ARTWORK & DETAILS CHECKLIST FOR APPROVAL

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DATE: JANUARY 29, 2021
CLIENT: TGIF PHARMACEUTICAL TRADING
JOB TITLE: TRIMOTOL (NEW PM'S)
DESCRIPTION: INSERT **(FOR APPROVAL)**

COLORS

PROCESS COLORS:
N/A | N/A
N/A | BLACK

PANTONE COLORS:

SIZE/DIMENSION

LENGTH: 170 mm
WIDTH: 105 mm

PREPARED BY:
MARIUS CRUZ
(KLCA GRAPHIC ARTIST)

PARACETAMOL
PHENYLEPHRINE Hydrochloride
DEXTROMETHORPHAN Hydrobromide

TRIMOTOL

325 mg/25 mg/10 mg Capsule
ANALGESIC / ANTIPYRETIC / NASAL DECONGESTANT / ANTITUSSIVE

Description of the Product
Encapsulated in hard black/ light green capsule containing 325 mg of Paracetamol, 25 mg of Phenylephrine Hydrochloride and 10 mg of Dextromethorphan Hydrobromide.

What is in the medicine?
Paracetamol – a para-aminophenol derivative, has analgesic and antipyretic properties and weak anti-inflammatory activity. Paracetamol is often the analgesic or antipyretic of choice, especially in the elderly and in patients in whom salicylates or other NSAIDs are contra-indicated. Such patients include asthmatics, those with a history of peptic ulcer, and children. It is given orally or as a rectal suppository for mild to moderate pain and for fever. It may also be given by intravenous infusion for the short-term treatment of moderate pain, particularly after surgery, and of fever. is readily absorbed from the gastrointestinal with peak plasma concentrations occurring about 10 to 60 minutes after oral administration. Paracetamol is distributed into most body tissue. It crosses the placenta and is present in breast milk.
Plasma – protein binding negligible at usual therapeutic concentrations but increases with increasing concentrations. The elimination half-life of paracetamol varies from about 1 to 3 hours. Paracetamol is metabolised mainly in the liver and excreted in the urine mainly as the glucuronide and sulfate conjugates. Less than 5% is excreted as unchanged paracetamol. A minor hydroxylated metabolite (N-acetyl-p-benzoquinoneimine), is usually produced in very small amounts by cytochrome P450 isoenzymes (mainly CYP2E1 and CYP3A4) in the liver and kidney. It is usually detoxified by conjugation with glutathione but may accumulate after paracetamol overdosage and cause tissue damage.
Phenylephrine Hydrochloride – Phenylephrine hydrochloride is a sympathomimetic with mainly direct effects on adrenergic receptors. It has mainly alpha-adrenergic activity and is without significant stimulating effects on the CNS at usual doses. Its pressor activity is weaker than that of noradrenaline but of longer duration. After injection it produces peripheral vasoconstriction and increased arterial pressure; it also causes reflex bradycardia. It reduces blood flow to the skin and to the kidneys. Phenylephrine and its salts are most commonly used, either topically or by mouth, for the symptomatic relief of nasal congestion. They are frequently included in preparations intended for the relief of cough and cold symptoms. For nasal congestion, a 0.25 to 1% solution may be instilled as nasal drops or a spray into each nostril every 4 hours as required, or phenylephrine hydrochloride may be given in usual oral doses of 10 mg every four hours (up to a maximum of 60 mg daily) or 12 mg up to four times daily. Phenylephrine has low oral bioavailability owing to irregular absorption and first-pass metabolism by monoamine oxidase in the gut and liver. When injected subcutaneously or intramuscularly it takes 10 to 15 minutes to act; subcutaneous and intramuscular injections are effective for up to about 1 hour and up to about 2 hours, respectively. Intravenous injections are effective for about 20 minutes. Systemic absorption follows topical application.
Dextromethorphan Hydrobromide – is a cough suppressant used for the relief of non-productive cough; it has a central action on the cough centre in the medulla. It is also an antagonist of *N-methyl-D-aspartate* (NMDA) receptors. Although structurally related to morphine, dextromethorphan has no classical analgesic properties and little sedative activity. Dextromethorphan hydrobromide is reported to act within half an hour of an oral dose and to exert an effect for up to 6 hours. It is given orally in doses of 10 to 20 mg every 4 hours, or 30 mg every 6 to 8 hours, to a usual maximum of 120 mg in 24 hours. It is rapidly absorbed from the gastrointestinal tract. It is metabolized in the liver and excreted in the urine are unchanged dextromethorphan and demethylated metabolites including dextorphan which has some cough suppressant activity. Dextromethorphan Hydrobromide is a cough suppressant used for the relief of non-productive cough; it has a central action on the cough centre in the medulla.

Strength of the medicine
Each capsule contains:
Paracetamol . . . . . 325 mg
Phenylephrine Hydrochloride . . . . . 25 mg
Dextromethorphan Hydrobromide . . . . . 10 mg

What is this medicine used for?
Relief of symptoms associated with cough; nasal congestion, headache and fever.

How much and how often should you use this medicine?
Adult – 1 capsule every 6 hours or as prescribed by the physician.

When should you not take this medicine?
Paracetamol should be given with care to patients with impaired kidney or liver function. It should also be given with care to patients with alcohol dependence.
Phenylephrine Hydrochloride- Phenylephrine hydrochloride is irritant and may cause local discomfort at the site of application; extravasation of the injection may even cause local tissue necrosis.
Dextromethorphan Hydrobromide should not be given to patients at risk of developing respiratory failure. Caution is needed in patients with a history of asthma and it should not be given during an acute attack. Care is also advisable in patients with bronchitis, emphysema, or in other conditions where chronic or persistent cough occurs.

What other medicine or food should be avoided while taking this medicine?
Paracetamol- The risk of paracetamol toxicity may be increased in patients receiving other potentially hepatotoxic drugs or drugs that induce liver microsomal enzymes. The absorption of paracetamol may be accelerated by drugs such as metoclopramide. Excretion may be affected and plasma concentrations altered when given with probenecid.
Colestyramine reduces the absorption of paracetamol if given within 1 hour of paracetamol.

Phenylephrine Hydrochloride- As for Sympathomimetics, Phenylephrine has mainly direct alpha-agonist properties and is less liable than adrenaline or noradrenaline to induce ventricular fibrillation if used as a pressor agent during anaesthesia with inhalational anaesthetics such as cyclopropane and halothane; nevertheless, caution is necessary.
Since phenylephrine is absorbed through the mucosa, interactions may also follow topical application, particularly in patients receiving an MAOI (including a RIMA).
Dextromethorphan Hydrobromide- Severe and sometimes fatal reactions have been reported after use of dextromethorphan in patients receiving MAOIs. Dextromethorphan is primarily metabolized by the cytochrome P450 isoenzyme CYP2D6; the possibility of interactions with inhibitors of this enzyme, including amiodarone, haloperidol, propafenone, quinidine, SSRIs, and thioridazine, should be borne in mind.

How should you keep this medicine?
Store at temperatures not exceeding 30°C.

Signs and symptoms of overdose
Paracetamol- Overdosage with paracetamol can result in severe liver damage and sometimes acute renal tubular necrosis. Prompt treatment with acetylcysteine or methionine is essential.
Phenylephrine Hydrochloride- Overdose of phenylephrine hydrochloride can cause a rapid rise in blood pressure. Symptoms of overdose include headache, vomiting, hypertension, reflex bradycardia, and cardiac arrhythmias including ventricular extrasystoles and ventricular tachycardia, and may cause a sensation of fullness in the head and tingling of the extremities. Consider using an a-adrenergic antagonist.
Dextromethorphan Hydrobromide- There have been few of overdosage or accidental poisoning (usually in children) due to dextromethorphan, including rare fatalities. Naloxone may be effective in reversing toxicity. Extrapyramidal reactions were seen in a child who ingested dextromethorphan.

Care that should be taken when taking this medicine?
It should be used with care in patients with cardiac disease, high blood pressure & thyroid disease.

Undesirable effects of this medicine
Paracetamol- Adverse effects of paracetamol are rare and usually mild, although haematological reactions including thrombocytopenia, leucopenia, pancytopenia, neutropenia, and agranulocytosis have been reported. Skin rashes and other hypersensitivity reactions occur occasionally. Hypotension has been reported rarely with parenteral use.
Phenylephrine Hydrochloride- As for Sympathomimetics, phenylephrine has mainly alpha-agonist effects. It has a longer duration of action than noradrenaline and an excessive vasopressor response may cause a prolonged rise in blood pressure. It induces tachycardia or reflex bradycardia and should therefore be avoided in severe hyperthyroidism and used with caution in severe ischaemic heart disease. Patients with diabetes mellitus or prostatic hyperplasia should also avoid phenylephrine. Since phenylephrine is absorbed through the mucosa systemic effects may follow application to the eyes or the nasal mucosa. In particular, phenylephrine 10% eye drops can have powerful systemic effects. They should be avoided or only used with extreme caution in infants, the elderly, and in patients with cardiac disease, significant hypertension, or advanced arteriosclerosis. Fatalities have been reported in patients with pre-existing cardiovascular disease.
Dextromethorphan Hydrobromide- Adverse effects with dextromethorphan appear to be rare and may include dizziness and gastrointestinal disturbances. Excitation, confusion, and respiratory depression may occur after overdosage. Dextromethorphan has been subject to abuse, but there is little evidence of dependence of the morphine type.

WARNING
Do not use with any other drug containing acetaminophen (PARACETAMOL) (prescription or non-prescription).
If you are not sure whether a drug contains acetaminophen (PARACETAMOL), ask a doctor or pharmacist.

Pregnancy and Lactation
Paracetamol is generally considered to be the analgesic of choice in pregnant patients. However, the frequent use of paracetamol (defined as most days or daily use) in late pregnancy may be associated with an increased risk of persistent wheezing in the infant which may persist into childhood. No adverse effects have been seen in breast-fed infants whose mothers were receiving paracetamol, and the American Academy of Pediatrics considers that it is therefore usually compatible with breast feeding. The BNF also considers that the amount of paracetamol distributed into breast milk is too small to be harmful to a breast-fed infant.
Phenylephrine Hydrochloride- Phenylephrine has been assigned to pregnancy category C by the FDA. Animal studies have not been reported. There are no controlled data in human pregnancy. Phenylephrine is only recommended for use during pregnancy when benefit outweighs risk. Small amounts of phenylephrine are secreted in breast milk.
Dextromethorphan Hydrobromide- Anti-tussive use during pregnancy has not been reported to increase the risk of teratogenic effects. However, there are no controlled data in human pregnancy. Excretion of this drug into breast milk has not been studied, however, usual doses are unlikely to cause harm to a nursing infant, especially infants older than 2 months.

ADR REPORTING STATEMENT
"For suspected adverse drug reaction, report to the FDA: www.fda.gov.ph" Seek medical attention immediately at the first sign of any adverse drug reaction.

Availability
Alu/Clear PVC Blister Pack x 10's (Box of 100's)

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DRP-1252

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CHECKLIST FOR CLIENT

PLEASE CHECK THE FOLLOWING:

GRAPHICS & TEXT	☐ CONFORMS	☐ WITH CORRECTIONS
COLORS	☐ CONFORMS	☐ WITH CORRECTIONS
SIZE / DIMENSION	☐ CONFORMS	☐ WITH CORRECTIONS

☐ 1ST READING ☐ 2ND READING ☐ 3RD READING

CLIENT'S REMARKS

APPROVED AND CHECKED BY:

(Date & Signature Over Printed Name)

***NOTE:**
CLIENT has responsibility to proofread and review all artwork produced during the project. As a result, the client is fully responsible for any errors in spelling, typography, illustrative layout, photography or other errors discovered after printing or reproduction or for any work performed by third-parties selected by the CLIENT. Approved Artwork/Proof will be our basis for final printing.

"**IMPORTANT!** Digital color output may not be 100% the same during actual printing. Digital printout may vary from the actual printing color."