shorter and with green tops): up to 20 g

The effect of alcohol can be potentiated if tranylcypromine is taken concomitantly.

4.6 Fertility, pregnancy and lactation

Pregnancy

There are insufficient data for the use of tranylcypromine in pregnant women. Similarly, animal studies are insufficient in respect of the reproductive toxicity of tranylcypromine (see section 5.3). Negative effects of tranylcypromine in pregnancy are possible due to frequently found hypertension and reduced placental perfusion.
Therefore, tranylcypromine should not be used in the first trimester of pregnancy and only if urgently indicated in the second and third trimesters.
If tranylcypromine is prescribed for a woman of childbearing age, she should be advised to contact her doctor immediately if she is planning to have a baby or if she thinks that she may be pregnant so that her medication can be changed in due time.

Lactation

It is not known whether tranylcypromine is excreted in human breast milk. Small quantities of tranylcypromine can pass into breast milk in animals. A risk to the newborns/infants cannot be excluded. Tranylcypromine Eignapharma should not be used during breast-feeding. Breastfeeding should be discontinued if treatment with tranylcypromine is urgently indicated.

Fertility
There are no data on effects on fertility.

4.7 Effects on ability to drive and use machines

Tranylcypromine has a small or moderate influence on ability to drive and use machines.
This applies to a greater extent if alcohol is consumed or in combination with other substances that can act on the central nervous system. Therefore, at the start of the treatment patients should not drive a car or other vehicles, operate electric tools and machines or carry out other potentially dangerous work. The further procedure depends on the individual responsiveness in the course of treatment.

4.8 Undesirable effects

The following frequency categories form the basis for classification of undesirable effects:

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)
Not known (cannot be estimated from the available data)
If a manic episode occurs, tranylcypromine should be discontinued immediately (see section 4.4).

The following undesirable effects occur in particular at the beginning of the treatment: Sleep disorders, hypotension, orthostatic reactions (orthostatic dysregulation).

System organ class	**Very common**	**Common**	**Uncommon**	**Rare**	**Very rare**	**Unknown**
Blood and lymphatic system disorders				Anaemia, leukaemia, neutropenia, agranulocytosis, thrombopenia		
Psychiatric disorders		Anxiety, agitation, restlessness		Psychological dependence, hallucinations,[a] confusion[a]		Suicidal thoughts, suicidal behaviour[b]
Nervous system disorders[c]	Insomnia, sleep disturbances	Dizziness, dry mouth, tiredness		Cerebral seizures, polyneuropathies[a]		
Eye disorders				Difficulty in focusing[a]		
Cardiac disorders		Palpitations				
Vascular disorders	Hypotension, orthostasis reaction (orthostatic dysregulation)	Hypertension	Hypertensive crisis that may be accompanied by tachycardia, flushing, headache (especially occipital pain), stiffness of the neck, nausea, vomiting and photophobia. In individual cases, especially if the dietary requirements are not observed (see section 4.4) or in the case of drug interactions (see section 4.5), they may cause intracranial haemorrhages.	Oedema		
Disorders of the gastrointestinal				Constipation, diarrhoea		

tract[d]						
Liver and biliary tract disorders				Liver function disorders,[a] increase in liver enzyme activity[a]		
Skin and subcutaneous tissue disorders				Sweating, allergic skin rashes[a]	Hair loss	
Skeletal musculoskeletal, connective tissue and bone disorders[e]				Muscle spasms, muscle pains, joint pain[a]		
Kidney and urinary tract disorders[f]					Reduced urine production that corresponds to the syndrome of inadequate ADH secre-tion	
Disorders of the genital organs and of the mammary gland				Anorgasmia, erectile impotence, ejaculation disorders		
General disorders and administration site conditions[g]		Weight gain, weight loss, Weakness		Hyperthermia[a]		

[a] Frequency indication: rare/very rare.
[b] Cases of suicidal ideation or attempted suicide during treatment with tranylcypromine or shortly after discontinuation of treatment have been reported (see section 4.4).
[c] There are reports that tranylcypromine has led to tremor, drowsiness and light-headedness in patients.
[d] There are reports that tranylcypromine has led to nausea with and without vomiting as well as non-specific gastrointestinal symptoms in patients.
[e] There are reports that tranylcypromine has led to muscle twitching in patients.
[f] There are reports that tranylcypromine has led to dysuria in patients.
[g] There are reports that tranylcypromine has led to breast pain, sensations of cold and states of exhaustion in patients.

Ear and labyrinth disorders
There are reports that tranylcypromine has led to tinnitus in patients.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions viathe HPRA Pharmacovigilance Website: www.hpra.ie

4.9 Overdose

Symptoms
No symptoms are likely from a single large dose.

Treatment
No specific treatment is indicated.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Sulfur-containing imidazole derivatives.
ATC Code: H03B B01

Mechanism of action:
Carbimazole, a thionamide, is a pro-drug which undergoes rapid and virtually complete metabolism to the active metabolite, thiamazole, also known as methimazole. The method of action is believed to be inhibition of the organification of iodide and the coupling of iodothyronine residues which in turn suppress the synthesis of thyroid hormones.

5.2 Pharmacokinetic properties

Absorption
Carbimazole is rapidly metabolised to thiamazole. After oral ingestion, peak plasma concentrations of thiamazole, the active moiety, occur at 1 to 2 hours.

Distribution
The total volume of distribution of thiamazole is 0.5 1/kg. Thiamazole is concentrated in the thyroid gland. This intrathyroidal concentration of thiamazole has the effect of prolonging its activity. However, thiamazole has a shorter half-life in hyperthyroid patients than in normal controls and so more frequent initial doses are required while the hyperthyroidism is active.

Biotransformation
Thiamazole is moderately bound to plasma proteins. Carbimazole has a half-life of 5.3 to 5.4 hours. It is possible that the plasma half-life may also be prolonged by renal or hepatic disease. See section 4.2. Thiamazole crosses the placenta and appears in breast milk. The plasma:milk ratio approaches unity.

Elimination
Over 90% of orally administered carbimazole is excreted in the urine as thiamazole or its metabolites. The remainder appears in faeces. There is 10% enterohepatic circulation.

5.3 Preclinical safety data

There are no preclinical data of relevance to the prescriber which are additional to that already included in other sections of the Summary of Product Characteristics.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Tablet core:

microcrystalline cellulose
lactose anhydrous
maize starch
silica, colloidal anhydrous

Film-coating:

polyvinyl alcohol (partially hydrolized)
titanium dioxide (E171)
macrogol 4000
talc

6.2 Incompatibilities

Not applicable

6.3 Shelf life

30 months

6.4 Special precautions for storage

This medicinal product does not require any special storage conditions.

6.5 Nature and contents of container

Blisters composed of white PVC/PVdC blisters sealed with laminated paper/aluminium foil lidding.
Packs containg 28 film-coated tablets.

6.6 Special precautions for disposal

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

7 MARKETING AUTHORISATION HOLDER

Neuraxpharm Ireland Limited
4045 Kingswood Road
Citywest
Dublin 24
Ireland

8 MARKETING AUTHORISATION NUMBER

PA23229/012/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of First Authorisation: 10th February 2023

10 DATE OF REVISION OF THE TEXT