For the use of a Registered Medical Practitioner or a Hospital or a Laboratory only

TRINICALM FORTE

1. Generic Name

Trifluoperazine + Benzhexol Hydrochloride + Chlorpromazine Hydrochloride tablets

2. Qualitative and quantitative composition

TRINICALM FORTE

Each film coated tablet contains:

Chlorpromazine Hydrochloride I.P..... 50 mg

Trifluoperazine Hydrochloride I.P……..5 mg

Benzhexol Hydrochloride I.P.....2 mg

Colour: Lake of carmoisine, Lake of Brilliant Blue & Titanium Dioxide I.P.

Excipients: LACTOSE, STARCH, MAGNESIUM STEARATE, TALC, POLYVINYL PYRROLIDONE (K-30), ISO PROPYL ALCOHOL, LAKE OF BRILLIANT BLUE, LAKE OF CARMOSINE, TITANIUM DIOXIDE, HYDROXY PROPYL METHYL CELU, ETHYL CELLULOSE, METHANOL, METHYLENE CHLORIDE, PROPYLENE GLYCOL.

3. Dosage form and strength

Dosage form: Film Coated Tablet

Strength: Chlorpromazine 50 mg, Trifluoperazine 5 mg and Benzhexol 2mg

4. Clinical particulars

4.1 Therapeutic indication

Trinicalm Forte is indicated for the management of schizophrenia in adults.

4.2 Posology and method of administration

Posology

Triniclam forte must be taken as directed by physician.

Method of administration

For oral use.

4.3 Contraindications

TRINICALM FORTE

• Hypersensitivity to the active substance or to any of the excipients.

• Do not use trifluoperazine in comatose patients, particularly if associated with other central nervous system depressants.

• Do not use in those with existing blood dyscrasias or known liver damage.

• Patients with uncontrolled cardiac decompensation should not be given trifluoperazine.

• Hypothyroidism

• Bone marrow depression

• Phaeochromocytoma

• Myasthenia gravis

• Risk of angle-closure glaucoma

• Risk of urinary retention related to urethroprostatic disorders

• History of agranulocytosis

• Dopaminergic antiparkinsonism agents

• Nursing mothers

• Citalopram, escitalopram.

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

4.4 Special warnings and precautions for use

Trifluoperazine:

Trifluoperazine' should be discontinued as the first sign of clinical symptoms of tardive dyskinesia and Neuroleptic Malignant Syndrome.

Patients on long-term phenothiazine therapy require regular and careful surveillance with particular attention to tardive dyskinesia and possible eye changes, blood dyscrasias, liver dysfunction and myocardial conduction defects, particularly if other concurrently administered drugs have potential effects in these systems.

Care should be taken when treating elderly patients, and the initial dosage should be reduced. Such patients can be especially sensitive, particularly to extrapyramidal and hypotensive effects. Patients with cardiovascular disease including arrhythmias should also be treated with caution. Because 'Trifluoperazine' may increase activity, care should be taken with patients who have angina pectoris. If an increase in pain is noted, the drug should be discontinued. Patients who have demonstrated bone marrow suppression or jaundice with a phenothiazine should not be re-exposed to 'Trifluoperazine' (or any trifluoperazine) unless in the judgement of the physician the potential benefits of treatment outweigh the possible hazard.

In patients with Parkinson's disease, symptoms may be worsened, and the effects of levodopa reversed. Since phenothiazines may lower the convulsive threshold, patients with epilepsy should be treated with caution, and metrizamide avoided. Although 'Trifluoperazine' has minimal anticholinergic activity, this should be borne in mind when treating patients with narrow angle glaucoma, myasthenia gravis or prostatic hypertrophy.

Nausea and vomiting as a sign of organic disease may be masked by the anti-emetic action of 'Trifluoperazine'.

Acute withdrawal symptoms including nausea, vomiting and insomnia have been described after abrupt cessation of high doses of antipsychotic drugs.

Recurrence of psychotic symptoms may also occur, and the emergence of involuntary movement disorders (such as akathisia, dystonia and dyskinesia) has been reported.

Therefore, a gradual withdrawal is advisable.

Phenothiazines should be used with care in extremes of temperature since they may affect body temperature control.

Cases of venous thromboembolism (VTE) have been reported with antipsychotic drugs. Since patients treated with antipsychotics often present with acquired risk factors for VTE, all possible risk factors for VTE should be identified before and during treatment with Trifluoperazine and preventive measures undertaken

Increased Mortality in Elderly people with Dementia

Data from two large observational studies showed that elderly people with dementia who are treated with antipsychotics are at a small increased risk of death compared with those who are not treated. There are insufficient data to give a firm estimate of the precise magnitude of the risk and the cause of the increased risk is not known.

Trifluoperazine is not licensed for the treatment of dementia-related behavioural disturbances.

Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine.

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

Benzhexol:

Anticholinergic medications, including benzhexol, should not be withdrawn abruptly in patients on long-term therapy, to avoid recurrence of the original symptoms and possible anticholinergic rebound. Prescribers should be aware that benzhexol may be the subject of abuse due to its euphoric or hallucinogenic properties.

Since atropine-like drugs may cause psychiatric symptoms such as confusion, delusion and hallucinations, benzhexol should be used with extreme caution in elderly patients.

As benzhexol may provoke or exacerbate tardive dyskinesia, it is not recommended for use in patients with this condition.

Since benzhexol has been associated with clinical worsening of myasthenia gravis, the drug should be avoided or used with great caution in patients with myasthenia gravis.

Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsoprtion or sucrase-maltase insufficiency should not take this medicine.

Chlorpromazine:

Blood Dyscrasias: All patients must be advised that, if they experience fever, sore throat or any other infection, they should inform their physician immediately and undergo a complete blood count. Treatment will be discontinued if any marked changes (hyperleucocytosis, granulocytopenia) are observed in the latter.

As agranulocytosis has been reported, regular monitoring of the complete blood count is recommended. The occurrence of unexplained infections or fever may be evidence of blood dyscrasia (see Section 4.8) and requires immediate haematological investigation.

Neuroleptic malignant syndrome: treatment must be interrupted in the event of unexplained hyperpyrexia since this can be one of the signs of neuroleptic malignant syndrome (pallor, hyperthermia, disorders of autonomic function, altered consciousness, muscle rigidity). Signs of autonomic instability, such as hyperhydrosis and irregular blood pressure, can precede the onset of hyperthermia and as such constitute premonitory signs of the syndrome. While this neuroleptic-related effect can be of idiosyncratic origin, certain risk factors such as dehydration and brain damage would seem to indicate a predisposition.

Chlorpromazine should be avoided in patients with hypothyroidism, phaeochromocytoma, myasthenia gravis and prostate hypertrophy. It should be avoided in patients known to be hypersensitive to phenothiazines or with a history of narrow angle glaucoma or agranulocytosis.

Acute withdrawal symptoms, including nausea, vomiting and insomnia, have very rarely have been reported following the abrupt cessation of high doses of neuroleptics. Relapse may also occur, and the emergence of extrapyramidal reactions has been reported. Therefore, gradual withdrawal is advisable.

In schizophrenia, the response to neuroleptic treatment may be delayed. If treatment is withdrawn, the recurrence of symptoms may not become apparent for some time.

Neuroleptic phenothiazines may potentiate QT interval prolongation which increases the risk of onset of serious ventricular arrhythmias of the torsade de pointes type, which is potentially fatal (sudden death). QT prolongation is exacerbated, in particular, in the presence of bradycardia, hypokalaemia, and congenital or acquired (i.e. drug induced) QT prolongation. If the clinical situation permits, medical and laboratory evaluations should be performed to rule out possible risk factors before initiating treatment with a neuroleptic agent and as deemed necessary during treatment.

Where clinically possible, the absence of any factors favouring the onset of ventricular arrhythmias should be ensured before administration:

• bradycardia less than 55 beats per minute;

• hypokalaemia;

• hypocalcaemia;

• hypomagnesaemia;

• starvation;

• alcohol abuse;

• concomitant therapy with other drugs to prolong QT interval;

• congenital long QT interval;

• ongoing treatment with any drug which could induce marked bradycardia (<55 beats per minute), hypokalaemia, intracardiac conduction depression or QT prolongation.

With the exception of emergencies, it is recommended that the initial work up of patients receiving a neuroleptic should include an ECG.

Except under exceptional circumstances, this drug must not be administered to patients with Parkinson's disease.

The concomitant use of chlorpromazine with lithium, other QT prolongation agents, and dopaminergic antiparkinsonism agents is not recommended.

The onset of paralytic ileus, potentially indicated by abdominal bloating and pain, must be treated as an emergency.

Cases of venous thromboembolism (VTE) sometimes fatal, have been reported with antipsychotic drugs. Since patients treated with anti-psychotics often present with acquired risk factors for VTE, all possible risk factors for VTE should be identified before and during treatment with Chlorpromazine and preventive measures undertaken.

Stroke: In randomised clinical trials versus placebo performed in a population of elderly patients with dementia and treated with certain atypical antipsychotic drugs, a 3-fold increase of the risk of cerebrovascular events has been observed. The mechanism of such risk increase is not known. An increase in the risk with other antipsychotic drugs or other populations of patient cannot be excluded. Chlorpromazine should be used with caution in patients with stroke risk factors.

Elderly Patients with Dementia: Elderly patients with dementia-related psychosis treated with antipsychotic drugs are at an increased risk of death. Analyses of seventeen placebo-controlled trials (modal duration of 10 weeks), largely in patients taking atypical antipsychotic drugs, revealed a risk of death in drug-treated patients of between 1.6 to 1.7 times the risk of death in placebo-treated patients. Over the course of a typical 10-week controlled trial, the rate of death in drug-treated patients was about 4.5% compared to a rate of about 2.6% in the placebo group. Although the cause of death in clinical trials with atypical antipsychotics were varied, most of the deaths appeared to be either cardiovascular (e.g., heart failure, sudden death) or infectious (e.g., pneumonia) in nature. Observational studies suggest that, similar to atypical antipsychotic drugs, treatment with conventional antipsychotic drugs may increase mortality. The extent to which the findings of increased mortality in

observational studies may be attributed to the antipsychotic drug as opposed to some characteristic(s) of the patient is not clear.

As with all anti-psychotic drugs, Chlorpromazine should not be used alone where depression is predominant. However, it may be combined with antidepressant therapy to treat those conditions in which depression and psychosis coexist.

Chlorpromazine Tablets are not licensed for the treatment of dementia-related behavioural disturbances.

Because of the risk of photosensitisation, patients should be advised to avoid exposure to direct sunlight. In those frequently handling preparations of phenothiazines, the greatest care must be taken to avoid contact of the drug with the skin.

Hyperglycaemia or intolerance to glucose has been reported in patients treated with Chlorpromazine Tablets. Patients with an established diagnosis of diabetes mellitus or with risk factors for the development of diabetes who are started on Chlorpromazine Tablets should get appropriate glycaemic monitoring during treatment.

• The following populations must be closely monitored after administration of chlorpromazine.

o epileptics, since chlorpromazine may lower the seizure threshold. Treatment must be discontinued if seizures occur.

o elderly patients presenting with heightened susceptibility to orthostatic hypotension, sedation and extrapyramidal effects; chronic constipation (risk of paralytic ileus), and potentially prostatic hypertrophy. It should be used with caution particularly during very hot or cold weather (risk of hyper-, hypothermia).

o patients presenting with certain forms of cardiovascular disease, since this class of drug has quinidine-like effects and can induce tachycardia and hypotension.

o patients with severe liver and/or renal failure because of the risk of accumulation.

• Patients on long-term treatment should receive regular ophthalmological and haematological examinations.

• Patients are strongly advised not to consume alcohol and alcohol-containing drugs throughout treatment (see Section 4.5).

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

• This medicine contains less than 1 mmol sodium (23 mg) per tablet, that is to say essentially, 'sodium free'.

• Since there is a potential to impact on cognitive function, children should undergo a yearly clinical examination to evaluate learning capacity. The dosage should be adjusted regularly as a function of the clinical status of the child.

4.5 Drugs interactions

Chlorpromazine:

Adrenaline must not be used in patients overdosed with Chlorpromazine.

Antichlolinergic drugs may reduce the antipsychotic effect of Chlorpromazine and the mild anticholinergic effect of Chlorpromazine may be enhanced by other anticholinergic drugs possibly leading to constipation, heat stroke etc.

The action of some drugs may be opposed by Chlorpromazine; these include amphetamine, levodopa, clonidine, guanethidine and adrenaline.

Increases or decreases in the plasma concentrations of a number of drugs e.g. propranolol Phenobarbital have been observed but were not of clinical significance.

Simultaneous administration of deferoxamine and prochlorperazine has been observed to induce a transient metabolic encephalopathy characterised by loss of consciousness for 48-72 hours. It is possible this may occur with Chlorpromazine since it shares many of the pharmacological properties of prochlorperazine.

There is an increased risk of agranulocytosis when neuroleptics are used concurrently with drugs with myelosuppressive potential, such as carbamazepine or certain antibiotics and cytotoxics.

Combinations contraindicated

Dopaminergics (quinagolide, cabergoline), not including dopaminergic antiparkinsonism agents, are contraindicated (see Section 4.3): reciprocal antagonism of the dopaminergic agent and neuroleptic. Citalopram and escitalopram are contraindicated.

Combinations not recommended

Dopaminergic antiparkinsonism agents (amantadine, bromocriptine, cabergoline, levodopa, lisuride, pergolide, piribedil, ropinirole) are not recommended: reciprocal antagonism of the antiparkinsonism agent and neuroleptic (see Section 4.4). Neuroleptic-induced extrapyramidal syndrome should be treated with an anticholinergic rather than a dopaminergic antiparkinsonism agent (dopaminergic receptors blocked by neuroleptics).

Levodopa: reciprocal antagonism of levodopa and the neuroleptic. In Parkinson's patients, it is recommended to use the minimal doses of each drug.

QT prolonging drugs: there is an increased risk of arrhythmias when chlorpromazine is used with concomitant QT prolonging drugs (including certain antiarrhythmics and other antipsychotics including sultopride) and drugs causing electrolyte imbalance (see Section 4.4).

Alcohol: alcohol potentiates the sedative effect of neuroleptics. Changes in alertness can make it dangerous to drive or operate machinery. Alcoholic beverages and medication containing alcohol should be avoided (see Section 4.4).

Lithium (high doses of neuroleptics): concomitant use can cause confusional syndrome, hypertonia and hyperreflexivity, occasionally with a rapid increase in serum concentrations of lithium (see Section 4.4). There have been rare cases of

neurotoxicity Lithium can interfere with the absorption of neuroleptic agents.

Combinations requiring precautions

Antidiabetic agents: concomitant administration of high chlorpromazine doses (100 mg/day), and antidiabetic agents can lead to an increase in blood sugar levels (decreased insulin release). Forewarn the patient and advise increased self-monitoring of blood and urine levels. If necessary, adjust the antidiabetic dosage during and after discontinuing neuroleptic treatment.

Topical gastrointestinal agents (magnesium, aluminium and calcium salts, oxides and hydroxides): decreased GI absorption of phenothiazine neuroleptics. Do not administer phenothiazine neuroleptics simultaneously with topical GI agents (administer more than 2 hours apart if possible).

CYP1A2 inhibitors

Administration of chlorpromazine with CYP1A2 inhibitors, in particular strong or moderate inhibitors may lead to an increase of chlorpromazine plasma concentrations. Therefore, patients may experience a chlorpromazine dose-dependent adverse drug reaction.

There is a possible pharmacokinetic interaction between inhibitors of CYP2D6, such as phenothiazines and CYP2D6 substrates.

Combinations to be taken into consideration

Antihypertensive agents: potentiation of the antihypertensive effect and risk of orthostatic hypotension (additive effects). Guanethidine has adverse clinically significant interactions documented.

Atropine and other atropine derivatives: imipramine antidepressants, histamine H1-receptor antagonists, anticholinergic, antiparkinsonism agents, atropinic antispasmodics, disopyramide: build up of atropine-associated adverse effects such as urinary retention, constipation dry mouth and heat stroke etc.

Other CNS depressants: morphine derivatives (analgesics, antitussives and substitution treatments), barbiturates, benzodiazepines, anxiolytics other than benzodiazepines, hypnotics, sedative anti-depressants, histamine H1 receptor antagonists, central antihypertensive agents increased central depression. Changes in alertness can make it dangerous to drive or operate machinery.

Trifluoperazine

Potentiation may with CNS depressants such as alcohol, hypnotics, anaesthetics and strong analgesics, or with antihypertensives or other drugs with hypotensive activity, anticholoinergics or antidepressants. Phenothiazines may antagonise the action of guanethidine and levodopa. Trifluoperazine may aggravate Parkinsonism and antagonise the action of levodopa. They may lower the convulsive threshold. Hence patients with epilepsy should be treated with caution.

Desferrioxamine should not be used in combination with 'Trifluoperazine', since prolonged unconsciousness has occurred after combination with the related

prochlorperazine.

Trifluoperazine may diminish the effect of oral anticoagulants.

The combination of lithium and trifluoperazine should only be used with extreme caution. It has been associated with an increased risk of severe extrapyramidal effects and neurotoxicity, with sleep walking described in some patients. However, it has also been noted that serum levels of phenothiazines can be reduced to non-therapeutic concentrations by concurrent lithium administration.

Antacids can reduce the absorption of phenothiazines.

Benzhexol:

Monoamine oxidase inhibitors (MAOI's), antihistamines, disopyramide, phenothiazines and tricyclic antidepressants increase the side effects of blurred vision and dry mouth, constipation, urinary retention. MAOI's, amantidine and some tricyclic antidepressents may also cause excitation, confusion and hallucination.

4.6 Use in special population (such as pregnant women, lactating women, paediatric patients, geriatric patients etc.)

Pregnancy

Trifluoperazine

Trifluoperazine Tablets have been available since 1958. There are some animal studies that indicate a teratogenic effect, but results are conflicting. There is no clinical evidence (including follow-up surveys in over 800 women who had taken low-dose Trifluroperazine during pregnancy) to indicated that Trifluroperazine has a teratogenic effect on man. Nevertheless, drug treatment should be avoided in pregnancy unless considered essential, especially during the first trimester.

Neonates exposed to antipsychotics (including Trifluoperazine) 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.

Chlorpromazine

There is inadequate evidence of the safety of chlorpromazine in human pregnancy. There is evidence of harmful effects in animals, so like other drugs, it should be avoided in pregnancy unless the physician considers it essential. It may occasionally prolong labour and at such a time should be withheld until the cervix is dilated 3-4cm. Possible adverse effects on the foetus include lethargy or paradoxical hyperexcitability, tremor and low Apgar score.

A large amount of exposure to chlorpromazine during pregnancy did not reveal any teratogenic effect.

It is advised to keep an adequate maternal psychic balance during pregnancy in order to avoid decompensation. If a treatment is necessary to ensure this balance, the treatment should be started or continued at effective dose all through the pregnancy.

Neonates exposed to antipsychotics (including chlorpromazine) 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, bradycardia, tachycardia, feeding disorder, meconium ileus, delayed meconium passage, abdominal bloating. Consequently, newborns should be monitored carefully in order to plan appropriate treatment.

Benzhexol

There is inadequate information regarding the use of benzhexol in pregnancy. Reported animal studies are insufficient with regard to effects on pregnancy, embryonal/foetal development, parturition and postnatal development. The potential risk for humans is unknown. Benzhexol should not be used during pregnancy unless clearly necessary.

Breast-feeding

Chlorpromazine being excreted in milk, breast-feeding is not recommended during treatment.

Trifluroperazine crosses the placenta and passes into the milk of lactating dogs; breast feeding should only be allowed at the discretion of the physician.

It is unknown whether benzhexol is excreted in human breast milk. The excretion of benzhexol in milk has not been studied in animals. Infants may be very sensitive to the effects of antimuscarinic medications. Benzhexol should not be used during breast feeding.

Fertility

A decrease in fertility was observed in female animals treated with chlorpromazine. In male animals data are insufficient to assess fertility.

In humans, because of the interaction with dopamine receptors, chlorpromazine may cause hyperprolactinaemia which can be associated with impaired fertility in women. In men, data on consequences of hyperprolactinaemia are insufficient with regard to fertility.

4.7 Effects on ability to drive and use machines

The attention of patients, particularly drivers and machine operators, should be drawn to the risk of drowsiness with this medication especially at the start of treatment. Patients should be warned of the possibility of disturbances of the central nervous system.

4.8 Undesirable effects

Trifluoperazine

The following undesirable effects may occur with the use of Trifluoperazine in the following requencies:

Rare (≥1/10,000 to <1/1,000);

Very rare (<1/10,000)

Not known (cannot be estimated from the available data).

The following effects have been reported and are listed below by body system:

System organ class	Frequency	Undesirable effects
Blood and lymphatic system disorders	Very rare	Blood dyscrasias[6] such as agranulocytosis, pancytopenia, leucopenia and thrombocytopenia
Endocrine disorders	Not known	Hyperprolactinaemia[1], galactorrhoea[1], amenorrhoea[1], gynaecomastia[1]
Metabolism and nutrition disorders	Not known	Anorexia, weight gain
Psychiatric disorders	Not known	Unpleasant symptoms[2], Confusion
Nervous system disorders	Rare	Extrapyramidal symptoms[3], Neuroleptic malignant syndrome[4]
	Not known	Tardive dyskinesia[5], drowsiness, dizziness, transient restlessness, insomnia
Eye disorders	Very rare	Retinopathy, lenticular opacities
	Not known	Blurred vision
Cardiac disorders	Very rare	Tachycardia
	Rare	Serious arrhythmias
Vascular disorders	Not known	Mild postural hypotension, venous thromboembolism, pulmonary

		embolism, deep vein thrombosis
Gastrointestinal disorders	Rare	Extrapyramidal symptoms
	Not known	Dry mouth
	Very rare	Constipation
Hepatobiliary disorders	Very rare	Cholestatic jaundice
Skin and subcutaneous tissue disorders	Not known	Photosensitivity reactions
	Very rare	Skin pigmentation
Musculoskeletal and connective tissue disorders	Not known	Muscular weakness
Renal and urinary disorders	Very rare	Urinary hesitancy and retention
Pregnancy, puerperium and perinatal conditions	Not known	Drug withdrawal syndrome neonatal
General disorders and administration site conditions	Not known	Lassitude, oedema, Withdrawal reactions
	Very rare	Hyperpyrexia
Investigations	Rare	ECG changes with prolongation of the QT interval and T-wave changes

Adverse reactions tend to be dose-related and to disappear.

[1]Hyperprolactinaemia may occur at higher dosages with associated effects such as galactorrhoea, amenorrhoea or gynaecomastia; certain hormone-dependent breast neoplasms may be affected.

[2]Trifluoperazine even at low dosage may cause unpleasant symptoms of being dulled or, paradoxically, of being agitated.

[3]Extrapyramidal symptoms are rare at oral daily dosages of 6mg or less; they are considerably more common at higher dosage levels. These symptoms include parkinsonism; akathisia, with motor restlessness and difficulty in sitting still; and acute dystonia or dyskinesia, which may occur early in treatment and may present with torticollis, facial grimacing, trismus, tongue protrusion and abnormal eye movements including oculogyric crises. These effects are likely to be particularly severe in children. Such reactions may often be controlled by reducing the dosage or by stopping medication. In more severe dystonic reactions, an anticholinergic antiparkinsonism drug should be given.

[4]The neuroleptic malignant syndrome is a rare but occasionally fatal complication of treatment with various neuroleptic drugs, and is characterised by hyperpyrexia, muscle rigidity, altered consciousness and autonomic instability. Intensive symptomatic treatment, following discontinuation of 'Trifluoperazine', should include cooling. Intravenous dantrolene has been suggested for muscle rigidity.

[5]Tardive dyskinesia of the facial muscles, sometimes with involuntary movements of the extremities, has occurred in some patients on long-term, high-dosage and, more rarely, low-dosage phenothiazine therapy, including 'Trifluoperazine'. Symptoms may appear for the first time either during or after a course of treatment; they may become worse when

treatment is stopped. The symptoms may persist for many months or even years, and while they gradually disappear in some patients, they appear to be permanent in others. Patients have most commonly been elderly, female or with organic brain damage. Particular caution should be observed in treating such patients. If tardive dyskinesia occurs, 'Trifluoperazine' should be discontinued. Anticholinergic antiparkinsonism agents may aggravate the condition. Since the occurrence of tardive dyskinesia may be related to length of treatment and total cumulative dosage, 'Trifluoperazine' should be given for as short a time and at as low a dosage as possible.

[6]Signs of persistent infection should be investigated.

Chlorpromazine

The following undesired events, listed by body system, have been reported with the following frequencies: very common (≥1/10), common (≥1/100 to <1/10), uncommon (≥1/1000 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).

System organ class	**Very common (≥1/10)**	**Common (≥1/100 to <1/10)**	**Not known (cannot be estimated from available data)**
Blood and lymphatic system disorders			Agranulocytosis Leukopenia
Immune system disorders			Systemic lupus erythematosus Antinuclear antibody positive[1] Bronchospasm Anaphylactic reactions
Endocrine disorders		Hyperprolactinaemia Amenorrhoea	Galactorrhoea Gynaecomastia Erectile dysfunction Impotence Female sexual arousal disorder
Metabolism and nutrition disorders	Weight increased	Glucose tolerance impaired (see Section 4.4)	Hyperglycaemia (see Section 4.4) Hypertriglyceridaemia Hyponatraemia Inappropriate antidiuretic hormone secretion
Psychiatric disorders		Anxiety	Lethargy Mood altered
Nervous system disorders	Sedation[2] Somnolence[2]	Hypertonia Convulsion	Torticollis Oculogyric crisis

	Dyskinesia (Acute dystonias or dyskenias, unusally transitory are more common in children and young adults and usually occur within the first 4 days of treatment or after dosage increases) Tardive dyskinesia[3] Extrapyramidal disorder Akathisia often after large initial dose		Trismus Akinesia Hyperkinesia Neuroleptic malignant syndrome (hyperthermia, rigidity, autonomic dysfunction and altered consciousness) (see Section 4.4.) Parkinsonism (more common in adults and the elderly. It usually develops after weeks or months of treatment) to include tremor, rigidity or other features of Parkinsonism
Eye disorders			Accommodation disorder[4] Deposit eye[5] Ocular changes[7]
Cardiac disorders		Electrocardiogram QT Prolonged (as with other neuroleptics) (see Section 4.4) , ST depression, U-Wave and T-Wave changes	Cardiac arrhythmias including Ventricular arrhythmia, a-v block, Ventricular fibrillation Ventricular tachycardia Torsade de pointes Cardiac arrest has been reported during neuroleptic phenothiazine therapy, possibly related to dosage. Pre-existing cardiac disease, old afe, hypokalaemia and concurrent tricyclic antidepressants may predispose. Sudden death/sudden cardiac death (with possible causes of cardiac origin as well as cases of unexplained sudden death, in patients receiving neuroleptic

			phenothiazines) (see Section 4.4)
Vascular disorders	Orthostatic hypotension (Elderly or volume depleted subjects are particularly susceptible: it is more likely to occur after intramuscular administration).		Embolism venous Pulmonary embolism (sometimes fatal) Deep vein thrombosis (see Section 4.4)
Respiratory, thoracic and mediastinal disorders			Respiratory depression Nasal stuffiness
Gastrointestinal disorders	Dry mouth Constipation (see Section 4.4)		Colitis ischaemic Ileus paralytic (see Section 4.4) Intestinal perforation (sometimes fatal) Gastrointestinal necrosis (sometimes fatal) Necrotising colitis (sometimes fatal) Intestinal obstruction
Hepatobiliary disorders			Jaundice cholestatic[6] Hepatocellular Liver injury[6] Cholestatic liver injury[6] Mixed liver injury
Skin and subcutaneous tissue disorders			Dermatitis allergic Angioedema Contact skin sensitisation may occur rarely in those frequently handling preparation of chlorpromazine (see section 4.4) Skin rashes Urticaria Photosensitivity reaction
Renal and urinary disorders			Urinary retention[4]

Pregnancy, puerperium and perinatal conditions			Drug withdrawal syndrome neonatal (see Section 4.6)
Reproductive system and breast disorders			Priapism
General disorders and administration site conditions			Temperature regulation disorder Insomnia Agitation

[1] may be seen without evidence of clinical disease

[2] particularly at the start of treatment

[3] particularly during long term treatment; may occur after the neuroleptic is withdrawn and resolve after reintroduction of treatment or if the dose is increased

[4] ilinked to anticholinergic effects

[5] in the anterior segment of the eye caused by accumulation of the drug but generally without any impact on sight

[6] A premonitory sign may be a sudden onset of fever after one to three weeks of treatment followed by the development of jaundice. Chlorpromazine jaundice has the biochemical and other characteristics of obstructive (cholestatic) jaundice and is associated with obstructions of the canaliculi by bile thrombi; the frequent presence of an accompanying eosinophilia indicates the allergic nature of this phenomenon. Liver injury, sometimes fatal, has been reported rarely in patients treated with chlorpromazine. Treatment should be withheld on the development of jaundice.

[7] The development of a metallic greyish-mauve coloration of exposed skin has been noted in some individuals, mainly females, who have received chlorpromazine continuously for long periods (four to eight years).

Benzhexol Hydrochloride

5 to 10% of patients cannot tolerate fully effective doses. Side-effects such as dry mouth and blurred vision are not uncommon. Dizziness, mild nausea or nervousness may be experienced by 30 to 50 per cent of patients on benzhexol. The reactions may be less pronounced as treatment continues. Suppurative parotitis skin rashes dilation of the colon, paralytic ileus, and delusions and hallucinations occur rarely. Patients with arteriosclerosis or with idiosyncrasy may show mental confusion, agitation nausea and vomiting. Potential side-effects associated with the use of any atropine-like drugs include constipation, drowsiness, urinary hesitancy or retention, tachycardia, dilation of the pupil, increased intra-ocular tension, weakness, and headache. Occasionally giddiness and staggering occurs. Large doses may cause cerebral stimulation. When intolerable side- effects occur with doses that fail to control the motor symptoms of the disease, other drugs must be employed along with benzhexol, or the agents must be withdrawn. Caution should be observed when

benzhexol is administered to patients with prostatic enlargement, coronary insufficiency, or cardiac failure. Tachycardia may result from vagal inhibition and induce angina of effort in patients with coronary heart disease. The effects of benzhexol and other parasympatholytics may be enhanced by the concomitant administration of other drugs with parasympatholytic properties, such as some antihistamines and phenothiazines and tricyclic antidepressants.

Reporting of side effects

If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via any point of contact of Torrent Pharma available at:

http://www.torrentpharma.com/index.php/site/info/adverse_event_reporting

By reporting side effects, you can help provide more information on the safety of this medicine.

4.9 Overdose

Trifluoperazine

Symptoms

Signs and symptoms will be predominantly extrapyramidal; hypotension may occur.

Management

Treatment consists of gastric lavage together with supportive and symptomatic measures. Do not induce vomiting. Extrapyramidal symptoms may be treated with an anticholinergic antiparkinsonism drug. Treat hypotension with fluid replacement; if severe or persistent, noradrenaline may be considered. Adrenaline is contra-indicated and dobutamine should be considered.

Chlorpromazine

Toxicity and treatment of overdosage: Symptoms of chlorpromazine overdosage include drowsiness or loss of consciousness, hypotension, tachycardia, E.C.G. changes, ventricular arrhythmias and hypothermia, Parkinsonism, convulsions and coma. Severe extra-pyramidal dyskinesias may occur.

Treatment should by symptomatic with continuous respiratory and cardiac monitoring (risk of prolonged QT interval) until the patient's condition resolves.

If the patient is seen sufficienly soon (up to 6 hours) after ingestion of a toxic dose, gastric lavage may be attempted. Pharmacological induction of emesis is unlikely to be of any use. Activated charcoal should be given. There is no specific antidote. Treatment is supportive.

Generalised vasodilatation may result in circulatory collapse; raising the patient's legs may suffice, in severe cases, volume expansion by intravenous fluids may be needed; infusion fluids should be warmed before administration in order not to aggravate hypothermia.

Positive inotropic agents such as dopamine may be tried if fluid replacement is insufficient to correct the circulatory collapse. Peripheral vasoconstriction agents are not generally recommended; avoid use of adrenaline.

Ventricular or supraventricular tachyarrhythmia's usually respond to restoration of normal body temperature and correction of circulatory or metabolic disturbances. If persistent or life threatening, appropriate antiarrhythmic therapy may be considered. Avoid lidocaine and, as far as possible, long acting antiarrhythmic drugs.

Pronounced central nervous system depression requires airway maintenance or, in extreme circumstances, assisted respiration. Severe dystonic reactions usually respond to procyclidine (5-10 mg) or orphenedrine (20-40 mg) administered intramuscularly or intravenously. Convulsions should be treated with intravenous diazepam.

Neuroleptic malignant syndrome should be treated with cooling. Dantrolene sodium may be tried.

Benzhexol Hydrochloride:

Tachycardia, rapid or stertorous respiration, hyperpyrexia, restlessness, confusion and excitement, and hallucinations passing into delirium. In case of overdosage, treatment is symptomatic and supportive.

5. Pharmacological properties

5.1 Mechanism of Action

Trifluoperazine

Pharmacotherapeutic group: Phenothiazine typical antipsychotics

A piperazine, phenothiazine tranquiliser with potent anti-psychotic, anxiolytic and antiemetic activity.

Chlorpromazine

Pharmacotherapeutic Group: Antipsychotics. Chlorpromazine is a phenothiazine neuroleptic.

Chlorpromazine has depressant actions on the Central Nervous System, with alpha-adrenergic blocking and anticholinergic activities. It inhibits Dopamine and Prolactin release-inhibitory factor, thus stimulating the release of Prolactin. It increases the turnover of Dopamine in the brain.

Benzhexol Hydrochloride

Benzhexol hydrochloride resembles atropine in its peripheral actions on autonomic effector cells, having an inhibitory effect on the parasympathetic nervous system.

5.2 Pharmacodynamic properties

Trifluoperazine

A piperazine, phenothiazine tranquiliser with potent anti-psychotic, anxiolytic and antiemetic activity, and a pharmacological profile of moderate sedative and hypotensive properties and fairly pronounced tendency to cause extra pyramidal reactions.

Chlorpromazine

It has anti-emetic, anti-puritic, serotonin-blocking and weak anti-histamine properties and slight ganglion blocking activity. It inhibits the heat regulating centre in the brain, and is analgesic and can relax skeletal muscle.

Due to its action on the autonomic system it produces vasodilatation, hypotension and tachycardia.

Salivary and gastric secretions are reduced.

Benzhexol Hydrochloride

It is one half as active as atropine on smooth muscle and one third as active as a mydriatic. It possesses about one tenth the potency of atropine on salivary glands and cardiac-vagal mechanisms. On the C.N.S., the actions of benzhexol likewise resembles those of atropine.

5.3 Pharmacokinetic properties

Trifluoperazine

Absorption

Trifluoperazine is well absorbed from the gastrointestinal tract but is subject to considerable first-pass metabolism in the gut wall.

Owing to the first-pass effect, plasma concentrations following oral administration are much lower than those following intramuscular injection. Moereover, there is very wide intersubject variation in plasma concentration.

Biotransformation

Paths of metabolism include hydroxylation and conjunction with glucuronic acid, N-oxidation, oxidation of a sulphur atom, and de-alkylation.

Distribution

It is extensively bound to plasma proteins. It is widely distributed in the body and crosses the blood-brain barrier to achieve higher concentrations in the brain than in the plasma.

Elimination

It is also extensively metabolised in the liver and is excreted in the urine and faeces in the form of numerous active and inactive metabolies; there is evidence of enterohepatic recycling.

Together with its metabolites, it crosses the placental barrier and is excreted in the milk. Inactive ingredients in the tablets include sucrose.

Chlorpromazine

Chlorpromazine is rapidly and widely distributed in the body. It is metabolised in the liver and excreted in the urine and bile. Whilst plasma concentration of chlorpromazine itself rapidly declines excretion of chlorpromazine metabolites is very slow. The drug is highly bound to plasma protein. It readily diffuses across the placenta. Small quantities have been detected in milk from treated women. Children require smaller dosages per kg than adults.

Benzhexol is well absorbed from the gastro-intestinal tract.

6. Nonclinical properties

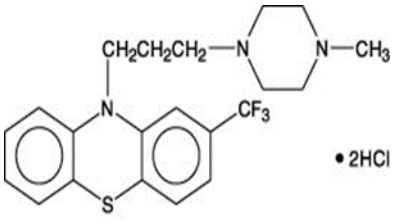
6.1 Animal Toxicology or Pharmacology

Preclinical studies undertaken in dogs have demonstrated that trifluoperazine crosses the placenta and passes into the milk of lactating dogs.

7. Description

Trifluoperazine is chemicaly 10-H –Phenothiazine, 10-[3-(4-methyl-1-piperazinyl)propyl]-2-(triflurомethyl)-, dihyrochloride.

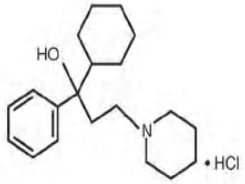
The structure formula is:



$C_{21}H_{24}F_3N_3S \bullet 2HCl$ M.W. 480.42

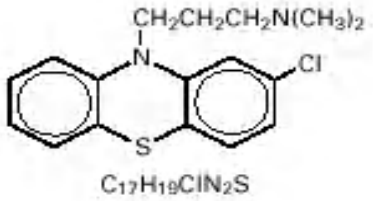
Benzhexol Hydrochloride is a white or slightly off white, crystalline powder, having not more than a very faint odor.

Benzhexol Hydrochloride is the substituted piperidine salt, 1-piperidinepropanol,α-cyclohexyl-α-phenyl-,hydrochloride,(±)-. The structural formula is:



$C_{20}H_{31}NO \bullet HCl$ M.W. = 337.93

Chlorpromazine is 10-(3-dimethylaminopropyl)-2-chlorphenothiazine, a dimethylamine derivative of phenothiazine. It is present in oral and injectable forms as the hydrochloride salt, and in the suppositories as the base.



$C_{17}H_{19}ClN_2S$

Descrption of formulation:

Purple coloured, round, biconvex, film coated tablets

8. Pharmaceutical particulars

8.1 Incompatibilities

Not applicable.

8.2 Shelf-life

Do not use later than the date of expiry.

8.3 Packaging information

TRINICALM FORTE is available in blister pack of 15 tablets

8.4 Storage and handing instructions

Keep in dry place, protect from light.

9. Patient Counselling Information

TRINICALM FORTE

(Trifluoperazine + Benzhexol Hydrochloride + Chlorpromazine tablets)

- Read all of this leaflet carefully before you start taking this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 9.4.

What is in this leaflet

9.1 What TRINICLAM FORTE is and what it is used for

The active substances of TRINICLAM FORTE is Trifluoperazine + Benzhexol Hydrochloride + Chlorpromazine tablets

Trinicalm Forte is used for the management of schizophrenia in adults.

9.2 What you need to know before you take TRINICLAM FORTE

Do not use TRINICLAM FORTE:

• You know that you are allergic TRINICLAM FORTE or any of the

other ingredients of TRINICLAM FORTE.

• You are suffering from liver problems, blood disorders, inability of the heart to

maintain adequate circulation causing breathlessness and swelling of the ankles.

• You have previously had to stop taking other medicines for psychiatric problems like Trifluoperazine (known as phenothiazines) because they have affected your blood cells or caused jaundice (yellowing of the skin and eyes). Ask your doctor about this.

• You are having a special X-ray examination of the brain or spinal cord involving a chemical called metrizamide (your doctor will be able to help you).

• have a low number of blood cells (bone marrow depression)

• have increased pressure in the eye (glaucoma)

• are taking a dopaminergic antiparkinsonism drug

• are breast-feeding

• are taking citalopram or escitalopram

• have a history of low white blood cell count

• have urine retention due to a prostate disorder

Warnings and precautions

Talk to your doctor or pharmacist before taking TRINICLAM FORTE Tablets if you:

● or someone else in your family has a history of blood clots, as medicines like these have been associated with formation of blood clots

● have liver or kidney disease

● have epilepsy or have had fits (seizures)

● have Parkinson's disease

● have hypothyroidism (reduced activity of the thyroid gland)

● have heart disease such as heart failure

● have ever had a stroke

● have myasthenia gravis (a condition where muscles become easily tired and weak leading to difficulty breathing)

● have phaeochromocytoma (high blood pressure due to a tumour near the kidney)

Other medicines and TRINICLAM FORTE

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines, including medicines bought without a prescription.

This is because Chlorpromazine Tablets can affect the way some other medicines work. Also some medicines can affect the way Chlorpromazine Tablets work.

- In particular, tell your doctor or pharmacist if you are taking any of the following:
- medicines for indigestion and heartburn (antacids)
- medicines for diabetes
- medicines for high blood pressure or prostate problems such as doxazosin
- and terazosin
- medicines for Parkinson's disease such as levodopa
- medicines for fits (epilepsy) such as carbamazepine or phenobarbital
- medicines to control your heartbeat such as amiodarone, disopyramide or
- quinidine
- medicines to help you sleep (sedatives)
- medicines for depression
- other medicines used to calm emotional and mental problems such as
- olanzapine or prochlorperazine.

Please tell your doctor or pharmacist if you are taking or have recently taken any other medicines, including medicines obtained without a prescription. The effects of these medicines may change, especially if you are taking:

- sleeping tablets.
- anaesthetics used prior to surgery.
- strong pain killers (e.g. codeine).
- medicines which result in lowering of blood pressure (e.g. guanethidine).
- anticholinergic medicines used to reduce saliva and lung secretions (e.g.
- atropine, procyclidine).
- antidepressants (e.g. other phenothiazines, lithium).
- medicines for fits (anticonvulsants).
- medicines for Parkinson's disease (e.g. levodopa).
- blood thinning medicines (anticoagulants such as warfarin).
- medicines used to treat iron poisoning (desferrioxamine).
- antacids used to treat indigestion.
- medicines for psychiatric conditions (neuroleptics)

Pregnancy and breast-feeding

Do not take Trifluoperazine Tablets if you are pregnant, think you may be pregnant or are planning to become pregnant or while breast feeding, unless your doctor decides that treatment is essential.

It is particularly important not to take Trifluoperazine Tablets during the first three months of pregnancy.

The following symptoms may occur in newborn babies, of mothers that have used Trifluoperazine in the last trimester (last three months of their pregnancy): shaking, muscle stiffness and/or weakness, sleepiness, agitation, breathing problems and difficulty in feeding. If your baby develops any of these symptoms you may need to contact your doctor.

The following symptoms may occur in newborn babies of mothers that have used Chlorpromazine in the last trimester (last three months) of their pregnancy: shaking, muscle stiffness and/or

weakness, sleepiness, agitation, breathing problems and difficulty in feeding. If your baby develops any of these symptoms you may need to contact your doctor.

Do not breast-feed if you are being given Chlorpromazine. This is because small amounts may pass into the mother's milk. If you are breast-feeding or planning to breast-feed talk to your doctor or pharmacist before taking this medicine.

Chlorpromazine may make it difficult for a woman to get pregnant due to it reducing her fertility.

Driving and using machines

Do not drive or use tools or machines if this medicine makes you feel drowsy or if it has affected your eyesight

9.3 How to take TRINICLAM FORTE

Always take Trifluoperazine Tablets exactly as your doctor has told you. You should check with your doctor or pharmacist if you are not sure.

Swallow the tablets with a glass of water. The tablets can be taken with or without food.

Your doctor will decide on a suitable dose depending on your condition.

Take special care with Trifluoperazine Tablets and tell your doctor if you

are:

• if you or any member of your family is suffering from any disease involving

the heart and blood vessels (cardiovascular disease) including chest pain

(angina) and irregular heart beats.

• suffering from a brain disorder causing tremors, rigidity and slowing of

movement (Parkinson's disease).

• suffering from fits (epilepsy).
• suffering from an eye disease called narrow angle glaucoma which causes increased pressure inside the eye, abnormal muscle weakness (Myasthenia gravis) or enlargement of prostate gland.
• exposed to extremes in temperature as this medicine can affect body temperature control.
• an elderly person.
• if you suffer from loss of cognitive (memory, language, intelligence) ability - dementia.
• if you or someone else in your family has a history of blood clots, as medicines like these have been associated with formation of blood clots.
• you have had a stroke or you have any of the following that can increase your risk of having a stroke.
• a heart attack.
• a TIA (transient ischaemic attack). This is a type of stroke where symptoms last less than 24 hours.
• an artificial heart valve.
• uncontrolled high blood pressure.
• diabetes.
• high cholesterol.
• a family history of strokes.
• you smoke.
• you drink excess alcohol (this tends to weaken blood vessels and can raise blood pressure).

If you take more TRINICLAM FORTE than you should

Talk to a doctor or go to hospital straight away. Take the medicine pack with you a so the doctor knows what you have taken.

Signs of overdose may include drowsiness, low body temperature, low blood pressure, twisting your limbs, stiffness, shaking, unusual heart beats and coma.

If you forget to take TRINICLAM FORTE

Do not take a double dose (two doses at the same time) to make up for a forgotten dose. Skip the missed dose then go on as before.

If you stop taking TRINICLAM FORTE

Keep taking TRINICLAM FORTE until your doctor tells you to stop. The doctor will lower your dose gradually. If you stop taking the

medicine suddenly you may get withdrawal symptoms. Signs include:

● feeling or being sick and difficulty sleeping (insomnia)

● your original symptoms becoming worse

● movements that you cannot control.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

9.4 Possible side effects

Trifluoperazine:

Blood clots in the veins especially in the legs (symptoms include swelling, pain and redness in the leg), which may travel through blood vessels to the lungs causing chest pain and difficulty in breathing. If you notice any of these symptoms seek medical advice immediately.

Like all medicines, Trifluoperazine Tablets can sometimes cause side effects, although not everybody gets them.

Stop taking Trifluoperazine Tablets immediately and call your doctor if you experience signs of allergic reaction.

Signs of an allergic reaction include a rash, swallowing or breathing problems, swelling of your lips, face, throat or tongue.

Tell your doctor straight away if you notice any of the following serious side effects:

• Rarely patients may develop Neuroleptic Malignant Syndrome. This causes a high temperature, rigid muscles, drowsiness, occasional loss of consciousness, and requires emergency admission to hospital for treatment.

• If you have chest pain (angina) and your pain is getting worse.

• Rarely, Trifluoperazine Tablets can affect certain types of breast cancers or lead to breast enlargement in men or to inappropriate milk production or altered menstrual cycle (e.g. periods stop).

• If you suffer from a sore throat, high fever, feel very tired, become pale, develop bruises and nose bleeds. These may indicate blood problems developing as a result of using this medicine.

• Very occasionally, medicines such as Trifluoperazine Tablets can have effects on muscle control.

If this happens, symptoms can include slurred speech, odd movements of the face, particularly of the tongue, eyes, head or neck (such as twisting of the neck which causes an unnatural positioning of the head, rigid muscles, tremors or restlessness and difficulty in sitting still.) Some patients (especially on high doses of this medicine) experience problems with muscle control which may continue for years.

Such patients may experience constant chewing or tongue movements or other gentle movements of the neck, head or trunk.

Uncontrollable movements of the arms and legs have also been reported in these patients.

• Very rarely, patients may experience a fast or irregular heartbeat, constipation, difficulty or inability to pass urine or a high temperature.

• Occasionally, some patients have complained of feeling slowed down, whilst others of being agitated.

• If you have angina and your pain is getting worse.

• There have been very rare reports of jaundice (yellowing of skin and whites of eyes), eye problems, skin colouring (pigmentation) and blood problems.

• In elderly people with dementia, a small increase in the number of deaths has been reported for patients taking antipsychotics compared with those not receiving antipsychotics. Some patients may also experience weakness, drowsiness, dizziness, restlessness, difficulty in sleeping, dry mouth, blurred vision or eye problems, muscle weakness, loss of appetite, faintness on standing up, weight gain, water retention causing swelling or confusion.

If any of the side effects become serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

Chlorpromazine:

Very common (may affect more than 1 in 10 people)

● you have movements that you cannot control, mainly of the tongue, mouth, jaw, arms and legs

● trembling, muscle stiffness or spasm, slow movement, producing more saliva that usual or feeling restless

Common (may affect up to 1 in 10 people)

● you have a fit (seizure)

● alteration of the heart rhythm (called 'prolongation of the QT interval', seen on ECG, electrical activity of the heart).

Not known (frequency cannot be estimated from the available data)

● you have an allergic reaction. The signs may include: rash, itching, fever, difficulty in breathing or wheezing, chills, swollen eyelids, lips, tongue or throat

● you have a very fast, uneven or forceful heartbeat (palpitations). You may also have breathing problems such as wheezing, shortness of breath, tightness in the chest and chest pain. These could be signs of very serious life threatening heart problems

●you have joint aches and pains, swollen joints, feel tired or weak with chest pain and shortness of breath. These could be signs of an illness called 'systemic lupus erythematosus' (SLE)

● you have yellowing of the skin or eyes (jaundice) and your urine becomes darker in colour. These could be signs of liver damage you have frequent infections such as fever, severe chills, sore throat or mouth ulcers. These could be signs of a blood problem called ‘leucopenia’

● you have a high temperature, sweating or stiff muscles,

fast heartbeat, fast breathing and feel confused, drowsy or agitated. These could be signs of a serious but rare side effect called ‘neuroleptic malignant syndrome’

● you get a bloated feeling and cramping pain in the abdomen (stomach) be sick (vomit), have indigestion, heartburn, upset stomach, constipation, loss of appetite, dry mouth. This could be caused by an obstruction or blockage of the intestine

● you have pain in your abdomen with vomiting and diarrhoea

● you have a long lasting painful erection of the penis

● you bruise more easily than usual. This could be because of a blood disorder called ‘thrombocytopenia’.

● you have blood clots in the veins especially in the legs (symptoms include swelling, pain and redness in theleg), which may travel through blood vessels to the lungs causing chest pain and difficulty in breathing. If you notice any of these symptoms seek medical advice immediately

Tell your doctor or pharmacist as soon as possible if you have any of the following side effects:

Very common (may affect more than 1 in 10 people)

● feeling dizzy, lightheaded or faint when you stand or sit up quickly (due to low blood pressure).

Not known (frequency cannot be estimated from the available data)

● you are breathing more slowly or less deeply than normal

● changes in skin or eye colour after having Chlorpromazine for a long time

● problems with eyesight

● rigid or stiff muscles, trembling or shaking, difficulty moving

● passing large amounts of urine, excessive thirst and having a dry mouth or skin. You may be more likely get infections such as thrush. This could be due to

too much sugar in your blood (hyperglycaemia)

● unusual eye movements (including rolling of the eyes)

● your neck becomes twisted to one side

● your jaw is tight and stiff

● you have difficulty in passing water (urine)

● feeling tired, weak, confused and have muscles that ache, are stiff or do not work well. This may be due to low sodium levels in your blood.

Tell your doctor or pharmacist if any of the following side effects gets serious or lasts longer than a few days:

Very common (may affect more than 1 in 10 people)

● dry mouth

● feeling drowsy or sleepy

● putting on weight.

Common (may affect up to 1 in 10 people)

● abnormal production of breast milk in men and women

● loss of menstrual periods

● feeling anxious.

Not known (frequency cannot be estimated from the available data)

● breast enlargement in men

● difficulty in getting or keeping an erection (impotence)

● reduced sexual desire in women

● difficulty sleeping (insomnia)

● feeling agitated

● being more sensitive to the sun than usual

● stuffy nose

● skin rashes

● tiredness, low mood.

Withdrawal effects: If this medicine is stopped suddenly nausea, vomiting and difficulty sleeping (insomnia), tremor (shaking), jerky body movements and the

inability to control movements of the hands and body can occur.

If any of the side effects get serious, or if you notice any side effects not mentioned in this leaflet, please tell your doctor or pharmacist.

Reporting of side effects

If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via any point of contact of Torrent Pharma available at: http://www.torrentpharma.com/index.php/site/info/adverse_event_reporting.

By reporting side effects, you can help provide more information on the safety of this medicine.

9.5 How to store TRINICLAM FORTE.

Keep in dry place, protect from light.

9.6 Contents of the pack and other information

What TRINICLAM FORTE contains

TRINICLAM FORTE consists of : Chlorpromazine 50 mg, Trifluoperazine 5 mg and Benzhexol 2mg as active substance.

Colour: Lake of carmoisine, Lake of Brilliant Blue & Titanium Dioxide I.P.

TRINICALM FORTE is available in blister pack of 15 tablets

10 Details of manufacturer

Manufactured by:

Torrent pharmaceuiticals ltd.

32 No. middle camp, NH-10,

East district, gangtok, Sikkim-737 135.

or

Windlas Biotech Limited (Plant-IV)

Plot No. 183 & 192,

Mohabewala Industrial Area,

Dehradun-248 110, Uttarakhand

11 Details of permission or licence number with date

Mfg Lic No.M/563/2010 Date: 06 dec 2021s

Windlas Biotech Limited (Plant-IV)

Mfg Lic No. 47/UA/2009

12 Date of revision

April 22

MARKETED BY

Torrent Pharmaceuticals Ltd.

IN/TRINICLAM FORTE/Apr-22/02/PI