Summary of Product Characteristics for Pharmaceutical Products

1. Name of the medicinal product:

Co-Depricap Capsule 3/25 mg

2. Qualitative and quantitative composition

Each capsule contains:
Olanzapine USP 3mg
Fluoxetine (as HCl) 25mg

Excipients with known effects
None.
For the full list of excipients, see section 6.1

3. Pharmaceutical form

Hard-gelatin capsule size No. "02" dark amethyst opaque cap and dark amethyst opaque body both imprinted with white NQ logo, containing yellow dry powder.

4. Clinical particulars

4.1 Therapeutic indications

Depressive Episodes Associated with Bipolar I Disorder:
Co-Depricap (Olanzapine and Fluoxetine HCl) Capsule is indicated for the acute treatment of depressive episodes associated with Bipolar I Disorder in adults.
Treatment Resistant Depression:
Co-Depricap (Olanzapine and Fluoxetine HCl) Capsule is indicated for the acute treatment of Treatment Resistant Depression (Major Depressive Disorder in adults who do not respond to 2 separate trials of different antidepressants of adequate dose and duration in the current episode).

4.2 Posology and method of administration

Posology
Depressive Episodes Associated with Bipolar I Disorder:
Co-Depricap (Olanzapine and Fluoxetine HCl) Capsule should be administered once daily in the evening, generally beginning with the 6mg/25mg capsule. While food has no appreciable effect on the absorption of Olanzapine and Fluoxetine HCl Capsule given individually, the effect of food on the absorption of Olanzapine and Fluoxetine HCl Capsule has not been studied. Dosage adjustments, if indicated, can be made according to efficacy and tolerability. Antidepressant efficacy was demonstrated with Co-Depricap (Olanzapine and Fluoxetine HCl) Capsule in a dose range of Olanzapine 6mg to 12mg and Fluoxetine 25mg to 50mg. The safety of doses above 18mg/75mg has not been evaluated in clinical studies. It is generally accepted that Bipolar I Disorder, including the depressive episodes associated with Bipolar I Disorder, is a chronic illness requiring chronic treatment. The physician should periodically re-examine the need for continued pharmacotherapy.

Treatment Resistant Depression:
Co-Depricap (Olanzapine and Fluoxetine HCl) Capsule should be administered once daily in the evening, generally beginning with the 6mg/25mg capsule. While food has no appreciable effect on the absorption of Olanzapine and Fluoxetine given individually, the effect of food on the absorption of Co-Depricap (Olanzapine and Fluoxetine HCl) Capsule has not been studied. Dosage adjustments, if indicated, can be made according to efficacy and tolerability. Antidepressant efficacy was demonstrated with Co-Depricap (Olanzapine and Fluoxetine HCl) Capsule in a dose range of Olanzapine 6mg to 18mg and Fluoxetine 25mg to 50mg. The safety of doses above 18mg/75mg has not been evaluated in clinical studies. It is generally accepted that Treatment Resistant Depression (Major Depressive Disorder in adult patients who do not respond to 2 separate trials of different antidepressants of adequate dose and duration in the current episode) is a chronic illness requiring chronic treatment. The physician should periodically re-examine the need for continued pharmacotherapy.

Dosage Summary

- Adult Starting Dose: 6 mg olanzapine with 25 mg fluoxetine (6 mg/25 mg, once daily in the evening.
- Adult Maximum Dose: 12 mg/50 mg once daily.
- Pediatric Bipolar Depression Starting Dose: 3 mg/25 mg once daily (for ages 10 to 17 years).
- Pediatric Bipolar Depression Maximum Dose: 12 mg/50 mg.
- Starting dose in patients predisposed to hypotensive reactions, hepatic impairment, or with potential for slowed metabolism: 3 mg/25 mg to 6 mg/25 mg. Escalate dose cautiously.

Method of Administration
For oral administration.

4.3 Contraindications

Olanzapine and Fluoxetine HCl Capsule is contra-indicated, if patient is hypersensitive to active substances and any of its excipients.
Co-depricap is also contraindicated when taken together with the following medicines:

- Monoamine Oxidase Inhibitors (MAOI): Because of the risk of serotonin syndrome, do not use MAOIs intended to treat psychiatric disorders with fluoxetine/olanzapine or within 5 weeks of stopping treatment with fluoxetine/olanzapine. Do not use fluoxetine/olanzapine within 14 days of stopping an MAOI intended to treat psychiatric disorders. In addition, do not start fluoxetine/olanzapine in a patient who is being treated with linezolid or intravenous methylene blue.
- Pimozide: Do not use. Risk of QT interval prolongation.

- Thioridazine: Do not use. Risk of QT interval prolongation. Do not use thioridazine within 5 weeks of discontinuing fluoxetine/olanzapine combination.

4.4 Special warnings and precautions for use

Clinical Worsening and Suicide Risk:

Patients with Major Depressive Disorder (MDD), both adult and paediatric, may experience worsening of their depression and/or the emergence of suicidal ideation and behaviour (suicidality) or unusual changes in behaviour, whether or not they are taking medications and this risk may persist until significant remission occurs. Suicide is a known risk of depression and certain other psychiatric disorders; and these disorders themselves are the strongest predictors of suicide.

Neuroleptic Malignant Syndrome (NMS):

A potentially fatal symptom complex sometimes referred to as NMS has been reported in association with administration of drugs, including Olanzapine.

Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS):

Discontinue if DRESS is suspected.

Metabolic Changes:

Atypical antipsychotic drugs have been associated with metabolic changes including hyperglycemia, dyslipidemia, and weight gain.

Hyperglycemia and Diabetes Mellitus:

In some cases, extreme and associated with ketoacidosis or hyperosmolar coma or death. Monitor for symptoms of hyperglycemia. Perform fasting blood glucose testing before beginning, and periodically during treatment.

Dyslipidemia:

Appropriate clinical monitoring is recommended, including fasting blood lipid testing before beginning, and periodically during, treatment.

Weight gain:

Consider potential consequences of weight gain. Monitor weight regularly.

Serotonin Syndrome:

Serotonin syndrome has been reported with SSRIs and SNRIs, including fluoxetine/olanzapine, both when taken alone, but especially when co-administered with other serotonergic agents. If such symptoms occur, discontinue fluoxetine/olanzapine combination and serotonergic agents and initiate supportive treatment. If concomitant use of fluoxetine/olanzapine with other

serotonergic drugs is clinically warranted, patients should be made aware of a potential increased risk for serotonin syndrome, particularly during treatment initiation and dose increases.

Angle-Closure Glaucoma:
Angle-closure glaucoma has occurred in patients with untreated anatomically narrow angles treated with antidepressants.

Allergic Reactions and Rash:
Discontinue upon appearance of rash or allergic phenomena.

Activation of Mania/Hypomania:
Screen for Bipolar Disorder and monitor for activation of mania/hypomania.

Tardive Dyskinesia:
Discontinue if clinically appropriate.

Orthostatic Hypotension:
Can be associated with bradycardia and syncope. Risk is increased during initial dose titration. Use caution in patients with cardiovascular disease or cerebrovascular disease, and those conditions that could affect hemodynamic responses.

Leukopenia, Neutropenia, and Agranulocytosis:
Has been reported with antipsychotics, including fluoxetine/olanzapine. Patients with a history of a clinically significant low white blood cell count (WBC) or drug induced leukopenia/neutropenia should have their complete blood count (CBC) monitored frequently during the first few months of therapy. Consider discontinuing fluoxetine/olanzapine at the first sign of a clinically significant decline in WBC in the absence of other causative factors.

Seizures:
Use cautiously in patients with a history of seizures or with conditions that lower the seizure threshold.

Increased Risk of Bleeding: SSRIs increase the risk of bleeding.
Use with NSAIDs, aspirin, warfarin, or other drugs that affect coagulation may potentiate the risk of gastrointestinal or other bleeding.

Hyponatremia:
Can occur in association with syndrome of inappropriate antidiuretic hormone (SIADH). Consider discontinuing fluoxetine/olanzapine if symptomatic hyponatremia occurs (SIADH).

Potential for Cognitive and Motor Impairment:
Has potential to impair judgment, thinking, and motor skills. Caution patients about operating machinery.

QT Prolongation:
QT prolongation and ventricular arrhythmia including Torsade de Pointes have been reported with fluoxetine. Use with caution in conditions that predispose to arrhythmias or increased fluoxetine exposure. Use cautiously in patients with risk factors for QT prolongation.

Anticholinergic (antimuscarinic) Effects:
Use with caution with other anticholinergic drugs and in patients with urinary retention, prostatic hypertrophy, constipation, history of paralytic ileus or related conditions.

Hyperprolactinemia:
May elevate prolactin levels.

Long Elimination Half-Life of Fluoxetine:
Changes in dose will not be fully reflected in plasma for several weeks.

Sexual Dysfunction:
Fluoxetine/Olanzapine use may cause symptoms of sexual dysfunction.

4.5 Interaction with other medicinal products and other forms of interaction

Mono Amine Oxidase Inhibitors (MAOI):
Olanzapine and Fluoxetine HCl should not be used in combination with MAOI or within a minimum of 14 days of discontinuing therapy with MAOI. There have been reports of serious, sometimes fatal reactions (including rigidity, myoclonus, autonomic instability with possible rapid fluctuations of vital signs, and mental status changes that include extreme agitation progressing to delerium and coma) in patients receiving Fluoxetine in combination with an MAOI, and in patients who have recently discontinued Fluoxetine and are then started on MAOI.

CNS Acting Drugs:
Caution is advised if the concomitant administration of Olanzapine and Fluoxetine HCl and other CNS active drugs is required. In evaluating individual cases, consideration should be given to use lower initial doses of the concomitantly administered drugs, using conservative titration schedules, and monitoring of clinical status.

Drugs Metabolized by CYP2D6:
Fluoxetine is a potent inhibitor of CYP2D6 enzyme pathway.

Tricyclic Antidepressants (TCAs):
Monitor TCA levels during co-administration with fluoxetine/olanzapine or when fluoxetine/olanzapine has been recently discontinued.

Antihypertensive Agent:
Enhanced antihypertensive effect.

Levodopa and Dopamine Agonists:
May antagonize levodopa/dopamine agonists.

Benzodiazepines:
May potentiate orthostatic hypotension and sedation.

Clozapine:
May elevate clozapine levels.

Haloperidol:
Elevated haloperidol levels have been observed.

Carbamazepine:
Potential for elevated carbamazepine levels and clinical anticonvulsant toxicity.

Phenytoin:
Potential for elevated phenytoin levels and clinical anticonvulsant toxicity.

Alcohol:
May potentiate sedation and orthostatic hypotension.

Fluvoxamine:
May increase olanzapine levels; a lower dose of the olanzapine component of fluoxetine/olanzapine fixed-dose combination should be considered.

Drugs that Interfere with Haemostasis: (e.g., NSAIDs, Aspirin, Warfarin, etc.):
May potentiate the risk of bleeding.

Drugs Tightly Bound to Plasma Proteins:
Fluoxetine may cause shift in plasma concentrations.

Drugs that Prolong the QT Interval:
Do not use fluoxetine/olanzapine in combination with thioridazine or pimozide. Use fluoxetine/olanzapine with caution in combination with other drugs that prolong the QT interval.

4.6 Pregnancy and Lactation

Fluoxetine

Pregnancy

Some epidemiological studies suggest an increased risk of cardiovascular defects associated with the use of fluoxetine during the first trimester. The mechanism is unknown. Overall the data suggest that the risk of having an infant with a cardiovascular defect following maternal fluoxetine exposure is in the region of 2/100 compared with an expected rate for such defects of approximately 1/100 in the general population.

Epidemiological data have suggested that the use of SSRIs in pregnancy, particular in late pregnancy, may increase the risk of persistent pulmonary hypertension in the new-born (PPHN). The observed risk was approximately 5 cases per 1000 pregnancies. In the general population 1 to 2 cases of PPHN per 1000 pregnancies occur.

Fluoxetine should not be used during pregnancy unless the clinical condition of the woman requires treatment with fluoxetine and justifies the potential risk to the foetus. Abrupt discontinuation of therapy should be avoided during pregnancy. If fluoxetine is used during pregnancy, caution should be exercised, especially during late pregnancy or just prior to the onset of labour since some other effects have been reported in neonates: irritability, tremor, hypotonia, persistent crying, difficulty in sucking or in sleeping. These symptoms may indicate either serotonergic effects or a withdrawal syndrome. The time to occur and the duration of these symptoms may be related to the long half-life of fluoxetine (4-6 days) and its active metabolite, norfluoxetine (4-16 days).

Observational data indicate an increased risk (less than 2-fold) of postpartum haemorrhage following SSRI/SNRI exposure within the month prior to birth.

Breast Feeding

Fluoxetine and its metabolite norfluoxetine, are known to be excreted in human breast milk. Adverse events have been reported in breastfeeding infants. If treatment with fluoxetine is considered necessary, discontinuation of breastfeeding should be considered; however, if breastfeeding is continued, the lowest effective dose of fluoxetine should be prescribed.

Fertility

Animal data have shown that fluoxetine may affect sperm quality. Human case reports with some SSRIs have shown that an effect on sperm quality is reversible.

Impact on human fertility has not been observed so far.

Olanzapine
Pregnancy
There are no adequate and well-controlled studies in pregnant women. Patients should be advised to notify their physician if they become pregnant or intend to become pregnant during treatment with olanzapine. Nevertheless, because human experience is limited, olanzapine should be used in pregnancy only if the potential benefit justifies the potential risk to the foetus.

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

Breast-feeding
In a study in breast-feeding, healthy women, olanzapine was excreted in breast milk. Mean infant exposure (mg/kg) at steady state was estimated to be 1.8% of the maternal olanzapine dose (mg/kg). Patients should be advised not to breast feed an infant if they are taking olanzapine.

Fertility
Effects on fertility are unknown

4.7 Effects on ability to drive and use machines

Has potential to impair judgment, thinking, and motor skills. Caution patients about driving and operating machinery.

4.8 Undesirable effects

Commonly Observed Adverse Reactions in Short-Term Controlled Studies Including Depressive Episodes Associated with Bipolar I Disorder and Treatment Resistant Depression include:
Sexual Dysfunction:
In the pool of controlled Olanzapine and Fluoxetine HCl studies in patients with Bipolar depression, there were higher rates of the treatment-emergent adverse reactions decreased and abnormal in the Olanzapine and Fluoxetine HCl group than in the placebo group. Sexual dysfunction, including priapism has been reported with all SSRIs.

Body as a Whole:
Frequent: chills, neck rigidity, photosensitivity reaction;
Rare: death.

Cardiovascular System:
Frequent: vasodilatation;
Infrequent: QT-interval prolonged.

Digestive System:
Frequent: diarrhea; Infrequent: nausea and vomiting;
Rare: gastrointestinal hemorrhage, liver fatty deposits.

Nervous System:
Infrequent: buccoglossal syndrome, coma, depersonalization, emotional hypokinesia, movement disorder;
Rare: hyperkinesia, libido increased, withdrawal syndrome.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of benefit/risk balance of the medicinal product. Health care professionals are asked to report any suspected adverse reactions via the Pharmacy and Poisons Board, Pharmacovigilance Electronic Reporting System (PvERS) https://pv.pharmacyboardkenya.org

4.9 Overdose

No specific antidote for either Fluoxetine or Olanzapine overdose is known. Treatment should be supportive and symptomatic.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Fluoxetine- ATC CODE: N06AB03
Olanzapine- ATC CODE: N05AH03
Mechanism of Action
The mechanism of action of olanzapine and fluoxetine in the listed indications, is unclear. However, the combined effect of olanzapine and fluoxetine at the monoaminergic neural systems (serotonin, norepinephrine, and dopamine) could be responsible for the pharmacological effect.

Pharmacodynamics
Olanzapine binds with high affinity to the following receptors: serotonin 5HT2A/2C, 5HT6 (Ki=4, 11, and 5 nM, respectively), dopamine D1-4 (Ki=11 to 31 nM), histamine H1 (Ki=7 nM), and adrenergic α1 receptors (Ki=19 nM). Olanzapine is an antagonist with moderate affinity binding for serotonin 5HT3 (Ki=57 nM) and muscarinic M1-5 (Ki=73, 96, 132, 32, and 48 nM, respectively). Olanzapine binds weakly to GABAA, BZD, and β-adrenergic receptors (Ki>10 μM).
Fluoxetine is an inhibitor of the serotonin transporter and is a weak inhibitor of the norepinephrine and dopamine transporters.

5.2 Pharmacokinetic properties

Fluoxetine/Olanzapine Combination — Fluoxetine (administered as a 60 mg single dose or 60 mg daily for 8 days) caused a small increase in the mean maximum concentration of olanzapine (16%) following a 5 mg dose, an increase in the mean area under the curve (17%) and a small decrease in mean apparent clearance of olanzapine (16%). In another study, a

similar decrease in apparent clearance of olanzapine of 14% was observed following olanzapine doses of 6 or 12 mg with concomitant fluoxetine doses of 25 mg or more. The decrease in clearance reflects an increase in bioavailability. The terminal half-life is not affected, and therefore the time to reach steady state should not be altered. The overall steady-state plasma concentrations of olanzapine and fluoxetine when given as the combination in the therapeutic dose ranges were comparable with those typically attained with each of the monotherapies. The small change in olanzapine clearance, observed in both studies, likely reflects the inhibition of a minor metabolic pathway for olanzapine via CYP2D6 by fluoxetine, a potent CYP2D6 inhibitor, and was not deemed clinically significant. Therefore, the pharmacokinetics of the individual components is expected to reasonably characterize the overall pharmacokinetics of the combination.

Absorption and Bioavailability

Fluoxetine/Olanzapine Combination — Following a single oral 12 mg/50 mg dose of SYMBYAX, peak plasma concentrations of olanzapine and fluoxetine occur at approximately 4 and 6 hours, respectively. The effect of food on the absorption and bioavailability of fluoxetine/olanzine has not been evaluated. The bioavailability of olanzapine, and the bioavailability of fluoxetine given were not affected by food. It is unlikely that there would be a significant food effect on the bioavailability of fluoxetine/olanzapine.

Olanzapine — Olanzapine is well absorbed and reaches peak concentration approximately 6 hours following an oral dose. Food does not affect the rate or extent of olanzapine absorption. It is eliminated extensively by first pass metabolism, with approximately 40% of the dose metabolized before reaching the systemic circulation.

Fluoxetine — Following a single oral 40 mg dose, peak plasma concentrations of fluoxetine from 15 to 55 ng/mL are observed after 6 to 8 hours. Food does not appear to affect the systemic bioavailability of fluoxetine, although it may delay its absorption by 1 to 2 hours, which is probably not clinically significant.

Distribution

Fluoxetine/ Olanzapine — The in vitro binding to human plasma proteins of olanzapine and fluoxetine in combination is similar to the binding of the individual components.

Olanzapine — Olanzapine is extensively distributed throughout the body, with a volume of distribution of approximately 1000 L. It is 93% bound to plasma proteins over the concentration range of 7 to 1100 ng/mL, binding primarily to albumin and α1-acid glycoprotein.

Fluoxetine — Over the concentration range from 200 to 1000 ng/mL, approximately 94.5% of fluoxetine is bound in vitro to human serum proteins, including albumin and α1-glycoprotein. The interaction between fluoxetine and other highly protein-bound drugs has not been fully evaluated.

Metabolism and Elimination

Fluoxetine/Olanzapine — Fluoxetine/Olanzapine therapy yielded steady-state concentrations of norfluoxetine similar to those seen with fluoxetine in the therapeutic dose range.

Olanzapine — Olanzapine displays linear pharmacokinetics over the clinical dosing range. Its half-life ranges from 21 to 54 hours (5th to 95th percentile; mean of 30 hr), and apparent plasma clearance ranges from 12 to 47 L/hr (5th to 95th percentile; mean of 25 L/hr). Administration of olanzapine once daily leads to steady-state concentrations in about 1 week that are approximately twice the concentrations after single doses. Plasma concentrations, half-life, and clearance of olanzapine may vary between individuals on the basis of smoking status, gender, and age.

Following a single oral dose of 14C-labeled olanzapine, 7% of the dose of olanzapine was recovered in the urine as unchanged drug, indicating that olanzapine is highly metabolized. Approximately 57% and 30% of the dose was recovered in the urine and faeces, respectively. In the plasma, olanzapine accounted for only 12% of the AUC for total radioactivity, indicating significant exposure to metabolites. After multiple dosing, the major circulating metabolites were the 10-N-glucuronide, present at steady state at 44% of the concentration of olanzapine, and 4′-N-desmethyl olanzapine, present at steady state at 31% of the concentration of olanzapine. Both metabolites lack pharmacological activity at the concentrations observed.

Direct glucuronidation and CYP450-mediated oxidation are the primary metabolic pathways for olanzapine. In vitro studies suggest that CYP1A2, CYP2D6, and the flavin-containing monooxygenase system are involved in olanzapine oxidation. CYP2D6-mediated oxidation appears to be a minor metabolic pathway in vivo, because the clearance of olanzapine is not reduced in subjects who are deficient in this enzyme.

Fluoxetine — Fluoxetine is a racemic mixture (50/50) of R-fluoxetine and S-fluoxetine enantiomers. In animal models, both enantiomers are specific and potent serotonin uptake inhibitors with essentially equivalent pharmacologic activity. The S-fluoxetine enantiomer is eliminated more slowly and is the predominant enantiomer present in plasma at steady state.

Fluoxetine is extensively metabolized in the liver to its only identified active metabolite, norfluoxetine, via the CYP2D6 pathway. A number of unidentified metabolites exist.

In animal models, S-norfluoxetine is a potent and selective inhibitor of serotonin uptake and has activity essentially equivalent to R- or S-fluoxetine. R-norfluoxetine is significantly less potent than the parent drug in the inhibition of serotonin uptake. The primary route of elimination appears to be hepatic metabolism to inactive metabolites excreted by the kidney.

Clinical Issues Related to Metabolism and Elimination
The complexity of the metabolism of fluoxetine has several consequences that may potentially affect the clinical use of fluoxetine/olannzapine.

Variability in Metabolism — A subset (about 7%) of the population has reduced activity of the drug metabolizing enzyme CYP2D6. Such individuals are referred to as "poor metabolizers" of drugs such as debrisoquin, dextromethorphan, and the tricyclic antidepressants (TCAs). In a study involving labeled and unlabeled enantiomers administered as a racemate, these individuals metabolized S-fluoxetine at a slower rate and thus achieved higher concentrations of S-fluoxetine. Consequently, concentrations of S-norfluoxetine at steady state were lower. The metabolism of R-fluoxetine in these poor metabolizers appears normal. When compared with normal metabolizers, the total sum at steady state of the plasma concentrations of the 4 enantiomers was not significantly greater among poor metabolizers. Thus, the net pharmacodynamic activities were essentially the same. Alternative nonsaturable pathways (non-CYP2D6) also contribute to the metabolism of fluoxetine. This explains how fluoxetine achieves a steady-state concentration rather than increasing without limit.

Because the metabolism of fluoxetine, like that of a number of other compounds including TCAs and other selective serotonin antidepressants, involves the CYP2D6 system, concomitant therapy with drugs also metabolized by this enzyme system (such as the TCAs) may lead to drug interactions [see Drug Interactions (7.7)].

Accumulation and Slow Elimination — The relatively slow elimination of fluoxetine (elimination half-life of 1 to 3 days after acute administration and 4 to 6 days after chronic administration) and its active metabolite, norfluoxetine (elimination half-life of 4 to 16 days after acute and chronic administration), leads to significant accumulation of these active species in chronic use and delayed attainment of steady state, even when a fixed dose is used. After 30 days of dosing at 40 mg/day, plasma concentrations of fluoxetine in the range of 91 to 302 ng/mL and norfluoxetine in the range of 72 to 258 ng/mL have been observed. Plasma concentrations of fluoxetine were higher than those predicted by single-dose studies, because the metabolism of fluoxetine is not

proportional to dose. However, norfluoxetine appears to have linear pharmacokinetics. Its mean terminal half-life after a single dose was 8.6 days and after multiple dosing was 9.3 days. Steady-state levels after prolonged dosing are similar to levels seen at 4 to 5 weeks.

The long elimination half-lives of fluoxetine and norfluoxetine assure that, even when dosing is stopped, active drug substance will persist in the body for weeks (primarily depending on individual patient characteristics, previous dosing regimen, and length of previous therapy at discontinuation). This is of potential consequence when drug discontinuation is required or when drugs are prescribed that might interact with fluoxetine and norfluoxetine following the discontinuation of fluoxetine.

5.3 Preclinical safety data

There is no evidence of carcinogenicity or mutagenicity from in vitro or animal studies.

6. Pharmaceutical Particulars

6.1 List of Excipients

Pregelatinized Starch
Sodium Lauryl Sulphate

6.2 Incompatibilities

None

6.3 Shelf-Life

24 months.

6.4 Special Precautions for storage

Store below 30^0C.
Protect from light and moisture.
Keep out of the reach of children.

6.5 Nature and Content of container

Co-Depricap 3mg/25mg Capsules are available in Alu-Alu pack size of 14's.

6.6 Special precautions for disposal and other handling

No special requirements. Dispose as per the local guidelines.

7. Marketing Authorization Holder

Nabiqasim Industries (Pvt.) Ltd.
17/24, Korangi Industrial Area, Karachi – Pakistan.

8. Marketing Authorization Number

CTD7796

9. Date of first authorization/renewal of the authorization
27/10/2023

10. Date of revision of the text
11/05/2025