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Provas® EZ Tablet

(Paracetamol + Diphenhydramine HCl + Phenylephrine HCl)

QUALITATIVE AND QUANTITATIVE COMPOSITION

Provas® EZ Tablet
Each film coated tablet contains:
Paracetamol BP.....325mg
Diphenhydramine Hydrochloride BP.....25mg
Phenylephrine Hydrochloride BP 5mg

PHARMACEUTICAL FORM

Tablet

CLINICAL PARTICULARS

THERAPEUTIC INDICATIONS:
For the relief of the symptoms associated with colds and influenza.
Temporarily relieves these symptoms of hay fever or other upper respiratory allergies:
- Headache.
- Nasal congestion, sneezing, runny nose, sinus congestion and pressure.
- Itchy watery eyes, itching of the nose or throat.
- Minor aches and pains.

POSOLOGY AND METHOD OF ADMINISTRATION
Adults and children 12 years and over: Two tablets every 4 hours. Do not take more than 10 tablets, in 24 hours or as prescribed by physician.
Children under 12 years: Not recommended for children under 12 years of age.
Hepatic Dysfunction: Caution should be exercised when administering this medicine to patients with severe hepatic impairment.
Renal Dysfunction: Caution should be exercised when administering this medicine to patients with moderate to severe renal impairment.

CONTRAINDICATIONS
- Contraindicated in individuals with known hypersensitivity to any active ingredient of the product.
- With any other drug containing acetaminophen (prescription or nonprescription).
- With any other product containing diphenhydramine hydrochloride, even one used on skin.
- Concomitant use of other sympathomimetic decongestants, beta-blockers or monoamine oxidase inhibitors (MAOIs) (certain drugs for depression, psychiatric or emotional conditions or Parkinson's disease) or within 14 days of stopping MAOI treatment. The concomitant use of MAOIs may cause a rise in blood pressure or hypertensive crisis.

SPECIAL WARNINGS AND PRECAUTIONS FOR USE:
- Severe liver damage may occur if you take more than 4,000mg of paracetamol in 24 hours, with other drugs containing paracetamol, 3 or more alcoholic drinks every day while using this product.
- Paracetamol may cause severe skin reactions. Symptoms may include skin reddening, blisters and rash. If a skin reaction occurs, stop use and seek medical help right away.
- Diphenhydramine hydrochloride may enhance the sedative effects of central nervous system depressants including alcohol, sedatives, opioid analgesics, antipsychotics and tranquilizers.
- Alcoholic beverages should be avoided while taking this product.
- If any of the symptoms like restlessness, sleep disturbances, hallucination, occur, this medicinal product should be stopped.
- Patients with the following conditions should be advised to consult a physician before using this product:
  - Acute or chronic asthma, a persistent or chronic cough such as occurs with chronic bronchitis or emphysema or where cough is accompanied by excessive secretions.
  - Prostatic hyperplasia, urine retention.
  - Patients with thyroid disease who are receiving thyroid hormones.
- Use with caution in patients with susceptibility to angle-closure glaucoma, severe hepatic impairment, moderate to severe renal impairment (particularly if accompanied by cardiovascular disease) or occlusive vascular disease. The hazards of overdose are greater in those with non-cirrhotic alcoholic liver disease.
- Do not use with any other product containing diphenhydramine hydrochloride, including topical formulations used on large areas of skin.
- Taking product with other paracetamol-containing products, could lead to overdose and should therefore be avoided.
- May cause drowsiness. This product should not be used to sedate a child.
- Concomitant use of decongestants and other cough and cold medicines should be avoided.
- Medical advice should be sought before taking this product in patients with liver disease, heart disease, high blood pressure, thyroid disease, diabetes, trouble urinating due to an enlarged prostate gland, a breathing problem such as emphysema or chronic bronchitis, glaucoma, in patients taking the blood thinning drug warfarin taking, sedatives or tranquilizers.

INTERACTION WITH OTHER MEDICINAL PRODUCTS AND OTHER FORMS OF INTERACTION:
Cardiac glycosides: Increased risk of dysrhythmias.
Ergot alkaloids (ergotamine & methysergide): Increased risk of ergotism.
Oxytocin: Risk of hypertension.
Anaesthetic agents: Concurrent use with halogenated anaesthetic agents such as chloroform, cyclopropane, halothane, enflurane or isoflurane may provoke or worsen ventricular arrhythmias.
Hepatic microsomal enzyme inducers: The use of drugs that induce hepatic microsomal enzymes, such as anticonvulsants and oral contraceptives, may increase the extent of metabolism of paracetamol, resulting in reduced plasma concentrations of the drug and a faster elimination rate.
Metoclopramide/domperidone/cholestyramine: The speed of absorption of paracetamol may be increased by metoclopramide or domperidone, and absorption reduced by cholestyramine.
Anticoagulants: The anticoagulant effect of warfarin and other coumarins may be enhanced by prolonged regular use of paracetamol with increased risk of bleeding; occasional doses have no significant effect.
Alcohol: Chronic alcohol intake can increase the hepatotoxicity of paracetamol overdose and may have contributed to the acute pancreatitis reported in one patient who had taken an overdose of paracetamol. Acute alcohol intake may diminish an individual's ability to metabolize large doses of paracetamol, the plasma half-life of which can be prolonged.
CNS depressants: Diphenhydramine hydrochloride may enhance the sedative effects of CNS depressants including barbiturates, hypnotics, opioid analgesics, anxiolytic sedatives, antipsychotics and alcohol.
Anti-muscarinic drugs: Diphenhydramine hydrochloride may have additive muscarinic action with other drugs, such as atropine and tricyclic antidepressants. This may result in tachycardia, mouth dryness, gastrointestinal disturbances (e.g., colic), urinary retention and headache.
Monoamine oxidase inhibitors (including moclobemide): Hypertensive interactions occur between sympathomimetic amines such as phenylephrine hydrochloride and monoamine oxidaseinhibitors (see contraindications).
Sympathomimetic amines: Concomitant use of phenylephrine hydrochloride with other sympathomimetic amines can increase the risk of cardiovascular side effects.
Beta-blockers and other antihypertensives (including debrisoquine, guanethidine, reserpine, methyldopa): Phenylephrine hydrochloride may reduce the efficacy of beta-blocking drugs and antihypertensive drugs. The risk of hypertension and other cardiovascular side effects may be increased.
Tricyclic antidepressants (e.g. amitriptyline): May increase the risk of cardiovascular side effects with phenylephrine hydrochloride.
Digoxin and cardiac glycosides: Increase the risk of irregular heartbeat or heart attack.
Warfarin and other coumarins: The anticoagulant effect of warfarin and other coumarins may be enhanced by prolonged regular daily use of paracetamol with increased risk of bleeding; occasional doses have no significant effect.

PREGNANCY AND LACTATION:
Pregnancy: This medicine, like most medicines, should not be used during pregnancy unless the potential benefit of treatment to the mother outweighs any possible risk to the developing foetus.

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Diphenhydramine hydrochloride is known to cross the placenta and, therefore, should only be used during pregnancy if considered essential by a doctor.
The safety of phenylephrine hydrochloride during pregnancy has not been established.
Breast-feeding: This product should not be used in breast feeding without medical advice.
Paracetamol and phenylephrine hydrochloride are excreted in breast milk, but not in a clinically significant amount.
Diphenhydramine hydrochloride is excreted into human breast-milk, but levels have not been reported. Although the levels are not thought to be sufficiently high enough after therapeutic doses to affect the infant, the use of diphenhydramine hydrochloride during breast-feeding is not recommended.

EFFECTS ON ABILITY TO DRIVE AND USE MACHINES:
May cause drowsiness. If affected, do not drive or operate machinery.

UNDESIRABLE EFFECTS:
Hypertension, hypotension, reflex tachycardia, tachycardia, severe peripheral and visceral vasoconstriction, dizziness, excitability, headache, restlessness, sedation, sleepiness, tremor, dermatologic rash, increased appetite, xerostomia, anaemia blood dyscrasias (neutropenia, pancytopenia, leukopenia), bilirubin and alkaline phosphatase may increase, urinary retention.

OVERDOSE:
Paracetamol: Liver damage is possible in adults who have taken 10g or more of paracetamol. Treatment with activated charcoal should be considered if the overdose has been taken within 1 hour.
Treatment with N-acetylcysteine may be used up to 24 hours after ingestion of paracetamol, 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.
Diphenhydramine hydrochloride: Following overdose in adults, moderate symptoms have been associated with ingestions of greater than 300-500mg and serious symptoms associated with doses greater than 1g diphenhydramine hydrochloride.
Young children may be more sensitive to the effects of overdose. Treatment of over dosage should be symptomatic and supportive. Measures to promote rapid gastric emptying (such as induced emesis or gastric lavage) and in cases of acute poisoning activated charcoal, may be useful. The intravenous use of physostigmine may be efficacious in antagonising severe anticholinergic symptoms.
Phenylephrine hydrochloride: Treatment should be as clinically appropriate. Severe hypertension may need to be treated with an alpha blocking drug such as phentolamine.

PHARMACOLOGICAL PROPERTIES

PHARMACODYNAMIC PROPERTIES:
Paracetamol: Paracetamol is an analgesic and antipyretic. The therapeutic effects of paracetamol are thought to be related to inhibition of prostaglandin synthesis, as a result of the inhibition of cyclo-oxygenase. The antipyretic action of paracetamol appears to stem from a direct action on the hypothalamic heat-regulating centres, producing peripheral vasodilation, and consequent loss of heat.
Diphenhydramine hydrochloride: Diphenhydramine hydrochloride is an antihistamine that competes with histamine for receptor sites on effector cells. The compound also possesses antispasmodic, antitussive, antiemetic, sedative and secretolytic effects.
Phenylephrine hydrochloride: Phenylephrine hydrochloride is a sympathomimetic decongestant; relieves symptoms resulting from irritation of upper respiratory tract tissue; shrinks swollen mucous membranes, reduces nasal congestion & tissue hyperemia.

PHARMACOKINETIC PROPERTIES:
Paracetamol: Paracetamol is rapidly absorbed from the gastrointestinal tract, with peak plasma concentrations occurring approximately 30 to 90 minutes following oral administration.
Paracetamol is incompletely available to the systemic circulation after oral administration since a variable proportion is lost through first pass metabolism. Oral bioavailability in adults appears to depend on the amount of paracetamol administered, increasing from 63% following a 500mg dose, to nearly 90% after 1 or 2g. Effects are apparent within 30 minutes and last for between 4 and 8 hours. Less than 50% is protein bound.
The compound is extensively metabolized in the liver to inactive conjugates of glucuronic and sulphonic acids (saturable) and to a hepatotoxic intermediate metabolite (first order) by P450 mixed function oxidase. The intermediate is detoxified by glutathione (saturable). Less than 4% is excreted unchanged in the urine.
Half-life for the drug usually lies in the range 2.75-3.25 hours although this may be mildly increased in chronic liver disease, or extended in acute paracetamol poisoning.
Diphenhydramine hydrochloride: Diphenhydramine hydrochloride is well absorbed from the gastrointestinal tract. Peak serum levels are reached between 2 and 2.5 hours after an oral dose. Duration of activity is between 4 and 8 hours. The drug is widely distributed throughout the body, including the CNS and some 78% is bound to plasma proteins. Estimates of the volume of distribution lie in the range 3.3-6.8L/kg.
Diphenhydramine hydrochloride experiences extensive first-pass metabolism, two successive N-demethylations, and the resultant amine is then oxidized to a carboxylic acid. Values for plasma clearance lie in the range 600-1300ml/min and the terminal elimination half-life lies in the range 3.4-9.3 hours. Little unchanged drug is excreted in the urine.
Phenylephrine hydrochloride: Phenylephrine hydrochloride is irregularly absorbed from the gastrointestinal tract and undergoes first-pass metabolism by monoamine oxidase in the gut and liver; orally administered phenylephrine hydrochloride has reduced bioavailability. It is excreted in the urine almost entirely as the sulphate conjugate.

SHELF LIFE
See expiry on the pack.

AVAILABILITY
Provas® EZ tablet in a pack of 30's

INSTRUCTIONS
Dosage: As advised by the physician.
To be sold on the prescription of a registered medical practitioner only.
Keep out of the reach of children.
Avoid exposure to heat, light and humidity.
Store between 15 to 30°C.
Improper storage may deteriorate the medicine.

پرووا س® ای زیڈ ٹیبلٹ

(پیراسیٹامول + ڈائفن ہائیڈرامین ہائیڈروکلورائیڈ + فینائل ایفرن ہائیڈروکلورائیڈ)

ہدایات:

خوراک: ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔
صرف رجسٹرڈ ڈاکٹر کے نسخے کے مطابق فروخت کریں۔
بچوں کی پہنچ سے دور رکھیں۔
دوا کو گرمی، روشنی اور نمی سے محفوظ ۱۵ سے ۳۰ ڈگری سینٹی گریڈ کے درمیان میں رکھیں ورنہ دوا خراب ہو جائیگی۔

Manufactured by:
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