OSAKA
Pharmaceuticals Pvt. Ltd.

SUMMARY OF PRODUCT CHARACTERISTICS
(As Per NAFDAC Template)

FLU-COF

ACETAMINOPHEN, PSEUDOEPHEDRINE HCL, DEXTROMETHORPHAN HYDROBROMIDE AND CHLORPHENIRAMINE MALEATE TABLETS

Manufactured by: **OSAKA PHARMACEUTICALS PVT. LTD.** Old National Highway No.8 Sankarda-391350 Dist.: Vadodara, India. Tel. No +91-265-2841451 Email: info@osakapharmaceutical.com	Marketed by: **VIXA PHARMACEUTICAL CO. LTD.** 13b Sunny Jigida Street, Off Celestial Way, Ogudu, Lagos, Nigeria.

1.3.1 Summary of Product Characteristics (SmPC)

1. Name of Medicinal Product

FLU-COF

ACETAMINOPHEN, PSEUDOEPHEDRINE HCL, DEXTROMETHORPHAN HYDROBROMIDE AND CHLORPHENIRAMINE MALEATE TABLETS

2. Qualitative and Quantitative Composition

Qualitative declaration:

Composition of the Drug product:

Each uncoated Caplet contains:

Acetaminophen USP 325mg

Pseudoephedrine HCL USP 30mg

Dextromethorphen Hydrobromide USP 15mg

Chlorpheniramine Maleate USP 2mg

Excipient q.s.

Qualitative & Quantitative Composition Formula:

Batch Size: 1,00,000 Tablets

Sr. No.	Name of raw material	Specification	Label claim Qty/Tab (mg)	% Overages	Qty / Tab with O.A (mg)	Qty. Per Batch size (Kg)	Function
Wet Granulation PART-1							
1.	Paracetamol	USP	325.00	-	325.00	331.50	Active
2.	Dextromethorphan Hydrobromide	USP	15.00	-	15.00	15.30	Active
3.	Chlorpheniramine Maleate	USP	2.00	-	2.00	2.040	Active
4.	Maize Starch	BP	98.00	-	105.84	107.956	Diluents

5.	Microcrystalline cellulose	BP	67.90	-	67.90	69.258	Diluents
6.	PVP K-30	BP	6.00	-	6.00	6.120	Binder
7.	Maize Starch	BP	32.00	8.0%	34.56	35.250	Binder
8.	Colour : Sunset yellow Supra	BP	0.30	-	0.30	0.306	Colour
9.	Methyl Paraben	BP	0.60	-	0.60	0.612	Preservative
10.	Propyl Paraben	BP	0.20	-	0.20	0.204	Preservative
11.	Purified Water	BP	NA	-	NA	Q.S	Solvent
Wet Granulation PART-2							
12.	Psuedoephedrine HCL	USP	30.00	-	30.00	30.600	Active
13.	Maize starch	BP	18.00	8.0	19.44	19.828	Diluents
14.	MCCP	BP	12.00	-	12.00	12.240	Diluents
15.	Sodium Starch glycolate	BP	2.00	-	2.00	2.040	Disintegrant
16.	PVP K-30	BP	2.00	-	2.00	2.040	Binder
17.	Isopropyl Alcohol	BP	NA	-	NA	25.00	Solvent
18.	Colour: Sunset yellow Lake	IHS	0.098	-	0.098	0.100	Colour
Lubrication							
19.	Cross Carmellose sodium	BP	7.70	-	7.70	7.854	Disintegrant
20.	Magnesium Stearate	BP	8.00	-	8.00	8.160	Lubricant
21.	Purified talc	BP	10.00	-	10.00	10.200	Lubricant
22.	Colloidal anhydrous silica	BP	3.00	-	3.00	3.060	Disintegrant
		Total			640.00	652.80	

3. Pharmaceutical form

Orange coloured, caplet shape biconvex uncoated tablet embossed with FLU-COF on one sided break line on other side.

4. Clinical particulars

Therapeutic indications

FLU-COF is a combination of a pain reliever, an antihistamine, a cough suppressant, and a decongestant. It is used to treat the aches and pains, cough, fever, congestion, runny nose and sneezing of a cold. This medicine will not treat an infection.

The relief of common cold symptoms (nasal mucus. nasal obstruction. sneeze. throat pain, cough chill. lever. headache. arthralgia. myalgia) FLU-COF caplets is a decongestant. antihistamine. cough suppressant. and analgesic combination. The decongestant works by constricting blood vessels and reducing swelling in the nasal passages. The antihistamine works by blocking the action of histamine, which helps reduce symptoms such as watery eyes and sneezing. The analgesic and cough suppressant work in the brain to decrease pain and to reduce a dry or unproductive cough.

Posology and method of administration

Caplet for oral use: Adults and children 15 years and above: take 1 caplet. 3 times a day or as directed by Me physician

12 yrs and older: Day time tablets (without chlorpheniramine): 2 tablets every 6 hours during waking hours as needed.

Night time tablets: 2 tablets every 6 hours during sleeping hours as needed.

Not to exceed a total of 8 tablets/day of day and night tablets combined.

Contraindications

1) If you are anaphylactic to Has drug (eg.. rash. Hare, pruntis. edema)
2) Asthma patient alter taking this drug or other anti-cold, antipyretic and analgesic

Special warnings and precautions for use

Ask a doctor or pharmacist before use it you are regularly drinking over three cups of alcohol per day or taking any other antipyretic and analgesics. Liver can be damaged if taken.

Pregnancy and Breast-Feeding: If you become pregnant while taking FLU-COF caplets. discuss with your doctor the benefits and risks of using FLU-COF caplets during pregnancy. It is

unknown if FLU-COF caplets is excreted in breast milk. Do not breast-feed while taking FLU-COF caplets.

Keep all medicine out of reach of children.

Precautions:

1) Family history to urticaria. contact dermatitis. bronchial asthma, allergic rhinitis. migrane, food allergy 2) Allergy experience to this drug (fever, rash, arthritis, asthma, pruntie)

3) Child below 14 years may be Infected by Chickenpox or influenza

4) Disease of Liver. kidney and thyrord disease. Diabetes, hypertension. weakling, high-fever

5) Glaucoma. dysuria

6) Pregnant or breast-feeding

7) People treated by MD or dentist

Interaction with other medicinal products and other forms of interaction

Drug Interaction: Some MEDICINES MAY INTERACT with FLU-COF caplets. Tell your health care provider if you am taking any other medicines, especially any of the following:

-Beta-blockers (eg. Propranolol), COMT inhibitors leg, toicapone), furazolidone, indomethacin, isoniazid. MAO inhibitors (eg. phenelzine). sodium oxybate (GHB), or tricyclic antidepressants (eg. amitriptyline) because side effects of FLU-COF caplets may be increased Anticoagulants leg. warfarin). digman or droxidopa because risk of bleeding. irregular heartbeat or heart attack may be increased. Bromomiptine or hydantoins (eg, phenytoin) because side effects may be increased by FLU-COF caplets .Guanadrel, guanethidine. mecamylamine, methyldopa, or reserpine because effectiveness may be decreased by FLU-COF caplets Ask your health care provider if FLU-COF caplets may interact with other medicines that you take. Check with your health care provider before you start. stop. or change the dose of any medicine.

Do not take this medicine with any of the following medications:

- cocaine
- ergot alkaloids like dihydroergotamine, ergonovine, ergotamine, methylergonovine
- MAOIs like Carbex, Eldepryl, Marplan, Nardil, and Parnate

- stimulant medicines like dextroamphetamine and others

This medicine may also interact with the following medications:

- alcohol
- bretylium
- furazolidone
- imatinib
- isoniazid
- linezolid
- mecamylamine
- medicines for anxiety or sleep
- medicines for blood pressure like atenolol, clonidine, doxazosin, methyldopa, metoprolol
- medicines for chest pain like isosorbide dinitrate, nitroglycerin
- medicines for enlarged prostate like tamsulosin
- medicines for sleep during surgery
- other medicines for cold, cough or allergy
- other medicines with acetaminophen
- procarbazine
- reserpine

This list may not describe all possible interactions. Give your health care provider a list of all the medicines, herbs, non-prescription drugs, or dietary supplements you use. Also tell them if you smoke, drink alcohol, or use illegal drugs. Some items may interact with your medicine.

Fertility, pregnancy and lactation

Not Applicable,

Effects on ability to drive and use machines

Not Applicable,

Undesirable effects

Constipation: diarrhea; dizziness; drowsiness; excitabitity', headache; loss of appetite; nausea; nervousness or anxiety: trouble sleeping: upset stomach: vomiting: weakness. Severe allergic reactions (rash: hives; difficulty breathing: tightness m the chest: swelling of the mouth, face, lips, or tongue): difficulty urinating or rnability to unnate. fast or irregular heartbeat, hallucinations; seizures: severe dizziness, lightheadedness, or headache: stomach pain: tremor: trouble sleeping: vision changes: yellowing al skin or eyes.

Overdose

Acetaminophen

Liver damage is possible in adults who have taken tog or more of Acetaminophen. Ingestion of 5g or more of Acetaminophen may lead to liver damage it the patient has risk factors.

Risk factors: If the patient

a, Is on long term treatment with cartiamampine, phenobarbitone, phenytoin. primidone. rifampicin, St Johns Wort or other drugs that induce hirer enzymes. Or

b. Regularly consumes ethanol in excess of recommended amounts. Or

c. Is likely to be glutathione deplete e.g. eating disorders, cystic fibrosis. HIV infection. starvation, cachexia.

Symptoms: Symptoms of Acetaminophen overd0Sage in the first 24 hours are pallor, nausea. vomiting. anorexia and abdominal pain. Liver damage may become apparent 12 to 48 hours after ingestion. Abnormalities of glucose metabolism and metabolic acidosis may occur. In severe poisoning, hepatic failure may progress to encephalopathy. haemorrhage. hypoglycaemia, cerebral oedema, and death. Acute renal failure with acute tubular necrosis. strongly suggested by loin pain, haematuria and proteinuria. may develop even in the absence of severe liver damage. Cardiac arrhylhmias and pancreatibs have been reported.

Management: Immediate treatment is essential in the management al Acetaminophen overdose. Despite a lack al significant early symptoms. pabents should be referred to hospital urgently for immediate medical attention. Symptoms may be limited to nausea or vomiting and may not

reflect the severity of overdose or the risk of organ damage. Management should be in accordance with established treatment guidelines. see 8NF overdose section. Treatment with activated charcoal should be considered it the overdose has been taken within 1 hour. Plasma Acetaminophen concentration should be measured at 4 hours or later after ingestion (earlier concentrations are unreliable). Treatment with el-acetylcysteine may be used up to 24 hours alter ingestion of Acetaminophen. however, the maximum protective effect is obtained up to 8 hours post-ingestion. The effectiveness of the antidote declines sharply after This time. If required the patient should be given intravenous N-acetylcysteine, in line with the established dosage schedule. If vomiting is not a problem. oral methionine may be a suitable alternative far remote areas. outside hospital. Management of patients who present with serious hepatiC dysfunction beyond 24h from ingestion should be discussed with the LAPIS or a liver unit.

Dextromethorphan Symptoms. Overdose is likely to result in effects similar to those listed under Adverse Reactions. The effects in overdosage will be potentiated by simultaneous ingestion of alcohol and psychotropic drugs.

Following large overdoses. additional symptoms may include excitation. mental confusion, restlessness. nervousness and irritability. stupor. ataxia, dystonia. hallucinations, psychosis and respiratory depression. fvlanagement: Supportive and symptomatic care should be provided as required.

If overdose is severe. nalaxone may be helpful. particulary for patients with respiratory depression.

Pseudoephedrine Hydrocholnde Symptoms: As with other sympathomimetics pseudoephedrine overdose will result in symptoms due to central nervous system and cardiovascular stimulation e.g. excitement. irritability, restlessness. tremor. hallucinations, hypertension, palpitations, arrhythmias and difficulty with mictuation. In severe cases. psychosis. convulsions, coma and hypertensive crisis may occur. Serum potassium levels may be low due to extracellular to intracellular shills in potassium.

Management: Treatment should consist of standard supportive measures. Beta-blockers should reverse the cardmvascular complications and the hypokalaemia.

Chlorpheniramine Maleate: Symptoms and signs include sedation. paradoxical stimulation of the COS, toxic psychosis. seizures. apnoea. convulsions. anticholinergic effects. dystonic reactions and cardiovascular collapse including arrhythmias.

Treatment includes gastric lavage or ernesis using ipecacuanha syrup. Following these measures activated charcoal and cathartics may be administered to minimise absorption. Other symptomatic and supportive measures should be provided with special attention to cardiac. respiratory. renal and hepatic functions and fluid and electrolyte balance. Treat hypotension and anhythmias vigorously CNS convulsions may be treated oath 10 diazepam or phenytoin. Haemopedusion may be used in severe cases

5. Pharmacological properties

Pharmacodynamic properties

Acetaminophen: Acetaminophen is a non.opiate. non-salicylate analgesic and antipyretic. The site and mechanism for the analgesic effect of acetaminophen has not been determined. The antipyretic effect at acetaminophen is accomplished through the inhibition of endogenous pyrogen action on the hypothalamic heat-regulating centers. Pseudoephedrine: Pseudoephedrine is a sympathomimetic agent with direct and indirect effects on adrenergic receptors. It has alpha and beta adrenergic activity and some stimulant effect on the central nervous system. The sympathomimett effect of pseudoephednne produces vasoconstriction which in turn relieves nasal congestion Dextromethorphan Hydrobromide: Dextromethorphan hydrobromide is a cough suppressant which has a central action on the cough centre M the medulla. It has no analgesic properties and little sedative activity. Chlorpheniramine Maleate: Chlorpheniramine is potent histamine Hi. receptor antagonist. Antihistamines diminish or abolish the actions of histamine in the body by competalwe reversible blockade of histamine Hl-receptor sees on tissues. Chlorpheniramine also has anticholinergic activity. Antihistamines act to prevent the release of histamine, prostaglandin and leukotrines and have been shown to prevent the migration of inflammatory mediators. The actions of chlorphenmine include inhibition of histamine on smooth muscle. cappillary permeability and hence reduction Of aedma and wheal in hypersneitivity reactions such as allergy and anaphylaxis

Pharmacokinetic properties

Acetaminophen: Acetaminophen is rapidly and completely absorbed from the gastrointestinal tract with peak plasma levels occurring about 025-2 hours after dosing. The absolute bioavailabilrly is about 80% and is independent of dose in normal therapeutic doses (5-20 mgrkg). It is not bound to plasma proteins. The volume of distribution is about 0.9 Mg. The plasma half-life ranges from 1-3 hours and is largely unaffected by age. It is metabolised in the liver and excreted in the unne as the glucurontde and sulphate coniugates.

Pseudoephedrine: Pseudoephedrine is readily and completely absorbed from the gastrointestinal tract. It is resistant to metabolism by monoamine oxidase and is largely excreted in the urine unchanged. II has an elimination half-tile of 5 to 8 hours but its urinary elimination and hence half-life is pH dependent. Pseudoephedrine is rapidly distributed throughout the body. its volume of distribution being 2 to &AG bodyweigh

Dextromethorphan Hydrobromide: Dextromethorphan hydrobromide is well absorbed from the gastrointestinal tract. It is metabolised in the liver and excreted in the urine as unchanged dextiomethorphan and demethylated metabolites including dextrorphan, which has some cough suppressant activity.

Chlorpheniramine Maleate: It is readily absorbed from the GI Tract. following oral administration, and is normally effective in 3010 60 minutes. The ell eels last to 4 to 6 hours. The plasma hall tile is estimated to be 12-15 hours. There is significant plasma protein binding. The drug is largely inactivated in the aver and excreted as metabolites in the urine. Chlorpheniramine is metabolised to the monodesmethyl and didesmethyl derivative. About 22% of an oral dose is excreted unchanged.

Preclinical safety data

Not Applicable,

6. PHARMACEUTICAL PARTICULARS

List of excipients

Sr. No.	Ingredients Name	Specification
1.	Maize Starch	BP

2.	Microcrystalline cellulose	BP
3.	PVP K-30	BP
4.	Maize Starch	BP
5.	Colour : Sunset yellow Supra	BP
6.	Methyl Paraben	BP
7.	Propyl Paraben	BP
8.	Purified Water	BP
9.	Sodium Starch glycolate	BP
10.	Isopropyl Alcohol	BP
11.	Cross Carmellose sodium	BP
12.	Magnesium Stearate	BP
13.	Purified talc	BP
14.	Colloidal anhydrous silica	BP

Incompatibilities: Not Applicable

Shelf-life: 36 Months

Special precautions for storage:

Store in a cool & dry place below 30°C. Keep medicines out of reach of children.

Nature and contents of container:

Each Alu/PVC Blister contains 4 Caplets and such 1 blister are packed in a monocarton along with pack insert and such 48 monocarton are packed in a outer carton.

Special precautions for disposal and other handling

No special instructions for use/handling

7- Marketing Authorization Holder:

VIXA PHARMACEUTICAL CO. LTD.

13b Sunny Jigida Street,

Off Celestial Way, Ogudu,

Lagos, Nigeria.

8- Marketing Authorization Number (s):

Product license / registration Number (s)

9- Manufacturer Name:

OSAKA PHARMACEUTICALS PVT. LTD.

OLD NATIONAL HIGHWAY NO.8, SANKARDA – 391 350, DIST. VADODARA, GUJARAT, INDIA.

10- Date of first authorization/renewal of the authorization:

11- Date of revision of the text:
