# SUMMARY OF PRODUCT CHARACTERISTICS

## 1 NAME OF THE MEDICINAL PRODUCT

Imipramine Tablets BP 25mg

## 2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains Imipramine Hydrochloride BP 25.0 mg.

Excipient with known effect:
Each tablet contains: 29.37 mg of lactose.
sucrose
tartrazine (E102)
amaranth (E123)

For the full list of excipients, see section 6.1.

## 3 PHARMACEUTICAL FORM

Tablet

## 4 CLINICAL PARTICULARS

### 4.1 Therapeutic indications

1. Treatment of depressive illness
2. Treatment of nocturnal enuresis in children

### 4.2 Posology and method of administration

Posology

Adults:
1 x 25mg up to three times daily, increasing stepwise to 150-200mg. This should be reached by the end of the first week and maintained until definite improvement has occurred. The subsequent maintenance dose should be individually determined by gradually reducing the dosage, usually to about 50-100mg daily.

In patients in hospital, i.e. severe cases, the dose may be increased to 100mg three times daily until a distinct improvement is seen. Again, the subsequent maintenance dose should be determined individually by reducing the dosage, usually to about 100mg daily.

Elderly:

Patients over 60 years may respond to lower doses of imipramine than those recommended above. Treatment should be initiated with 10mg daily, gradually increasing to 30-50mg daily. The optimum dose should be reached after about 10 days and then continued until the end of treatment.

*Paediatric population*

Children: (In the treatment of nocturnal enuresis only). The tablets should be administered just before bedtime.

6-7 years (weight 20-25kg or 44-55lbs): 25 mg daily
8-11 years (weight 25-35kg or 55-77lbs): 25 – 50 mg daily
Over 11 years (weight 35-54kg or 77-119lbs): 50 – 75 mg daily.

Children under 6 years: Not to be given to children under 6 years of age.

The dose should not exceed 75 mg daily. The maximum period of treatment should not exceed three months, and withdrawal should be gradual. If relapse should occur, treatment should not be re-instituted until a full physical examination has been carried out.

Method of administration:

For oral administration.

## 4.3 Contraindications

- Hypersensitivity to imipramine or to any of the excipients listed in section 6.1
- Cross-sensitivity to other tricyclic antidepressants of the dibenzazepine group.
- Any degree of heart block or other cardiac arrhythmias; recent myocardial infarction.
- Mania
- Porphyria
- Severe liver disease
- Narrow angle glaucoma
- Children under 6 years of age
- Retention of urine
- Concomitant therapy with selective, reversible MAO-A inhibitors such as moclobemide, or within 3 weeks of cessation of therapy.

## 4.4 Special warnings and precautions for use

Improvement in depression may not occur during the first two to four weeks of treatment and hence patients should be closely monitored during this period.

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 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. A meta-analysis of placebo-controlled clinical trials of antidepressant drugs 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 drug 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.

Blood sugar concentrations may be altered in diabetic patients.

Caution is required in patients with hyperthyroidism or during treatment with thyroid preparations as aggravation of unwanted cardiac effects may occur.

Before starting treatment it is advisable to check the patients' blood pressure because patients with hypotension or a labile circulation may react to the drug with a fall in blood pressure.

Caution is required when giving tricyclic antidepressants to patients with tumours of the adrenal medulla (e.g. phaeochromocytoma, neuroblastoma), as hypertensive crises may be provoked.

Many patients with panic disorders experience intensified anxiety symptoms at the start of treatment with antidepressants. This paradoxical initial increase in anxiety is most pronounced during the first few days of treatment and generally subsides within two weeks.

Concomitant treatment of imipramine and electroconvulsive therapy should only be resorted to under careful supervision.

Avoid if possible in patients with symptoms of bladder neck obstruction e.g. prostatic
hypertrophy.

Lengthy treatment with tricyclic antidepressants can lead to an increased incidence of dental caries. Regular dental check-ups are therefore advisable during long-term treatment.

Activation of psychosis has occasionally been observed in schizophrenic patients receiving tricyclic antidepressants. Hypomanic or manic episodes have also been reported during a depressive phase in patients with cyclic affective disorders receiving treatment with a tricyclic antidepressant. In such cases it may be necessary to reduce the dosage of Imipramine hydrochloride or

to withdraw it and administer an antipsychotic agent. After such episodes have subsided, low dose therapy with Imipramine hydrochloride may be resumed if required.

In predisposed and elderly patients, imipramine may, particularly at night, provoke pharmacogenic (delirious) psychoses, which disappear without treatment within a few days of withdrawing the drug. Agitation, confusion and postural hypotension may occur.

Abrupt withdrawal should be avoided because of possible adverse reactions (see section 4.8).

Hyponatraemia (usually in the elderly) has been associated with all types of antidepressants and should be considered in all patients who develop symptoms such as drowsiness, confusion or convulsions.

A swing from depression to hypomania or mania is possible in patients with bipolar affective disorders. In such cases it may be necessary to withdraw imipramine and administer drugs to control the mania. After such episodes have subsided, low-dose therapy with imipramine may be resumed if required.

Behavioural changes may occur in children receiving imipramine for treatment of nocturnal enuresis.

Tricyclic antidepressants are known to lower the convulsion threshold and Imipramine Hydrochloride should therefore be used with extreme caution in patients with epilepsy and other predisposing factors, e.g. brain damage of varying aetiology, concomitant use of neuroleptics, withdrawal from alcohol or drugs with anticonvulsive properties (e.g. benzodiazepines). It appears that the occurrence of seizures is dose dependent.

Caution is required when giving tricyclic antidepressants to patients with severe renal disease.

Although changes in the white blood cell count have been reported with imipramine only in isolated cases, periodic blood cell counts and monitoring for symptoms such as fever and sore throat are called for, particularly during the first few months of therapy (See section 4.8).

Because of its anticholinergic properties, imipramine should be used with caution in patients with a history of increased intra- ocular pressure, narrow angle glaucoma, or urinary retention (e.g. diseases of the prostate).

Caution is called for in patients with chronic constipation. Tricyclic antidepressants may cause paralytic ileus, particularly in the elderly and bedridden patients.

Decreased lacrimation and accumulation of mucoid secretions due to anticholinergic properties of tricyclic antidepressants may cause damage to the corneal epithelium in patients with contact lenses.

Imipramine may cause anxiety, feelings of unrest, and hyperexcitation in agitated patients and patients with accompanying schizophrenic symptoms.

Before general or local anaesthesia, the anaesthetist should be aware that the patient has been receiving imipramine. Anaesthetics given during tri/tetracyclic antidepressant therapy may increase the risk of arrhythmias and hypotension (see section 4.5).

*Serotonin syndrome*
Concomitant administration of Imipramine Tablets and buprenorphine/opioids may result in serotonin syndrome, a potentially life-threatening condition (see section 4.5).
If concomitant treatment with other serotonergic agents 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.

Periodic monitoring of hepatic enzyme levels is recommended in patients with liver disease.

Monitoring of cardiac function is indicated in elderly patients.

The tablets contain lactose. Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

The tablets contain sucrose: Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take this medicine.

The tablets also contain tartrazine (E102) which may cause allergic reactions.

## 4.5 Interaction with other medicinal products and other forms of interaction

Adrenergic neurone blockers: Imipramine may diminish or abolish the antihypertensive effects of guanethidine, debrisoquine, bethanidine, reserpine, α-methyldopa and clonidine. Patients requiring co-medication for hypertension should therefore be given antihypertensives of a different type (e.g. vasodilators).

Beta-blockers: Blood concentrations of imipramine may be increased by drugs such as labetalol and propranolol. The clinical importance of these interactions are uncertain.

Diuretics: Concurrent use of a tricyclic antidepressant and a diuretic may increase the risk of postural hypotension.

Alpha$_2$-adrenoceptor stimulants: concomitant use of apraclonidine or brimonidine should be avoided.

Sympathomimetic drugs: Imipramine may potentiate the cardiovascular effects of adrenaline (epinephrine), noradrenaline (norepinephrine), ephedrine, isoprenaline, phenylephrine and phenylpropanolamine (e.g. as contained in local anaesthetic preparations and nasal decongestants).

CNS depressants: Tricyclic antidepressants may also potentiate the CNS depressant effects of alcohol and central depressant drugs (e.g. barbiturates, benzodiazepines or general anaesthetics) (See section 4.4).

It also reduces the effect of oral contraceptives, the side-effects of which may be increased.

MAO inhibitors (MAOIs): Imipramine hydrochloride should not be administered for at least 3 weeks after discontinuation of treatment with MAO inhibitors (there is a risk of severe symptoms such as hypertensive crisis, hyperpyrexia, myoclonus, agitation, seizures, delirium and coma). This also applies when giving a MAO inhibitor after previous treatment with Imipramine. In both instances, Imipramine or the MAO inhibitor should initially be given in small, gradually increasing doses and its effects monitored. There is evidence to suggest that tricyclic antidepressants may be given as little as 24 hours after a reversible MAO inhibitor such as moclobemide, but the 3 week wash-out period must be observed if the MAO inhibitor is given after a tricyclic antidepressant has been used.

Cimetidine, methylphenidate: These drugs may increase the plasma levels of imipramine whose dosage should therefore be reduced.

Anticholinergic agents: Tricyclic antidepressants may potentiate the effects of these drugs (e.g. phenothiazine, antiparkinsonian agents, antihistamines, atropine, biperiden) on the eye, central nervous system, bowel and bladder.

Antiviral agents: Drugs such as ritonavir have been reported to increase plasma concentrations of antidepressant drugs.

Calcium channel blockers: Blood levels of imipramine may be increased by calcium channel blockers such as diltiazem and verapamil.

Nitrates: Reduced salivary secretion may lessen the effectiveness of sub-lingual nitrate preparations.

Dopaminergic agents: CNS toxicity may be enhanced when tricyclic antidepressants are used in conjunction with dopaminergic drugs such as selegiline and entacapone.

Centrally acting appetite suppressants: Concomitant use is not recommended due to the increased risk of CNS toxicity.

Antineoplastic drugs: concomitant use of altretamine should be avoided due to the risk of severe postural hypotension.

Liver enzyme inducers: Drugs which activate the hepatic mono-oxygenase enzyme system (carbamazepine, barbiturates, nicotine, phenytoin, and oral contraceptives) may accelerate the metabolism and lower the plasma concentrations of imipramine, resulting in decreased efficacy. Plasma levels of phenytoin and carbamazepine may

increase, with corresponding adverse effects. It may be necessary to adjust the dosage of these drugs.

Selective serotonin reuptake inhibitors (SSRIs): Co-medication may lead to additive effects on the serotonergic system. Fluoxetine and fluvoxamine may also increase plasma concentrations of imipramine, with corresponding adverse effects, resulting in increased plasma levels of tricyclic antidepressants, a lowered convulsion threshold and seizures.

Alprazolam and disulfiram: It may be necessary to reduce the dosage of imipramine if it is administered concomitantly with alprazolam or disulfiram.

Neuroleptics: Concomitant use may result in increased plasma levels of tricyclic antidepressants, a lowered convulsion threshold and seizures. Combination with thioridazine may produce severe cardiac arrhythmias.

Anticoagulants: Tricyclic antidepressants may potentiate the anti-coagulant effect of coumarin drugs by inhibiting hepatic metabolism of these anticoagulants. Careful monitoring of plasma prothrombin is therefore advised.

Oestrogens: There is evidence that oestrogens can sometimes paradoxically reduce the effects of imipramine yet at the same time cause imipramine toxicity.

Tricyclic antidepressants may also interact with the following drug classes:

- Analgesics: Possible increase in risk of side effects (nefopam), convulsions (tramadol), sedation (opioid analgesics) or ventricular arrhythmias.

- Anti-arrhythmics: Increased risk of ventricular arrhythmias with drugs, which prolong the QT interval.

- Muscle relaxants: Enhanced muscle relaxant effect of baclofen.

Quinidine: Tricyclic antidepressants should not be employed in combination with anti-arrhythmic agents of the quinidine type.

Buprenorphine/opioids as the risk of serotonin syndrome, a potentially life-threatening condition, is increased (see section 4.4).

## 4.6 Fertility, pregnancy and lactation

Pregnancy

There is no evidence of the safety of the drug in human pregnancy. There have been isolated reports of a possible connection between the use of tricyclic antidepressants and adverse effects (developmental disorders) on the foetus. Treatment with imipramine should be avoided during pregnancy, unless the anticipated benefits justify the potential risk to the foetus.

Neonates whose mothers had taken imipramine up till delivery have developed dyspnoea, lethargy, colic, irritability, hypotension or hypertension, tremor or spasms, during the first few hours or days. If possible, Imipramine should be gradually withdrawn at least 7 weeks before the calculated date of confinement.

Breast-feeding
As imipramine is excreted in breast milk, it should not be administered to nursing mothers unless considered essential when the mother should be advised to cease breast feeding.

## 4.7 Effects on ability to drive and use machines

Patients should be warned

- That blurred vision, drowsiness and other CNS symptoms may occur (see section 4.8).
- Against possible hazards such as driving a car, operating machinery or doing anything which may require alertness or quick actions.
- Alcohol or other drugs may potentiate these effects (see section 4.5).

## 4.8 Undesirable effects

If severe neurological or psychiatric reactions occur, Imipramine hydrochloride should be withdrawn.

Elderly patients are particularly sensitive to anticholinergic, neurological, psychiatric, or cardiovascular effects. Their ability to metabolise and eliminate drugs may be reduced, leading to a risk of elevated plasma concentrations at therapeutic doses.

The following frequency estimates are used: 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).

*Blood and lymphatic system disorders*:
Rare: agranulocytosis, bone marrow depression including leucopenia, eosinophilia, purpura, thrombocytopenia. It is advisable to perform blood counts during treatment with tritetracyclic antidepressants, especially if the patient develops fever, sore throat or other signs of infection. (see section 4.4).

*Immune system disorders:*
Rare: allergic alveolitis (pneumonitis) with or without eosinophilia, systemic anaphylactic/anaphylactoid reactions including hypotension.

*Endocrine disorders:*
Rare: SIADH (syndrome of inappropriate antidiuretic hormone secretion)

*Metabolism and nutrition disorders:*
Rare: Hyponatraemia, usually in the elderly, has been associated with all types of antidepressants (see section 4.4).

*Psychiatric Disorders:*
Behavioural changes in children may occur.
Common: fatigue, drowsiness, restlessness, delirium, confusion, disorientation and hallucination (particularly in geriatric patients and those suffering from Parkinson's

disease), increased anxiety, agitation, sleep disturbances, swings from depression to hypomania or mania.
Uncommon: activation of psychotic symptoms
Rare: aggressiveness

Paranoid delusion may be exacerbated during treatment with tricyclic antidepressants. These are more frequently seen in elderly patients or those on high doses.
Cases of suicidal ideation and suicidal behaviours have been reported during Imipramine therapy or early after treatment discontinuation (see section 4.4).

*Nervous system disorders:*
Very common: tremor
Common: paraesthesiae, headache, dizziness.
Uncommon: epileptic seizures/convulsions.
Rare: EEG changes, myoclonus, weakness, extrapyramidal symptoms, ataxia, speech disorder, drug fever.
Syncope has also been reported.

*Eye disorders:*
Very common: blurred vision, disorders of visual accommodation
Rare: glaucoma, mydriasis

*Ear and labyrinth disorders:*
Rare: Tinnitus

*Cardiac disorders:*
Very common: sinus tachycardia and clinically irrelevant ECG changes (T and ST changes) in patients of normal cardiac status, postural hypotension.
Common: arrhythmias and heart block follow the use of imipramine and may be the cause of sudden death in patients with cardiac disease, conduction disorders (widening of QRS complex and PR interval, bundle-branch block), palpitations.
Rare: increased blood pressure, cardiac decompensation, peripheral vasospastic reactions.

Cardiac arrhythmias and severe hypotension are likely to occur with high dosage or in deliberate overdosage. They may also occur in patients with pre-existing heart disease taking normal dosage.

*Vascular disorders:*
Very common: hot flushes

*Gastro-Intestinal disorders:*
Very common: constipation, dry mouth.
Common: nausea, vomiting, anorexia.
Rare: stomatitis, tongue lesions, abdominal disorders, and paralytic ileus have been reported.

*Hepatobiliary disorders:*
Common: elevated transaminases
Uncommon: impaired liver function
Rare: hepatitis with or without jaundice.

*Skin and subcutaneous tissue disorders:*
Very common: sweating

Common: allergic skin reactions (skin rash, urticaria)
Rare: oedema (local or generalised), photosensitivity, pruritus, petechiae, hair loss.

*Renal and urinary disorders:*
Common: disturbances of micturition, urinary retention.

*Reproductive system and breast disorders:*
Common: interference with sexual function
Rare: enlarged mammary glands, galactorrhoea

*General disorders and administration site conditions:*
Although not indicative of addiction, withdrawal symptoms following abrupt discontinuation of treatment: nausea, vomiting, abdominal pain, diarrhoea, insomnia, headache, nervousness, anxiety, irritability, excessive perspiration (see section 4.4).

Respiratory depression, agitation and withdrawal symptoms have been reported in neonates whose mothers received imipramine during the last trimester of pregnancy.

*Investigations:*
Very common: weight gain
Rare: increase or decrease in blood sugar and weight loss.

*Class effects:*
Epidemiological studies, mainly conducted in patients 50 years of age and older, show an increased risk of bone fractures in patients receiving SSRIs and TCAs. The mechanism leading to this risk is unknown.

**Reporting of suspected adverse reactions:**

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

## 4.9 Overdose

The signs and symptoms of overdose with imipramine are similar to those reported with other tricyclic antidepressants. Cardiac abnormalities and neurological disturbances are the main complications. In children, accidental ingestion of any amount should be regarded as serious and potentially fatal.

Signs and Symptoms: Symptoms generally appear within 4 hours of ingestion and reach a maximum severity after 24 hours. Owing to delayed absorption (increased anticholinergic effect due to overdose), long half-life and enterohepatic recycling of the drug, the patient may be at risk for up to 4-6 days. Major symptoms of overdosage include:

Central nervous system:
Drowsiness, stupor, coma, ataxia, restlessness, agitation, enhanced reflexes, muscular rigidity, athethoid and chloreiform movements, convulsions.

Cardiovascular system:
Hypotension, tachycardia, arrhythmia, conduction disorders, heart failure, in very rare cases cardiac arrest.

In addition, respiratory depression, cyanosis, shock, vomiting, fever, hydriasis, sweating and oliguria or anuria may occur.

Treatment:
There is no specific antidote to imipramine. Treatment is essentially symptomatic and supportive. Gastric lavage and forced emesis should be employed immediately if the patient is fully conscious to reduce absorption of the drug. If the patient has impaired consciousness, the airway should be secured with a cuffed endotracheal tube before beginning lavage, and vomiting should not be induced. These measures are recommended for up to 12 hours or even longer after the overdose, since the anticholinergic effect of the drug may delay gastric emptying. Activated charcoal should be administered to reduce drug absorption.

Patients presenting with major symptoms of overdosage, particularly children, should be nursed in an intensive care unit for at least 72 hours where full support of vital functions is possible.

Treatment of symptoms is based on modern methods of intensive care with continuous monitoring of cardiac function, blood gases and electrolytes, and if necessary emergency measures such as: anticonvulsive therapy, artificial respiration, insertion of a temporary cardiac pacemaker, plasma expander, dopamine or dobutamine administered by intravenous drip, resuscitation.

Any serious overdosage requires continuous cardiac monitoring for at least 48 hours and dysrhythmias must be treated on an individual basis. Respiratory insufficiency may necessitate intubation and ventilation, and convulsions may be controlled with intravenous diazepam.

Physostigmine should not be used following an overdosage of imipramine as it has been reported that physostigmine may cause severe bradycardia, asystole and seizures. Haemodialysis or peritoneal dialysis is ineffective because of the low plasma concentrations of imipramine.

# 5 PHARMACOLOGICAL PROPERTIES

## 5.1 Pharmacodynamic properties

Pharmacotherapeutic group
Tricyclic antidepressant. Noradrenaline (NA) and serotonin (5HT) re-uptake inhibitor. ATC code: NO6A A02

Mechanism of action
Imipramine is a tricyclic antidepressant and has several pharmacological with actions which include alpha-adrenolytic, antihistamine, anticholinergic and 5 HT-receptor blocking properties but exhibiting a less marked tendency to cause sedation. However, the main therapeutic activity is believed to be inhibition of the neuronal re-uptake of noradrenaline and 5HT. Imipramine is a so-called “mixed” re-uptake blocker, i.e. it inhibits the reuptake of NA and 5HT to about the same extent.

## 5.2 Pharmacokinetic properties

Absorption:
Imipramine is absorbed quickly and completely following oral administration.

The intake of food has no effect on its absorption and bioavailability. During its first passage through the liver, orally administered imipramine becomes partly converted to desmethylimipramine, a metabolite which likewise exhibits antidepressant activity.

During oral administration of 50 mg 3 times daily for 10 days, the mean steady state plasma concentrations of imipramine and desmethylimipramine were 33-85 ng/ml and 43-109ng/ml, respectively. Owing to lower clearance in the plasma, resulting in increased systemic availability, elderly patients require lower doses of imipramine than patients in intermediate age groups. Renal impairment is not expected to have any influence on the kinetics of unchanged imipramine and its desmethylimipramine metabolite, since both are excreted only in small amounts by the kidneys.

Distribution:
About 86% of imipramine binds to plasma proteins. Concentrations of imipramine in the cerebrospinal fluid and the plasma are highly correlated. The mean distribution volume is about 21L/kg. Imipramine and its metabolite desmethylimipramine both pass into breast milk in concentrations similar to those found in the plasma.

Biotransformation:
Imipramine is extensively metabolised in the liver. It is cleared mainly by demethylation and to a lesser extent by hydroxylation. Both metabolic pathways are under genetic control.

Elimination:
Imipramine is eliminated from the blood with a mean half-life of about 19 hours. About 80% is excreted in the urine and about 20% in the faeces, mainly in the form of inactive metabolites. Urinary excretion of unchanged imipramine and of the active metabolite desmethylimipramine is about 5% and 6% respectively. Only small quantities of these are excreted in the faeces.

Characteristics in patients: Owing to reduced metabolic clearance, plasma concentrations of imipramine are higher in elderly patients than in younger patients.

In children, the mean clearance and elimination of half-life does not differ significantly from adult controls but the between-patient variability is high.

In patients with severe renal impairment, no change occurs in renal excretion of imipramine and its biologically active unconjugated metabolites. However, steady-state plasma concentrations of the conjugated metabolites, which are considered to be biologically inactive are elevated. The clinical significance of this finding is not known.

## 5.3 Preclinical safety data

Imipramine has no mutagenic or carcinogenic potential. Studies in four species (mouse, rat, rabbit and monkey) led to the conclusion that orally administered imipramine has no teratogenic potential. Experiments with high doses of parenterally administered imipramine resulted mainly in severe maternal and embryotoxic effects, they were thus inconclusive with regard to teratogenic effects.

# 6 PHARMACEUTICAL PARTICULARS

## 6.1 List of excipients

**Ingredient:**
Lactose BP
Povidone BP
Isopropyl Alcohol BP
Maize Starch BP
Magnesium Stearate BP

**Coating Materials:**
Coating Varnish HSE
Talc BP
Syrup BP
Standard Coating Cream HSE
Opalux 2619 Tan Colour Coat H

## 6.2 Incompatibilities

None

## 6.3 Shelf life

24 months - blister packs

36 months - amber glass bottles

60 months - opaque plastic containers

## 6.4 Special precautions for storage

Keep out of reach of children

Protect from heat, light and moisture

## 6.5 Nature and contents of container

1. Amber glass bottles with screw caps, containing 50, 100, 250, 500 and 1000 tablets.

2. Opaque plastic containers (securitainers) with plastic caps, containing 28, 42, 50, 56, 84, 100, 112, 250, 500 and 1000 tablets.

3. Opaque plastic container composed of either high density polypropylene or high density polyethylene with a tamper-evident or child-resistant tamper-evident closure composed of high density polyethylene with a packing inclusion of standard polyether foam or polyethylene or polypropylene made filler, containing 28, 42, 50, 56, 84, 100, 112, 250, 500 and 1000 tablets.

4. Aluminium/opaque PVC blister packs, containing 28, 42, 50, 56, 84 and 112 tablets.

### 6.6 Special precautions for disposal

None stated

## SUMMARY OF PRODUCT CHARACTERISTICS

## 7 MARKETING AUTHORISATION HOLDER

Crescent Pharma Ltd
Key House, Sarum Hill, Basingstoke,
RG21 8SR,UK.

## 8 MARKETING AUTHORISATION NUMBER

PL 20416/0093

## 9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

29/01/2004 / 11/03/2009

## 10 DATE OF REVISION OF THE TEXT

30/09/2024