NOVOGOLD

PRODUCT INFORMATION

NOVOGOLD(cyproheptadine hydrochloride, MSD) is a serotonin and histamine antagonist with anticholinergic and sedative effects and is also recommended for the symptomatic treatment of allergic disorders and pruritic dermatoses, as well as certain types of vascular headaches.

DESCRIPTION

NOVOGOLD I
Yellow coloured coated caplets with “NOVO” embossed on one side and plain on other side

COMPOSITION

Each film coated tablet contains:-
Cyproheptadine Hydrochloride B.P eq.to Anhydrous Cyproheptadine Hydrochloride... 4 mg

PHARMACOLOGY

NOVOGOLD (cyproheptadine HCL, MSD) is a serotonin and histamine antagonist with anticholinergic and sedative effects. Anti serotonin and antihistamine drugs appear to compete with serotonin and histamine, respectively for receptor sites.

Animal studies have shown cyproheptadine hydrochloride to be an effective serotonin and histamine antagonist, comparable, in general, to that of the most active known substances.

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Cyproheptadine hydrochloride antagonises the following effects of serotonin in laboratory animals:

bronchoconstrictor (guinea pig)
vasodepressor (dog)
spasmogenic (isolated rat uterus)
oedema (rat)
lethal (Haemophilus pertussis-treated mouse)

In all these effects, cyproheptadine hydrochloride approaches, equals or surpasses the activity of specific serotonin antagonists, such as l-benzyl-2-methyl-5-methoxytryptamine (BAS) and l-benzyl-2-methyl-5-hydroxytryptamine (BMS). In contrast, specific antihistamines, even the most potent, show little or no serotonin antagonism. Thus, cyproheptadine hydrochloride must be considered a serotonin antagonist as well as a histamine antagonist.

Cyproheptadine hydrochloride antagonises or blocks the following effects of histamine in laboratory animals:

bronchoconstrictor (guinea pig)
vasodepressor (dog)
spasmogenic (isolated guinea pig ileum)
anaphylactic shock, active and passive (guinea pig, mouse)
increased gastric secretion (Heidenhain pouch dog)

That cyproheptadine hydrochloride protects both guinea pigs and mice against anaphylactic shock is unusual. In guinea pigs, the pulmonary aspects of anaphylactic shock are attributable to the release of endogenous histamine and can be controlled by substances with specific antihistaminic activity. In mice, however, where histamine release seems to be less important and serotonin release may be involved, specific antihistamines are of little value in protecting against anaphylaxis. Thus, the protective effect of cyproheptadine hydrochloride in mice may be an anti serotonin effect.

The inhibitory effect of cyproheptadine hydrochloride in histamine-induced gastric secretion is also unusual because specific antihistamines do not influence this effect of histamine.

Because of its marked activity as an antagonist of serotonin and histamine in laboratory animals, cyproheptadine hydrochloride was evaluated in man in situations where standard antihistamines are not effective.

In one evaluation, skin reactions were induced in test subjects by the intra dermal injection of histamine, serotonin, and histamine-releasing substances, such as Compound 48-80. The wheals and flares resulting from the injections were observed, as well as the degree of blueness of the wheals produced by intravenous injection of a protein dye, coomassie blue. Coomassie blue was used as an indicator of capillary leakage of plasma proteins because of its propensity for plasma binding and its safety for use in man. Cyproheptadine hydrochloride and two standard antihistamines were administered orally in moderate therapeutic doses. Only cyproheptadine hydrochloride led to a suppression of the whealing responses and the capillary damage demonstrated by the bluing reaction.

Acute and chronic toxicity studies in various laboratory animals indicate that cyproheptadine hydrochloride has an adequate margin of safety. In doses far greater than those in the therapeutic range, ataxia, sedation and tachycardia can be produced, but other objective signs of toxicity are not evident.

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The oral LD_{50} of cyproheptadine is 123 mg/kg, and 295 mg/kg in the mouse and rat, respectively.

There was no evidence of histomorphological changes in the various organs when doses approximating subacute lethal doses were administered to dogs, monkeys, rabbits, and mice. Twelve months of oral toxicity studies in dogs did not reveal functional or anatomical changes. In chronic toxicity studies in rats, only at dosages of 10 to 12 mg/kg/day, far in excess (approximately 200 times) of those required for pharmacodynamic effects, was reversible vacuolisation of the beta cells of the pancreatic islets noted. This was not observed in the other four species of animals used in the toxicity studies. After six months of continuous drug administration there was no evidence derangement of carbohydrate metabolism in man, as measured by serial blood sugar determinations and glucose tolerance tests.

Cyproheptadine hydrochloride has central nervous system effects in laboratory animals, including anticonvulsant and anti tremor activity and behavioural effects. It has weak peripheral anticholinergic activity and moderate local anaesthetic action. It exerts highly effective protection against burn shock in mice. Most of these properties are evident only with doses much larger than those used in therapy. In the rat, for instance, behavioural effects are produced only by doses 50-100 times greater than those required to produce anti serotonin activity.

Cyproheptadine is not a hormone, but has effects on certain endocrine systems in man, possibly as a result of its anti serotonin activity. It acts centrally to reduce ACTH secretion and thus tends to cause modest reductions in adrenal corticosteroid output and plasma cortisol levels. This effect has been studied with variable results in the treatment of Cushing's disease and Nelson's syndrome. Cyproheptadine may reduce plasma growth hormone levels during the early phase of sleep and in response to exogenous arginine or insulin, but does not reduce linear growth. Neither has an increase in linear growth in undersized children been demonstrated beyond that which would normally be expected as a result of improved nutrition. These endocrine effects of cyproheptadine have not been shown to have adverse clinical significance.

PHARMACOKINETICS AND METABOLISM

After a single 4 mg oral dose of ^{14}C-labelled cyproheptadine HCl in normal subjects, given as tablets or syrup, 2-20% of the radioactivity was excreted in the stools. Only about 34% of the stool radioactivity was unchanged drug, corresponding to less than 5.7% of the dose. At least 40% of the administered radioactivity was excreted in the urine. No significant difference in the mean urinary excretion exists between tablet and syrup formulations. No detectable amounts of unchanged drug were present in the urine of patients on chronic 12-20 mg daily doses of a NOVOGOLD syrup formulation. The principal metabolite found in human urine has been identified as a quaternary ammonium glucuronide conjugate of cyproheptadine. Elimination is diminished in renal insufficiency.

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INDICATIONS

As an anti-allergic-antipruritic

NOVOGOLD has a wide range of anti allergic and anti pruritic activity and can be used successfully in the treatment of acute and chronic allergies and pruritus, such as: dermatitis, including neurodermatitis and neurodermatitis circumscripta, eczema, eczematoid dermatitis, dermatographism, mild local allergic reactions to insect bites, hay fever and other seasonal rhinitis, perennial allergic and vasomotor rhinitis, allergic conjunctivitis due to inhalant allergens and foods, urticaria, angioneurotic oedema, drug and serum reactions, anogenital pruritus and pruritus of chickenpox.

NOVOGOLD may be used as therapy for anaphylactic reactions, adjunctive to adrenalin and other standard measures after the acute manifestations have been controlled.

In migraine and vascular types of headache

NOVOGOLD has been reported to have beneficial effects in a significant number of patients diagnosed as having vascular types of headache, such as migraine and histamine cephalalgia. Many patients who have not been able to obtain adequate relief from any other agent have reported amelioration of symptoms with NOVOGOLD. The characteristic headache and feeling of malaise may disappear within an hour or two after the first dose.

CONTRAINDICATIONS

Cyproheptadine should not be used for therapy of an acute asthmatic attack.

Newborn or Premature Infants

This drug should not be used in newborn or premature infants. Use in infants has been associated with apnea, cyanosis, and respiratory difficulty.

Nursing Mothers

Because of the higher risk of antihistamines for infants generally, and for newborn and prematures in particular, antihistamine therapy is contraindicated in nursing mothers.

Other Conditions

. Hypersensitivity to cyproheptadine and other drugs of similar chemical structure
. Monoamine oxidase inhibitor therapy (see DRUG INTERACTIONS)
. Angle-closure glaucoma
. Stenosing peptic ulcer
. Symptomatic prostatic hypertrophy
. Bladder neck obstruction
. Pyloroduodenal obstruction
. Elderly, debilitated patients

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PRECAUTIONS

Antihistamines should not be used to treat lower respiratory tract symptoms including those of acute asthma.

Paediatric Use

Safety and effectiveness in children below the age of two years have not been established.

Overdose of antihistamines, particularly in infants and children, may produce hallucinations, central nervous system depression, convulsions, respiratory and cardiac arrest, and death.

Antihistamines may diminish mental alertness; conversely, particularly in the young child, they may occasionally produce excitation.

Newborn or Premature Infants (See CONTRAINDICATIONS)

Activities Requiring Mental Alertness

Patients should be warned about engaging in activities requiring mental alertness and motor coordination, such as driving a car or operating machinery.

Antihistamines are more likely to cause dizziness, sedation, and hypotension in elderly patients.

Other

Rarely, prolonged therapy with antihistamines may cause blood dyscrasias.

Cyproheptadine has an atropine-like action and, therefore, should be used with caution in patients with:

- History of bronchial asthma
- Increased intraocular pressure
- Hyperthyroidism
- Cardiovascular disease
- Hypertension

Carcinogenicity/Mutagenicity And Impairment Of Fertility Cyproheptadine has not been evaluated in long term carcinogenicity studies.

Cyproheptadine at about 10 times the human dose had no effect on fertility in a two litter study in rats or a two generation study in mice.

Cyproheptadine did not produce chromosome damage in human lymphocytes or fibroblasts in vitro; high dose (10^{-4}M) were cytotoxic. Cyproheptadine did not have any mutagenic effect in the Ames microbial mutagen test; concentrations of above 500 mcg/plate inhibited bacterial growth.

Pregnancy (Cat A)

The use of any drug in pregnancy or in women of childbearing potential requires that the anticipated benefit be weighed against possible hazards to the embryo or foetus.

Reproduction studies have been performed in rabbits, mice, and rats at doses up to 32 times the human dose and have revealed no evidence of impaired fertility or harm to the foetus

due to cyproheptadine. There are, however, no adequate or well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

Use In Lactation

It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, and because of the potential for serious adverse reactions in nursing infants from NOVOGOLD, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother (see CONTRAINDICATIONS).

Drug Interactions

MAO inhibitors prolong and intensify the anticholinergic effects of antihistamines.

Antihistamines may have additive effects with alcohol and other CNS depressants, eg: hypnotics, sedatives, tranquillisers, anti anxiety agents.

Drugs with anti-serotonin activity, such as cyproheptadine, may interfere with serotonin-enhancing anti-depressant drugs.

Cyproheptadine may cause a false positive test result for tricyclic antidepressant drugs when evaluating a drug screen.(e.g. urine, serum).

ADVERSE REACTIONS

The side effects that appear frequently are drowsiness and somnolence. Many patients who complain initially of drowsiness may no longer do so after the first three or four days of continuous administration.

Adverse reactions which have been reported with the use of antihistamines:

Central Nervous System

sedation
sleepiness (often transient)
dizziness
disturbed co-ordination
confusion
restlessness
excitation
nervousness
tremor
irritability
aggressive behaviour
insomnia
paraesthesias
neuritis
convulsions
euphoria
hallucinations
hysteria
faintness

NOVOGOLD

Integumentary

allergic manifestation of rash and oedema
excessive perspiration
urticaria
photosensitivity

Special Senses

acute labyrinthitis
blurred vision
diplopia
vertigo
tinnitus

Cardiovascular

hypotension
palpitation
tachycardia
extrasystoles
anaphylactic shock

Haematological

Haemolytic anaemia
leucopoenia
agranulocytosis
thrombocytopoenia

Digestive System

cholestasis
hepatic failure
hepatitis
hepatic function abnormality
dryness of mouth
epigastric distress
anorexia
nausea
vomiting
diarrhoea
constipation
jaundice

Genitourinary

frequency of micturition
difficult micturition
urinary retention
early menses

Respiratory

dryness of nose and throat
thickening of bronchial secretions
tightness of chest and wheezing
nasal stuffiness
epistaxis

Miscellaneous

fatigue
chills
headache
increased appetite/weight gain

DOSAGE AND ADMINISTRATION

Children Under 2 years of Age

There is no recommended dosage schedule for children under 2 years of age.

ALLERGIES AND PRURITUS

Dosage must be individualised. Since the anti-allergic effect of a single dose usually lasts four to six hours, the daily requirement should be given in divided doses three times a day or as often as necessary to provide continuous relief.

Adults

The therapeutic range is from 4 mg to 20 mg a day, the majority of patients requiring 12 mg to 16 mg a day. An occasional patient may require as much as 32 mg a day for adequate relief. It is suggested that dosage be initiated with 4 mg three times a day and adjusted according to the size and response of the patient. The dosage is not to exceed 32 mg a day.

Children (7 - 14 years)

The usual dosage is 4 mg three times a day. This dosage may be adjusted as necessary according to the size and response of the patient. If an additional dose is required, it should be taken preferably at bedtime. The dosage is not to exceed 16 mg a day.

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Children (2 - 6 years)

It is suggested that dosage be initiated with 2 mg two or three times a day and adjusted as necessary according to the size and response of the patient. If an additional dose is required, it should be taken at bedtime. The total dosage is not to exceed 12 mg a day.

FOR MIGRAINE AND VASCULAR TYPES OF HEADACHE

For prophylaxis or treatment the recommended dosage is 4 mg initially, repeated in 1/2 hour if necessary; not to exceed 8 mg in a 4 to 6 hour period. Relief is usually obtained in responsive patients with 2 doses (total 8 mg) and maintained with 4 mg every 4 to 6 hours.

OVERDOSAGE

Signs and Symptoms

Antihistamine overdosage reactions may vary from central nervous system depression or stimulation to convulsions respiratory and cardiac arrest, and death especially in infants and children. Also, atropine-like signs and symptoms (dry mouth; fixed, dilated pupils; flushing, etc.) as well as gastrointestinal symptoms may occur.

Treatment

If vomiting has not occurred spontaneously the patient should be induced to vomit if conscious with syrup of ipecac.

If the patient is unable to vomit, perform gastric lavage followed by activated charcoal. Isotonic or 1/2 isotonic saline is the lavage of choice.

Precautions against aspiration must be taken especially in infants and children.

When life threatening CNS signs and symptoms are present, intravenous physostigmine salicylate may be considered. Dosage and frequency of administration are dependent on age, clinical response, and recurrence after response. (See package circulars for physostigmine products.)

Saline cathartics, such as milk of magnesia, draw water into the bowel by osmosis and therefore, are valuable for their action in rapid dilution of bowel content.

Stimulants should not be used.

Vasopressors may be used for hypotension.

Excipients:

Dibasic calcium phosphate, Maize starch, Gelatin, Sodium methyl paraben, Sodium propyl paraben.

NOVOGOLD

Film-coating

COLOUR NOVOMIX (YELLOW) -110067

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

4 years

6.4 Special precautions for storage

This medicinal product does not require any special storage conditions.

6.5 Nature and contents of container

10 TABLETS PACKED IN ALU –PVC BLISTER, PACKE, AND 3 BLISTER PACK IN MONO CARTON.

6.6 Special precautions for disposal

Any unused medicinal product or waste material should be disposed of in accordance with local

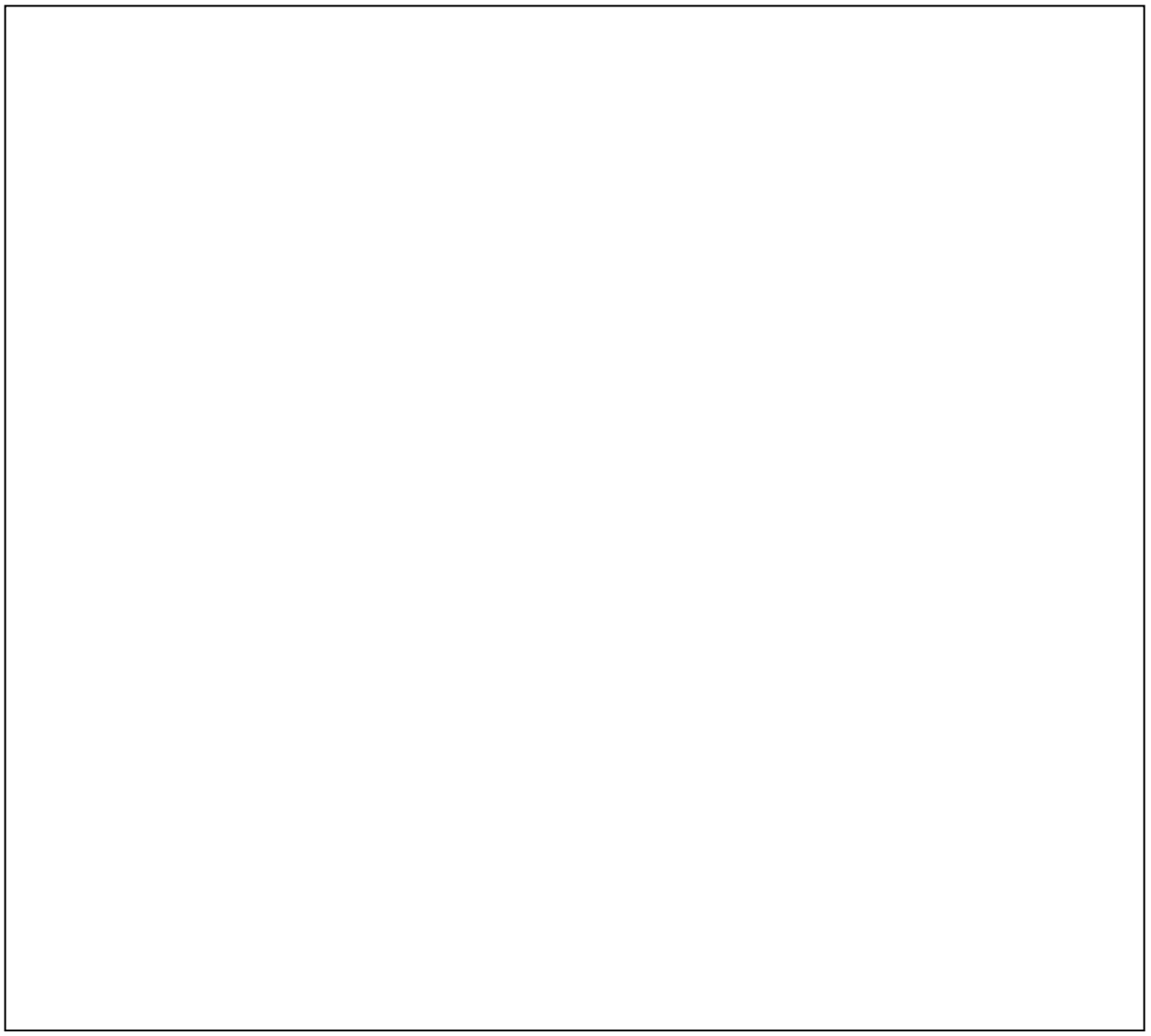
Requirements.

SOLE AGENT: - NCI PHARMACHEM INDUSTRIES

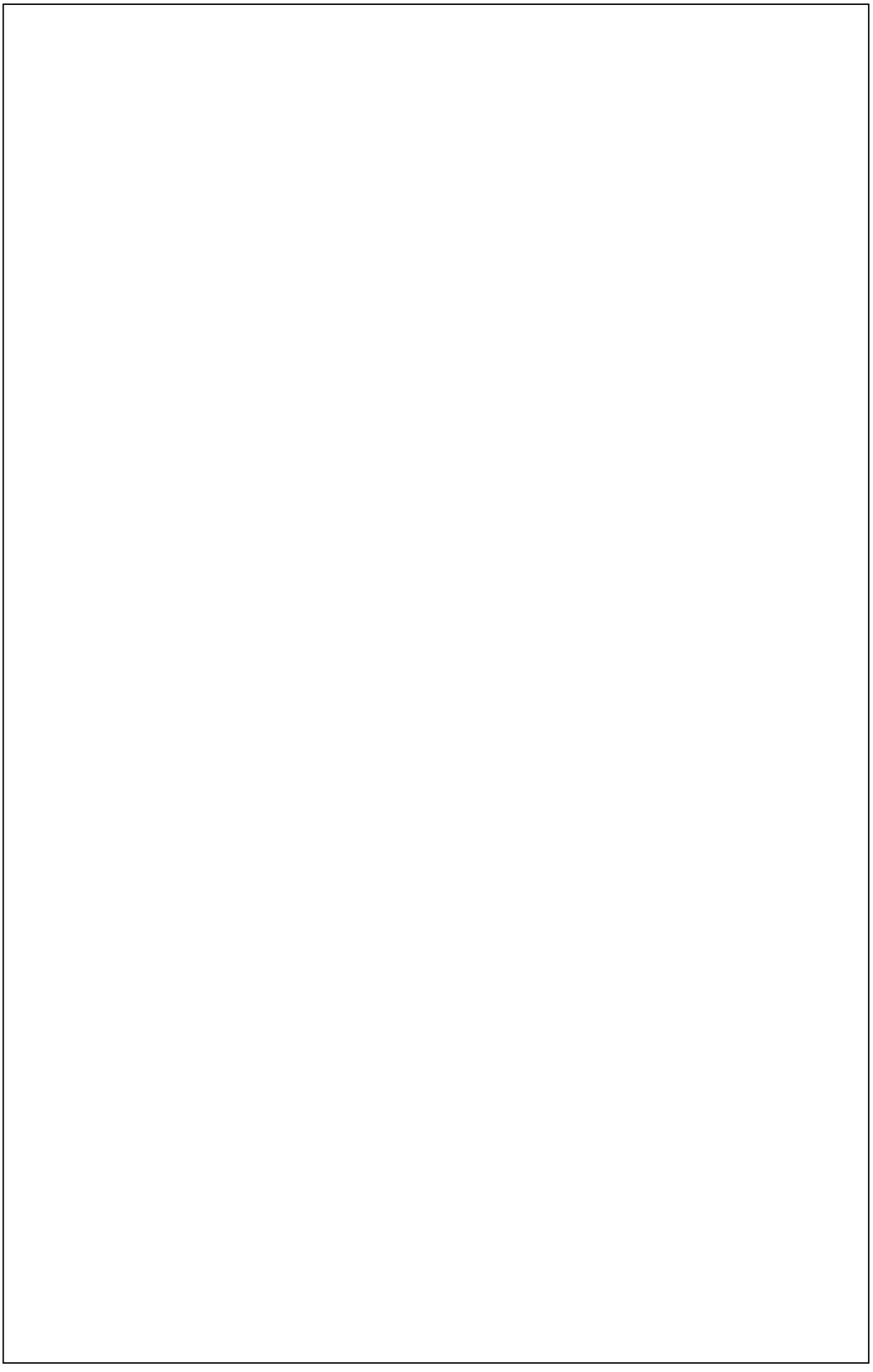
LAGOS, NIGERIA.

NAFDAC REG. NO. : 04-5056

NOVOGOLD



NOVOGOLD



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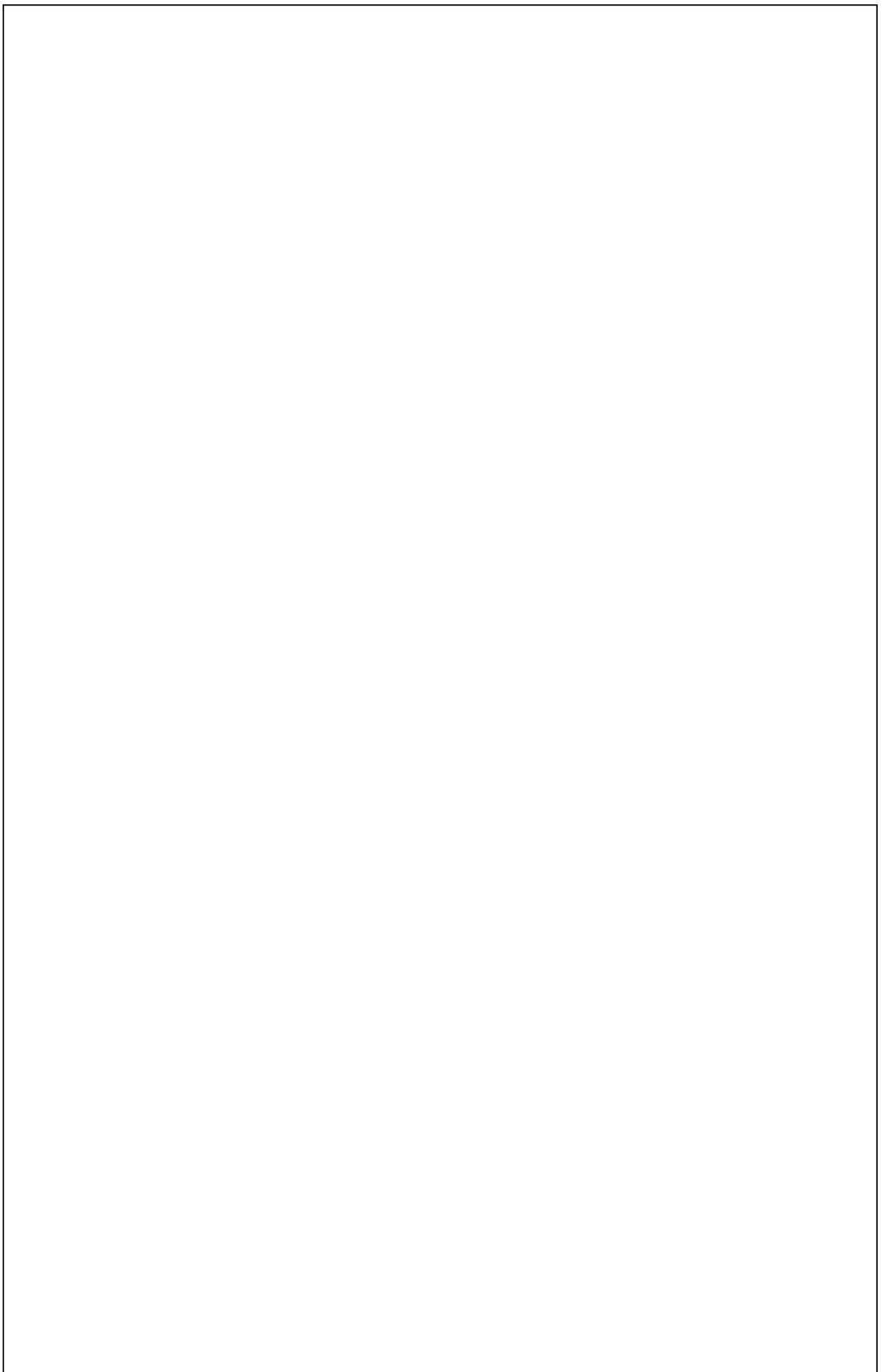

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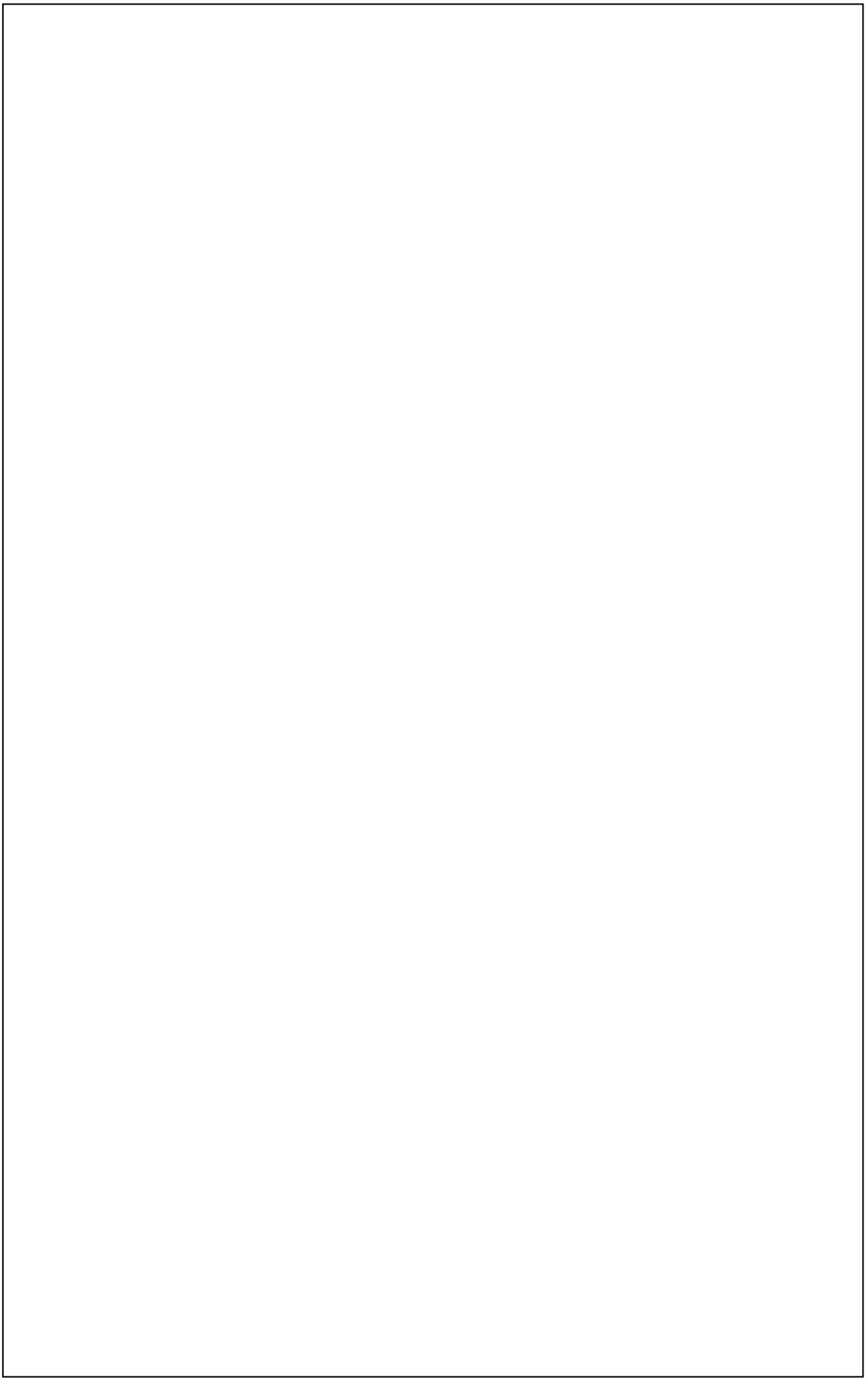

NOVOGOLD

be induced to vomit if conscious with syrup of Ipecac. If the patient is unable to vomiting perform gastric lavage followed by activated charcoal, isotonic or isotonic salline is the lavage of choice.

Precautions against aspiration aspiration ½ must be taken, especially in infants and children. When life threatening CNS signs and symptoms are present intravenous physostigmine salicylate may be considered dosage and frequency of administration are dependant on age, clinical respones and recurrence after reponse (See package circulare for physostigmine products.) Saline cathartics, such as milk of magnesia, draw water into the bowel by osmosis and therefor are valuable for their action in rapid dilution of bowel content. Stimulants should not be used. Vasopressors may be used to treat hypotension.

HOW SUPPLIED

NOVO GOLD Tablets supplied in blister of 10 tablets and pack size will be 3 x 10 tablets. Each film coated tablet contains 4 mg Cyproheptadine hydrochloride B.P. (Anhydrous).

Mfg. Lic. No KD-493
Nafdac Reg. No - 04 - 5056

Manufactured By
MANCARE
PHARMACEUTICAL PVT. LTD.
Plot. 60, V.M.I.E., Dhowali Village,
Vasai (w), Maharashtra, INDIA.

Marketed by

NCI pharma Chem Ind, Ltd.
29, Igbehinadun Street, Oshodi, Lagos, Negeria.

NOVO
GOLD

NOVOGOLD

NOVO GOLD CAPLET

Cyproheptadine Hydrochloride Tablets

NOVO GOLD (Cyproheptadine Hydrochloride B.P. 4mg) is aserotonin and histaminst with anticholinergic and sedative effects and is also recommended for the symptomatic treatment of allergic disorders and prurutic dermatoses, as well as certain types of vascular headaches.

INDICATION:

As an Antiallergic- Antipruritic

NOVO GOLD has a wide range of Antiallergic and Antipruritic activity and can be used successfully in the treatment of acute and chronic allergies and prurutic, such as dermatitis, including neurodermatitis and neurodermatitis circumscripta, eczema, eczematoid dermatities dermatographism, mild local allergic reaction to inset bites, hay fever and other seasonal rhinitis, perennial allergic and vasomotor rhinitis, allergic conjunctivitis due to inhalant allergic and foods, urticaria, angioneurotic edema, drug and serum reactions, anogenital pruritus and pruritus of chickenpox.

NOVO GOLD may be used as therapy for anaphylactic reactions, aduntive to epinephrine and other standard measures after the acute manifestation have been controlled.

In migraine and vascular types of headache

Novo Gold has been reported to have beneficial effects in significant number of patients diagonsed as having vascular types of headache, such as migraine and histamine cephalagia. Many patients who have not been able to obtain adequate relief from any other agent have reported amelioraion of symptoms With **NOVO GOLD**. The Characteristic headache and feeling of malaise may disappear within an hour or two after the first dose.

DOSAGE AND ADMINISTRATION:

Dosage recommendations

There is no recommended dosage schedule for children under two years of age.

Allergies and pruritus

Dosage must be individualized since the antiallergic effect of a single dose usually lasts four to six hours, the daily requirement should be given in divided doses three time a day or as often as necessary to provide continuous relief.

Adults

The therapeutic range is from 4 mg to 20 mg a day, the majority of patients requiring 12 mg to 16 mg a day. An occasional patient may require as much as 32 mg a day for adequate relief. It is suggested that dosage be initiated with 4 mg three times a day or one 8 mg capsule twice a day and adjusted according to the size and response of the patient. The dosage is not to exceed 32mg a day.

Children (7 to 14 years)

The usual dosage is 4 mg two or three times a day, This dosage may be adjusted as necessary according to the size and response of the patient. If a additional dose is required. It should be taken accordingly preferably at bed time. The dosage is not to exceed 16 mg a day.

Children (2 to 7 years)

It is suggested that dose be initiated with 2 mg or three times a day and adjusted as necessary according to the size and response of the patient. If an additional dose is required it should be taken at bedtime. The total dosage is not to exceed 12 mg a day.

For Migraine and vascular types of headaches

For prophylaxis or therapy, the recommended dosage is 4 mg initially. Repeated in ½ hour if necessary. Not to exceed 8 mg in 4 to 6 hour period. Relief usually is obtained in responsive patients with 2 doses (total 8 mg) and maintain with 4 mg every 4 to 6 hours.

CONTRAINDICATIONS

Cyproheptadine should not be used for therapy of an acute asthmaticattack.

Newborn or premature infants

This drugs should not be used in newborn or premature infants.

Nursing mothers

Because of the higher risk of antihistamines for infants generally and for newborn and premature in particlulars, antihistamine therapy is contraindicated in nursing mother.

Other conditions

- Hypersensitivity to cyproheptadine and other drugs of similar chemical structure
- Monoamine oxidase inhibitor therapy (see Drug Interactions)
- Angle - closure glaucoma.
- Stenosing peptic ulcer.
- Symptomatic prostatic hypertrophy.
- Bladder neck obstruction .
- Pyloroduodenal obstruction.
- Elderly, debilitated patients.

PRECAUTIONS

Antihistamines should not be used to treat lower respiratory tract symptoms including those of acute asthma.

Paediatric Use

Safety and effectiveness in children below the age of two years have not been established. Overdoses of antihistamines, particularly in infants and children, may produce hallucinations, central nervous system depression, convulsions and death. Antihistamines may diminish metal alertness, conversely, particularly in the young child, they may occasionally produce excitation.

Newborn or premature infants

(See contraindications)

Pregnancy

The use of any drug in pregnancy or in woman of child bearing potential required that the anticipated benefit be weight against possible hazards to the embryo or foetus.

Nursing mother

It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk and because of the potential for serious adverse reactions in nursing infants from **NOVO GOLD** a decision should be made whether to discontinue the drug, taking into account the importance of the drug to the mother.

(See Contraindications)

Activities requiring mental alertness

Patients should be warned about engaging in activities required mental alertness and motor co-ordination, such as driving a car or operation machinery.

Antihistamines are more likely to cause dizziness sedation any hypotesion in elderly patients.

Other

Rarely, prolonged therapy with antihstamines may cause blood dyscrassias.

Cyproheptadine has an atropine-like action and therefor, should be used with caution in patients with:

History of bronchial asthama.

Increase intraocular pressure.

Hyperthyroidism.

Cardiovascular disease.

Hypertension.

DRUG INTERACTIONS

MAO inhibitors prolog and intensify the anticholinergic effect of Antihistamines.

CNS depressants

Antihistamines may have additive effect with alcohol and otherCNS depressant, eg. Hyponotics, Sedatives, tranqulizers, antianxiety agents.

SIDE EFFECTS

The side effect that appear frequently are drowsiness and somnolence. Many patients who complain initially of drowsiness may no longer do so after the first three or four days continuous administration. Averse reaction which have been reported with the use of Antihistamines are as follow:

CENTRAL NERVOUS SYSTEM

Sedation
Sleepiness (often transient)
dizziness
Disturbed co- ordination
Confusion
Restlessness
Excitation
Nervousness
Tremor
Irritability
Insomnia
Paresthesias
Neuritis
Convulsion
Euphoria
Hallucination
Hysteria
Faintness

INTEGUMENTARY

Allergic manifestation of rash eema
Excessive perspiration
Urticaria
photo sensitivity

GENITOURINARY

Frequency of micturition
Difficult micturition
Urinary retention
Early menses

RESPIRATORY

Dryness of nose and throat
Thickening of bronchial secretion
Tightness of chest wheezing
Nasal stuffiness

SPECIAL SENSES

acute labyrinthisities
blurred vision
diplopia
vertigo
tinnitus

CARDIO VASCULAR

hypotention
palpitation
tachycardia
extra systoles
anaphylactic shock

HEMATOLOGIC

hemolytic anemia
leukopenia
agranulocytosis
thrombocytopenia

DIGESTIVE SYSTEM

dryess of mouth
epigastric distress
anorexia
vomitting
diarrhoea
constipation jaundice

MISCELLANEOUS

fatigue
Chills
headache

MANAGEMENT OF OVERDOSE

Antihistamine overdoseage reaction may vary from central nervous system depression or stimulation to convulsion and death especially in infants and children. Also atropine-like signs and symptoms (dry mouth, fixed dilated pupils flushing etc.) As well as gastrointestinal symptoms may occur.