Summary of Product Characteristics (SPC)

1. NAME OF THE FINISHED PHARMACEUTICAL PRODUCT:

Prof® Cold & Flu Film Coated Tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION:

200 mg Ibuprofen/30 mg Pseudoephedrine HCl/ 2 mg Chlorpheniramine Maleate

3. PHARMACEUTICAL FORM:

Film-coated tablet
Orange colored, oval shaped film coated tablets engraved with "MT" on one side and plain on the other side.

4. CLINICAL PARTICULARS:

4.1 Therapeutic Indication:

Temporarily relieves the combined symptoms associated with colds & sinusitis including:
Stuffy nose, fever, body aches, sore throat, headache , runny nose, sneezing, itchy, watery eyes, and sinus pain and pressure.

Ibuprofen reduces fever and pain.

Pseudoephedrine hydrochloride is a nasal decongestant.

Chlorpheniramine Maleate is an antihistamine.

4.2 Posology and method of administration:

Usual dose:

Adults and children over 12: 1 or 2 tablets should be taken every 4 to 6 hours as needed. Not to exceed six tablets in 24 hours, unless directed by a physician.
Do not give to children under 12 unless directed by a physician.

If more Prof Cold & Flu Tablets are taken
In case of overdose, call a doctor even If there are no symptoms.
If you forget to take Prof Cold & Flu
- Take the missed dose as soon as you remember.
-If it is almost time for your next dose, wait until then to take your medicine and skip the missed dose.
-Do not take two doses at the same time.

4.3 Contraindications:

Hypersensitivity to the active substances or to any of the excipients.

Patients with allergy to aspirin or other Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) or with a history of hypersensitivity reactions (e.g. bronchospasm, rhinitis, urticaria) in response to ibuprofen, aspirin or NSAIDs.

History of gastrointestinal bleeding or perforation, related to previous NSAIDs therapy.
Active or history of recurrent peptic ulcer/haemorrhage (two or more distinct episodes of proven ulceration or bleeding).

Patients with active peptic ulceration or a history of peptic ulceration.

Patients with phaeochromocytoma, closed angle glaucoma, diabetes or thyroid disease.

Patients with kidney disease.

Patients suffering from heart disease, circulatory problems, hypertension or coronary artery disease.

Patients taking other NSAIDs, pain-relievers or decongestants.
Patients receiving tricyclic antidepressants.

Patients currently receiving, or who have within the last two weeks received, monoamine oxidase inhibitors. (MAO inhibitor therapy)

Patients with severe heart failure.

Last trimester of pregnancy (see section 4.6).

Pre-coma states (due to Chlorpheniramine Maleate content)

4.4 Special warnings and special precautions for use :

The use of Prof Cold & Flu with concomitant NSAIDs including cyclooxygenase-2 selective inhibitors should be avoided.
Undesirable effects may be minimized by using the minimum effective dose for the shortest duration necessary to control symptoms.
If symptoms get worse or last more than 3 days or you experience any other symptoms not related to the original condition, treatment should be stopped unless directed otherwise by a doctor or healthcare professional.

Elderly: The elderly have an increased frequency of adverse reactions to NSAIDs especially gastrointestinal bleeding and perforation which may be fatal.

Gastrointestinal bleeding, ulceration and perforation: GI bleeding, ulceration or perforation, which can be fatal, has been reported with all NSAIDs at any time during treatment, with or without warning symptoms or a previous history of serious GI events.

The risk if GI bleeding, ulceration or perforation is higher with increasing NSAID doses, in patients with a history of ulcer, particularly if complicated with haemorrhage or perforation (see section 4.3), and in the elderly. These patients should commence treatment on the lowest dose available.

Combination therapy with protective agents (e.g. misoprostol or proton pump inhibitors) should be considered for these patients and also for patients requiring concomitant low dose aspirin or other drugs likely to increase gastrointestinal risk (see below and 4.5)

Patients with a history of GI toxicity, particularly when elderly, should report any unusual abdominal symptoms (especially GI bleeding) particularly in the initial stages of treatment.

Caution should be advised in patients receiving concomitant medications which could increase the risk of ulceration or bleeding such as oral corticosteroids, anticoagulants such as warfarin, selective serotonin-reuptake inhibitors or anti-platelet agents such as aspirin (see section 4.5).

When GI bleeding or ulceration occurs in patients receiving Prof Cold & Flu, the treatment should be withdrawn.
NSAIDs should be given with care to patients with a history of gastrointestinal disease (ulcerative colitis, Crohn's disease) as their condition may be exacerbated (see sections 4.8 –undesirable effects).

In patients with cardiac or hepatic impairment, caution is required since the use of NSAIDs may result in deterioration in renal function.

Prof Cold & Flu should be used with caution in patients with a history of peptic ulceration or inflammatory bowel disease.
Caution (discussion with doctor or pharmacist) is required prior to starting treatment in patients with a history of hypertension and/or heart failure as fluid retention and oedema have been reported in association with NSAID therapy. Undesirable effects may be minimised using the lowest effective dose for the shortest duration necessary to control symptoms (see GI and cardiovascular risks below)

Cardiovascular and cerebrovascular effects:
Clinical trial and epidemiological data suggest that use of some NSAIDs (particularly at high doses (2400mg daily) and in long term treatment may be associated with a small increased risk of arterial thrombotic events (for example myocardial infarction or stroke). Overall, epidemiological studies do not suggest that low dose ibuprofen (e.g. 1200mg daily) is associated with an increased risk of myocardial infarction.

Serious skin reactions, some of them fatal, including exfoliative dermatitis, Stevens-Johnson syndrome and toxic epidermal necrolysis, have been reported very rarely in association with the use of NSAIDs (see section 4.8). Patients appear to be at highest risk of these reactions early in the course of therapy, the onset of the reaction occurring in the majority of cases within the first month of treatment. Prof Cold & Flu should be discontinued at the first appearance of skin rash, mucosal lesions, or any other sign of hypersensitivity.

As NSAIDs can interfere with platelet function, they should be used with caution in patients with intra-cranial haemorrhage and bleeding diathesis.

Patients suffering from asthma, hypertension, heart disease, diabetes, liver cirrhosis, kidney disease, thyroid disease or prostatic hypertrophy should consult their doctor before using this product.

Bronchospasm may be precipitated in patients suffering from asthma or allergic disease.
There is some evidence that drugs which inhibit cyclo-oxygenase / prostaglandin synthesis may cause impairment of female fertility by an effect on ovulation. This is reversible on withdrawal of treatment.

The use of NSAIDs may impair female fertility and is not recommended in women attempting to conceive. In women who have difficulties conceiving and who are undergoing investigation of infertility, withdrawal of the product should be considered.

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

Due to the content of Chlorpheniramine, the following Special warnings and precautions should be considered:
- Chlorpheniramine in Prof Cold & Flu may act as a cerebral stimulant in children and occasionally in adults, giving rise to insomnia, nervousness, hyperpyrexia, tremors and epileptiform convulsions. Children and the elderly are more likely to experience the neurological anticholinergic effects and paradoxical excitation (e.g. increased energy, restlessness, nervousness).

- Chlorpheniramine in Prof Cold & Flu, may increase the effects of alcohol, therefore, concurrent use should be avoided.

- In common with other drugs having anticholinergic effects (due to Chlorpheniramine content), Prof Cold & Flu, should be used with caution in epilepsy, severe hypertension and cardiovascular disease, raised intra-ocular pressure including glaucoma; prostatic hypertrophy, severe hepatic impairment, severe renal impairment, bronchitis, thyrotoxicosis, bronchiectasis and bronchial asthma.

- Concurrent use of Prof Cold & Flu with drugs which cause sedation such as anxiolytics and hypnotics may cause an increase in sedative effects, and therefore, medical advice should be sought before taking this product concurrently with these medicines.

- Prof Cold & Flu, should not be used with other anti-histamine containing products, including antihistamine containing cough and cold preparations.

Keep out of the reach and sight of children.

4.5 Interaction with other medications and another forms of interaction:

It is considered unsafe to take Ibuprofen in combination with warfarin or heparin unless under direct medical supervision.

Not recommended combinations:

Animal studies show that acetylsalicylic acid reduces the plasma concentrations of Ibuprofen. Ibuprofen should not be used with other pain relievers such as NSAIDs.

Experimental data suggest that ibuprofen may inhibit the effect of low dose aspirin on platelet aggregation when they are dosed concomitantly. However, the limitations of these data and the uncertainties regarding extrapolation of ex vivo data to the clinical situation imply that no firm conclusions can be made for regular ibuprofen use, and no clinically relevant effect is considered to be likely for occasional ibuprofen use (see section 5.1).

Combinations requiring precautions:

Care should be taken in patients treated with any of the following drugs as interactions have been reported.

Anticoagulants, antihypertensives or thiazide diuretics:

NSAIDs may enhance the effects of anticoagulants and diminish the effects of antihypertensive or thiazide diuretics.

Diuretics: Reduced diuretic effect. Diuretics can increase the risk of nephrotoxicity of NSAIDs.

Cardiac Glycosides: NSAIDs may exacerbate cardiac failure, reduce GFR and increase plasma cardiac glycoside levels. Serum digitalis concentrations should therefore be monitored in patients with decreased renal function or congestive heart failure.

Phenytoin: Ibuprofen may increase the pharmacologically active free phenytoin. Patients taking Ibuprofen for long-term use should be monitored.

Lithium: Decreased elimination of lithium. This may result in clinically significant increases in lithium concentrations.

Methotrexate: Concomitant administration of Ibuprofen with moderate and high doses of methotrexate may lead to serious and fatal methotrexate toxicity. Patients with reduced renal function may be at additional risk of toxicity from the combination even when low doses of methotrexate (≥20 mg/week) are used.

Antacids: Certain antacids may increase the gastrointestinal absorption of Ibuprofen. This is considered to be of clinical relevance particularly during long-term use of Ibuprofen.

Cyclosporin: Increased risk of nephrotoxicity with NSAIDs.

Corticosteroids: Increased risk of gastro-intestinal bleeding or ulceration.

Anti-platelet agents and selective serotonin reuptake inhibitors (SSRIs): Increased risk of gastrointestinal bleeding (see section 4.4).

Aminoglycosides: Reduction in renal function in susceptible individuals decreased elimination of aminoglycosides and increased plasma concentrations.

Pseudoephedrine:

Pseudoephedrine may interact with:
The actions of other sympathomimetic drugs.
The antibacterial agent furazoline.
The action of Pseudoephedrine may be reduced by:
Guanethidine.
Reserpine.
Methyldopa.
The action of Pseudoephedrine may be reduced or enhanced by:
Tricyclic antidepressants.
Pseudoephedrine may reduce the action of:
Guanethidine.
Pseudoephedrine may increase the possibility of arrhythmias in patients taking:
Digitalis.
Quinidine.
Tricyclic antidepressants.

Chlorpheniramine Maleate:

Chlorpheniramine may have an additive effect when used concurrently with hypnotics and anxiolytics causing potentiation of drowsiness. A similar additive effect will result from concurrent usage of alcohol with chlorpheniramine.

The effects of anti-cholinergics e.g. some psychotropic drugs and atropine, may be potentiated by this product giving rise to tachycardia, mouth dryness, gastrointestinal disturbances e.g. dyskinesia, colic, urinary retention and headache.

As monoamine oxidase inhibitor therapy intensifies the anticholinergic effects of chlorpheniramine, concurrent therapy is contra-indicated.

Chlorpheniramine inhibits phenytoin metabolism and can lead to phenytoin toxicity.

4.6 Pregnancy and lactation:

Pregnancy:

Ibuprofen:

Whilst no teratogenic effect has been demonstrated in animal experiments, use of ibuprofen during pregnancy should be avoided during the first 6 months of pregnancy.

During the third trimester, ibuprofen is contraindicated as there is a risk of premature closure of the foetal ductus arteriosus with possible persistent pulmonary hypertension. The onset of labour may be delayed and duration of labour increased with an increased bleeding tendencyin both mother and child (see Section 4.3).

Pseudoephedrine:

Data on pregnancy outcomes after maternal exposure to pseudoephedrine are limited. Two analyses of health maintenance organisation pharmacy data identified 9 malformed infants among 902 first-trimester pseudoephedrine exposures suggesting no specific association with birth defects overall. However the related compounds epinephrine, ephedrine and phenylephrine have been associated with haemorrhages and cardiovascular and limb malformations in animal models. The vasoconstrictive effects of these drugs may indicate that their use in early pregnancy might increases the risk of vascular disruption defects.

Chlorpheniramine Maleate:

This product should not be used during pregnancy or lactation unless considered essential by the physician. Animal studies have not been conducted nor are there specific studies in human beings. Use during the third trimester may result in reactions in the newborn or premature neonates.

Lactation:

Ibuprofen:

In limited studies, ibuprofen appears in the breast milk in very low concentrations, and is unlikely to affect the breast fed infant adversely.

Pseudoephedrine:

Pseudoephedrine is excreted in breast milk in small quantities, but the effect of this on breast-fed infants is not known. It is estimated that 0.4% to 0.7% of a single dose of pseudoephedrine ingested by the mother will be excreted in breast milk over 24 hours.

In summary, caution should be exercised by balancing the potential benefit of treatment against any possible risks.

Chlorpheniramine Maleate:

Small amounts of anti-histamines are excreted in breast milk.

Use by nursing mothers is not recommended because of the risks of adverse effects in the infant. Antihistamines may inhibit lactation.

4.7 Effects on ability to drive and use machines:

This product may cause drowsiness and patients receiving it should not drive or operate machinery unless it has been shown that their physical and mental capacity remains unaffected.

4.8 Undesirable effects:

Gastro-intestinal: The most common observed adverse events are gastrointestinal in nature. Peptic ulcers, perforation or GI bleeding, sometimes fatal in the elderly, may occur (see section 4.4). Nausea, vomiting, diarrhoea, flatulence, constipation, dyspepsia, abdominal pain, abdominal distension, mouth ulcerations, melaena, haematemesis, ulcerative stomatitis, exacerbation of colitis and Crohn's disease (see section 4.4 – Special warnings and precautions for use) have been reported following administration. Less frequently, gastritis has been observed

Hypersensitivity reactions have been reported following treatment with Ibuprofen. These may consist of;

- non-specific allergic reaction and anaphylaxis,
- **Breathing:** respiratory tract reactivity comprising of asthma, aggravated asthma, bronchospasm or dyspnoea,
- **Skin:** assorted skin disorders, including rashes of various types, bruising pruritis, urticaria, purpura, angiodema and, less commonly, bullous dermatoses (including epidermal necrolysis and erythema multiforme). Very rarely, bullous reactions including Steven's – Johnson syndrome and toxic epidermal necrolysis.

Cardiovascular: Clinical trial and epidemiological data suggest the use ibuprofen (particularly at high doses 2400mg daily) and in long term treatment may be associated with a small increased risk of arterial thrombotic events (for example myocardial infarction or stroke) (see section 4.4). Oedema, hypertension, angina pectoris and cardiac failure have been reported in association with NSAID treatment.

Haematological: Impaired coagulation, bleeding, anaemia, haemolytic anaemia, leukopenia, thrombocytopenia, occasionally agranulocytosis and aplastic anaemia.

Renal: Haematuria, interstitial nephritis, renal papillary necrosis, nephrotic syndrome, proteinuria and renal failure have occasionally been reported.

Liver: Abnormal LFTs (Liver function tests), hepatitis (occasionally progressing to liver failure), jaundice.

Other: Insomnia, dizziness, excitability, anxiety, agitation, irritability, nervousness, restlessness, tinnitus, vertigo, visual disturbances, tremor, palpitations, tachycardia, dry mouth, loss of appetite, thirst, psychomotor hyperactivity, chest pain. Less frequently, difficulty in micturition and hallucinations. Rarely headache, hearing disturbance, exacerbation of colitis meningitis and aseptic meningitis.

Undesirable effects due to Chlorpheniramine Maleate Content:

Specific estimation of the frequency of adverse events for OTC products is inherently difficult (particularly numerator data). Adverse reactions which have been observed in clinical trials and which are considered to be common (occurring in ≥ 1% to <10% of subjects) or very common (occurring in ≥ 10% of subjects) are listed below by MedDRA System Organ Class. The frequency of other adverse reactions identified during post-marketing use is unknown.

Blood and Lymphatic system disorders:

Very rare: haemolytic anaemia, thrombocytopenic purpura. Other blood dyscrasias including agranulocytosis, anaemia, aplastic anaemia, eosinophilia, leucopenia and thrombocytopenia

Hepatobiliary disorders

Very rare: hepatitis including jaundice

Immune system disorders:

Unknown: allergic reactions, angioedema, anaphylactic reactions

Metabolism and nutritional disorders:

Unknown: anorexia

Psychiatric disorders:

Unknown: confusion*, excitation*, irritability*, nightmares*

Nervous system disorders*:

Very common: sedation, somnolence

Common: disturbance in attention, abnormal coordination, dizziness, headache

Eye disorders

Common: blurred vision

Vascular disorders:

Unknown: Hypotension

Respiratory, thoracic and mediastinal disorders:

Unknown: thickening of bronchial secretions

Gastrointestinal disorders:

Common: nausea, dry mouth

Unknown: vomiting, abdominal pain, diarrhoea, dyspepsia

Skin and subcutaneous disorders:

Unknown: exfoliative dermatitis, rash, urticaria, photosensitivity

Musculoskeletal and connective tissue disorders:

Unknown: muscle twitching, muscle weakness

Renal and urinary disorders:

Unknown: urinary retention

General disorders and administration site conditions:

Common: fatigue

Unknown: chest tightness

*Children and the elderly are more susceptible to neurological anticholinergic effects and paradoxical excitation (e.g. increased energy, restlessness, nervousness).

4.9 Overdose

Overdosage may result in nervousness, agitation, anxiety, irritability, restlessness, dizziness, tremor, vertigo, insomnia, nausea, abdominal pain, vomiting, epigastric pain, diarrhoea, bradycardia, palpitation, tachycardia, tinnitus, headache and gastrointestinal bleeding. Sedation, paradoxical stimulation of CNS, toxic psychosis, seizures, apnoea, convulsions, anticholinergic effects, dystonic reactions and cardiovascular collapse including arrhythmias.

Hyperkalemia, metabolic acidosis, hypertension or hypotension are also possible signs of overdose. Toxicity may manifest as drowsiness, excitation, disorientation or coma. The patient may develop convulsions. Hepatic function may be abnormal. Metabolic acidosis may occur and the prothrombin time/INR may be prolonged. Acute renal failure and liver damage may occur. In asthmatics, exacerbation of asthma is possible.

The estimated lethal dose of Chlorpheniramine Maleate is 25 to 50mg/kg body weight.

Due to the rapid absorption of Ibuprofen and Pseudoephedrine HCl from the gastro-intestinal tract, emetics and gastric lavage must be instituted within four hours of overdosage to be effective. Charcoal is effective only if given within one hour. Cardiac status should be monitored and the serum electrolytes measured.

If there are signs of cardiac toxicity, propanolol may be administered intravenously. A slow infusion of a dilute solution of potassium chloride should be initiated in the event of a drop in the serum potassium level. Despite hypokalaemia, the patient is unlikely to be potassium depleted, therefore overload must be avoided. Continued monitoring of the serum potassium is advisable for several hours after administration of the salt. For delirium or convulsions, intravenous administration of diazepam is indicated. Convulsions and marked CNS stimulation should be treated with parenteral diazepam.

5. PHARMACEUTICAL PROPERTIES:

Pharmacotherapeutic Group:

5.1 Pharmacodynamic properties

ATC code: M01AE51

Ibuprofen

Pharmacotherapeutic group: Propionic acid derivatives.

Pseudoephedrine Hydrochloride

Pharmacotherapeutic group: Nasal decongestants for systemic use, sympathomimetrics.

Chlorpheniramine Maleate:

Pharmacotherapeutic group: Antihistamines For Systemic Use, substituted Alkylamines

Ibuprofen is a non steroidal anti-inflammatory agent belonging to the Propionic Acid class of drugs. It has analgesic, antipyretic and anti-inflammatory properties.

Experimental data suggest that ibuprofen may inhibit the effect of low dose aspirin on platelet aggregation when they are dosed concomitantly. In one study, when a single dose of ibuprofen 400mg was taken within 8 h before or within 30 min after immediate release aspirin dosing (81mg), a decreased effect of ASA on the formation of thromboxane or platelet aggregation occurred. However, the limitations of these data and the uncertainties regarding extrapolation of ex vivo data to the clinical situation imply that no firm conclusions can be made for regular ibuprofen use, and no clinically relevant effect is considered to be likely for occasional ibuprofen use.

Pseudoephedrine Hydrochloride is a sympathomimetic agent which causes vasoconstriction of nasal mucosa, thereby reducing rhinorrhoea and nasal congestion.

Chlorpheniramine Maleate is a potent antihistamine (H1-receptor antagonist). Antihistamines diminish or abolish the actions of histamine in the body by competitive reversible blockade of histamine 1 receptor sites on tissues. Chlorpheniramine also has anticholinergic activity.

5.2 Pharmacokinetic properties

Ibuprofen is rapidly absorbed from the gastrointestinal tract with peak concentrations being achieved 45-90 minutes later. It is over 90% plasma protein bound in the circulation and has a short elimination half-life of 0.9-2.5 hours. Ibuprofen is primarily metabolised in the liver to 2-Hydroxyibuprofen and 2- carboxyibuprofen. These are excreted in the urine along with approximately 9% of unchanged drug.

Pseudoephedrine Hydrochloride is rapidly absorbed from the gasto-intestinal tract with peak plasma levels at 1-3 hours. It is partly metabolised in the liver like most sympathomimetics, but is mainly excreted unchanged in the urine.

Chlorpheniramine is well absorbed from the gastro-intestinal tract, following oral administration. The effects develop within 30 minutes, are maximal within 1 to 2 hours and last 4 to 6 hours. The plasma half-life has been estimated to be 12 to 15 hours. Chlorpheniramine is metabolised to the monodesmethyl and didesmethyl derivatives. About 22% of an oral dose is excreted unchanged in the urine. Only trace amounts have been found in the faeces.

5.3 Preclinical safety data

None stated.

6. PHARMACEUTICAL PARTICULARS:

6.1 List of excipients:

Tablets Core:

Microcrystalline Cellulose, Corn Starch, Croscarmellose Sodium, Povidone K30, Pregelatinized Starch, Colloidal Silicon Dioxide, Talc, Magnesium Stearate.

Tablets Coat:

Opadry, FD&C Red No 40. Lake, FD&C Yellow No 6. Lake, Simethicone Emulsion.

6.2 Incompatibilities:

Not applicable.

6.3 Shelf life:

2 years.

6.1 Special precautions for storage:

Store below 30° C

6.2 Nature and content of the container.

Two Aluminum-White PVC/PVDC of 10 Film Coated Tablets each, in a printed carton with folded leaflet.

Primary packaging:

Aluminum-White PVC/PVDC.

Secondary packaging:

Carton: A carton with an over printed information.

Leaflet*:* multi folded leaflet

Pack details:

Prof® Cold & Flu Film Coated Tablets: Two Aluminum-White PVC/PVDC of 10 Film Coated Tablets each packed in a printed carton with folded leaflet.

Pack size:

Packs of 20 Film Coated Tablets.

Hospital packs are available.

6.3 Instruction for use and handling:

- Medicament is a product which affects your health and its consumption contrary to instructions is dangerous for you.
- Strictly follow the doctor's prescription, the method of use and the instructions of the pharmacist who sold the medicament.
- The doctor and the pharmacist are experts in medicine, its benefits and risks.
- Do not by yourself interrupt the period of treatment prescribed for you.
- Do not repeat the same prescription without consulting your doctor.
- Keep medicament out of reach of children.

7. MARKETING AUTHORIZATION HOLDER

Tabuk Pharmaceutical Manufacturing Company
P.O. Box 3633
Tabuk - Saudi Arabia
Tel: 009661-4-4283030
Fax: 009661-4-4283031/421-0286
E-mail: tpmc@nournet.com.sa
Web site: www.tpmc.com.sa

8. NUMBER(S) IN THE NATIONAL REGISTER OF FINISHED PHARMACEUTICAL PRODUCTS

Marketing Authorization Number in Ethiopia: **06991/08264/REN/2021**

9. DATE OF FIRST AUTHORIZATION/ RENEWAL OF THE AUTHORIZATION

- Date of first authorization in Ethiopia: **01/02/2018**
- Date of latest renewal in Ethiopia: **30/12/2021**

10. DATE OF REVISION OF THE TEXT

August 2023