148 mm

210 mm

10 mm

75 mm

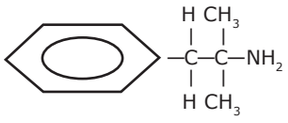
PRODUCT INFORMATION

DUROMINE®

(Phentermine)

NAME OF THE DRUG

Phentermine (phenyl tertiary butylamine, $C_{10}H_{15}N$)



DESCRIPTION

Each Duromine capsule contains phentermine as an ion-exchange resin complex equivalent to 15 or 30 mg phentermine depending on strength. The ion-exchange resin is quite stable, highly insoluble and without pharmacological effect until it reacts with cations (hydrogen, potassium, sodium etc) present in the gastrointestinal fluids. Phentermine is then released from the resin complex at a rate dependent on the total concentration of these cations. Since this concentration is fairly constant throughout the entire gastrointestinal tract, continuous and controlled ionic release occurs over a 10 to 14 hour period.

PHARMACOLOGY

Pharmacodynamic properties

Phentermine is a sympathomimetic amine with significant anorectic activity in animal models. Its appetite suppressant effect is generally considered to be exerted through the hypothalamus, but it is not certain that this is the only effect related to weight loss. Phentermine has major effects on the dopaminergic and noradrenergic nervous systems. The cardiovascular effects include a pressor response and increase in heart rate and force of contraction.

Pharmacokinetic properties

Absorption of phentermine is almost complete. The rate of absorption from the resin complex is significantly slower than that from the hydrochloride salt resulting in a lower and later peak blood level. Phentermine is readily absorbed from the gastro-intestinal tract. Following an oral dose of phentermine capsule, one study demonstrated urinary excretion of unchanged drug ranging from 62.7% to 84.8% in 72 hours. The remainder is metabolised in the liver. The half-life of phentermine is about 25 hours. In one study in volunteers acidification of the urine reduced the half-life to 7 - 8 hours.

INDICATIONS

Duromine is an anorectic agent indicated in the management of obesity as a short-term adjunct in a medically monitored comprehensive regimen of weight reduction based, for example, on exercise, diet (caloric/kilojoule restriction) and behaviour modification in obese patients with a body mass index (BMI) of 30 kg/m^2 or greater. The treatment with Duromine can be initiated in overweight patients with a lower BMI (25 to 29.9 kg/m^2) which increases the risk of morbidity from a number of disorders. Secondary organic causes of obesity should be excluded by diagnosis before prescribing this agent.

CONTRAINDICATIONS

Pulmonary artery hypertension; existing heart valve abnormalities or heart murmurs; moderate to severe arterial hypertension; cerebro-vascular disease; severe cardiac disease including arrhythmias, advanced arteriosclerosis; known hypersensitivity to sympathomimetic drugs; hyperthyroidism; agitated states or a history of psychiatric illnesses including anorexia nervosa and depression; glaucoma; history of drug/alcohol abuse or dependence; concomitant treatment with Monoamine Oxidase (MAO) Inhibitors or within 14 days following their administration.

PRECAUTIONS

Special Precautions

Duromine capsules are indicated only as short-term monotherapy for the management of exogenous obesity. The safety and efficacy of combination therapy with phentermine and any other drug products for weight loss have not been established. Therefore, coadministration of drug products for weight loss is not recommended.

Since the selective serotonin reuptake inhibitor (e.g. fluoxetine, sertraline, paroxetine), ergot-like drugs and clomipramine affect serotonin disposition there remains a theoretical risk that combination of these agents with phentermine may also be associated with cardiac valvular disease and is not recommended. There is no direct scientific evidence to confirm this theory.

Valvular Heart Disease: Serious regurgitate cardiac valvular disease, primarily affecting the mitral, aortic and/or tricuspid valves, has been reported in otherwise healthy persons who had taken a combination of fenfluramine or dexfenfluramine with phentermine for weight loss. The aetiology of these valvulopathies has not been established and their course in individuals after the drugs are stopped is not known. There have been no reported cases to date of valvular heart disease occurring with the use of phentermine alone.

Primary Pulmonary Hypertension (PPH): Cases of severe, sometime fatal primary pulmonary hypertension, have been reported in patients who have received anorectics. In a case-control epidemiological study, the duration of treatment with anorectic agents, not including phentermine, beyond three months significantly increases the risk of PPH. However, patients treated with phentermine require medical review at least every 3 months (Refer to "Dosage and Administration"). PPH has been reported in patients receiving fenfluramine/dexfenfluramine combined with phentermine. The possibility of an association between PPH and the use of phentermine alone cannot be ruled out; there have been very rare cases of PPH in patients who reportedly have taken phentermine alone. The initial symptom of PPH is usually dyspnoea.

Other early symptoms include: angina pectoris, syncope, lower extremity oedema or the unexplained onset or aggravation of diminished exercise tolerance. Under these circumstances, treatment should be immediately discontinued and the patient referred to a specialist unit for investigation.

Use with caution in the following circumstances:

Duromine should be used with caution in patients with mild hypertension. In the first days of treatment, determine that there is no loss of blood pressure control. In patients receiving Duromine, response to insulin and oral hypoglycaemic agents may vary due to alterations in dietary regimes. This should be kept in mind if Duromine is used in diabetic patients.

Duromine may impair the ability to perform activities requiring mental alertness, such as driving and operating machinery, and patients therefore should be cautioned accordingly. Inappropriate use has been reported with similar drugs and the possibility of this occurrence should be considered with Duromine.

Cardiovascular and cerebrovascular events have rarely been reported, mainly in association with rapid weight loss. Weight

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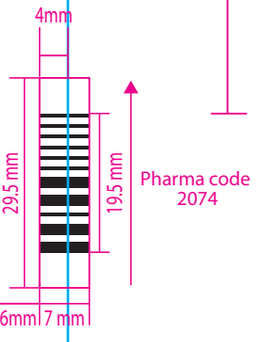

Size: 210 x 148 mm

PRODUCT INFORMATION	2.635 mm
DUROMINE	4.179 mm
(Phentermine)	2.053 mm

NAME OF THE DRUG	2.635 mm
Phentermine (phenyl tertiary butylamine, C	1.669 mm
DESCRIPTION	2.635 mm
Each Duromine capsule contains	1.669 mm

GROUP 24|7 WORLDWIDE™

inova pharmaceuticals

ARTWORK

Job No. : JB-02174 **V3**
UIC : A3080
SKU : 100190 100191

26.11.19 - V0 - Artwork build - Carina
29.11.19 - V1 - Amends - Carina
03.12.19 - V2 - Amends - Chanon
06.12.19 - V3 - Amends - Pornpawee

A3080_DUROMINE 15MG CAPSULE 30
Component : LEAFLET
Country : MY

Dieline Ref: PP-0442
EMO: DOUGLAS
Printer: Xxxxx Xxxxxxxxxxx

G247 File Name: 89214_A3080_DUROMINE 15MG CAPSULE 30_MY_LT_V3

Colour 100%

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Guide

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Any additonal information and technical check required by EMO on the Artwork BEFORE APPROVING.

148 mm

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75 mm

loss should be gradual and controlled in obese patients undergoing treatment with Duromine. Duromine should be used with caution in patients with established coronary artery disease. A single case of exacerbation of angina pectoris in a patient with established coronary artery disease has been reported.

Duromine should be used with caution in patients receiving psychotrophic drugs, including sedatives and agents with sympathomimetic activity. Duromine should be used with caution in epileptic patients. Duromine should be used with caution in patients receiving anti-hypertensive agents.

Effects on Laboratory Tests
There are no reports to-date to suggest that phentermine interferes with laboratory or diagnostic tests.

Carcinogenicity, Mutagenicity, Impairment of Fertility
Phentermine was not mutagenic in a bacterial gene mutation assay, however, studies to assess the potential for chromosomal damage have not been performed. No studies have been performed to determine the potential of phentermine for carcinogenesis. In rats, administration of phentermine at a dose 10 times the maximum human dose on a mg/m^2 basis abolished oestrous cycling. There is no information on the potential of phentermine to impair fertility in humans.

Use in pregnancy:
Weight reduction using appetite suppression drugs is not recommended during pregnancy. In rats, administration of phentermine during late gestation at a dose 7 times the maximum human dose on a mg/m^2 basis had no adverse effects on dams or offspring. There is no information on the teratological potential of phentermine. Because of inadequate evidence of safety in human pregnancy, Duromine should not be used in pregnant women.

Use in lactation:
There is no data available on the safety of Duromine in lactation and as such its use in lactating women should be avoided.

Interactions with other drugs:
Duromine should be used with caution in patients receiving sympathomimetic agents. Duromine antagonises adrenergic neurone blocking drugs such as clonidine, methyldopa and guanethidine and may decrease their hypotensive effect. The effects of Duromine are potentiated by Monoamine Oxidase Inhibitors (see Contraindications) and may result in a hypertensive crisis. The concurrent use of thyroid hormones with Duromine may increase the CNS stimulation that can occur with Duromine. Alcohol may increase CNS side effects such as dizziness, lightheadedness and confusion, and its concurrent use should be avoided with Duromine.

ADVERSE REACTIONS

Cardiovascular: Refer to "Special Precautions - Valvular Heart Disease and Primary Pulmonary Hypertension". The most common reported reactions are palpitations, tachycardia, elevation of blood pressure, precordial pain. Rare occurrences of cardiovascular or cerebrovascular events have been described with anorectic agents. In particular stroke, angina, myocardial infarction, cardiac failure and cardiac arrest have been reported.

Central Nervous System: Overstimulation, restlessness, nervousness, insomnia, tremor, dizziness and headache. Rarely euphoria may occur and this may be followed by fatigue and depression. Psychotic episodes and hallucinations are rare side effects.

Gastrointestinal: Nausea, vomiting, dry mouth, abdominal cramps, unpleasant taste, diarrhoea, constipation.

Other: Micturition disturbances, rash, impotence, changes in libido, facial oedema.

DOSAGE AND ADMINISTRATION

Adults and children over 12 years:
One capsule daily at breakfast, swallowed whole. Evening dosing should be avoided, as this agent may induce insomnia. It is recommended that treatment should be initiated under the care of physicians experienced in the treatment of obesity.

The recommended starting dose is 30 mg daily. The recommended maintenance dose, either continuous or intermittent is 15 to 30 mg daily depending on responsiveness. The recommended dose of Duromine should not be exceeded to increase the effect. Duromine should not be combined with other appetite suppressants. Patients require medical review after a defined course of treatment, which should not exceed three months.

Children under 12 years:
Duromine is not recommended for children under the age of twelve.

Elderly:
Duromine is not recommended for the elderly.

OVERDOSAGE

Symptoms
Initially irritability, rapid respiration, agitation, euphoria, restlessness, hyperreflexia, disorientation and tremor, aggressiveness, hallucinations and panic states may occur, followed by cardiac arrhythmias, convulsions, fatigue, central nervous system depression and coma. Cardiovascular consequences include hypertension, hypotension and circulatory collapse. Gastrointestinal symptoms include nausea, vomiting, diarrhoea and abdominal cramps.

Treatment
The treatment is largely symptomatic. The stomach should be emptied by gastric lavage and washed out with water if the preparation has been ingested within the last three or four hours. Gastric lavage, followed by activated charcoal, may be the optimal decontamination regimen for patients exhibiting CNS depression. Diazepam, preferably by mouth (cautiously by intravenous injection) can be used to control marked excitement and convulsions. Provided renal function is adequate, elimination of phentermine has been shown to be assisted by acidification of the urine. There is insufficient experience to recommend haemodialysis or peritoneal dialysis.

PRESENTATION

Capsules:

Duromine 15mg is a powder-filled, size 3 locking capsule with opaque green cap and opaque light grey colour body, marked with "Duromine15/Duromine15".

Duromine 30mg is a powder-filled, size 3 locking capsule with opaque reddish brown cap and opaque light grey colour body, marked with "Duromine30/Duromine30".

STORAGE CONDITIONS

Store below 30˚C

NAME AND ADDRESS OF MANUFACTURER

Douglas Manufacturing Ltd
Corner Te Pai Place and Central Park Drive Lincoln, Auckland, New Zealand

REVISION DATE

January 2020

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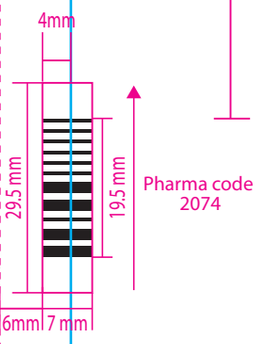

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