

## **SUMMARY OF PRODUCT CHARACTERISTICS**

### **1 NAME OF THE MEDICINAL PRODUCT**

Dibenyline Injection Concentrate.  
Phenoxybenzamine Injection Concentrate

### **2 QUALITATIVE AND QUANTITATIVE COMPOSITION**

#### Active Ingredient

Phenoxybenzamine hydrochloride BP 100 mg

#### Other Ingredients

Absolute ethyl alcohol	0.97 ml
Hydrochloric acid AR	13.60 mg
Propylene glycol	qs

### **3 PHARMACEUTICAL FORM**

Clear colourless glass ampoules containing clear colourless to mid-straw coloured liquid for intravenous injection.

### **4 CLINICAL PARTICULARS**

#### **4.1 Therapeutic indications**

In the management of phaeochromocytoma and as an adjunct to the treatment of severe shock not responding to conventional therapy in the presence of an adequate circulatory blood volume.

#### **4.2 Posology and method of administration**

Method of Administration: Intravenous

### Posology

Adults and Elderly: Must be diluted in physiological saline before use. Not more than one dose should be given in 24 hours, and not more than two doses in 48 hours.

Phaeochromocytoma: Dose titrated on daily basis: Guide daily dose 1 mg/kg body weight in 200 ml physiological saline over 2 hours.

Shock: 1 mg/kg body weight in 200-500 ml physiological saline over not less than 2 hours.

Patient should be recumbent and blood pressure must be determined every few minutes during infusion.

Children: Dosage in children has not been established.

## **4.3 Contraindications**

Do not use in patients who have had a cerebrovascular accident; or in the recovery period (usually 3-4 weeks) after acute myocardial infarction. Do not use in the presence of hypovolaemia in patients with severe shock.

## **4.4 Special warnings and precautions for use**

The patient should be recumbent. Blood pressure must be determined every few minutes during the administration. Facilities for rapid infusion of intravenous fluid should be available. The Dibenyline infusion should be slowed or stopped if there is a precipitous fall in blood pressure. This usually indicates an inadequate circulating blood volume, but occasionally may occur in the presence of an adequate blood volume in the hypertensives or in patients with carbon dioxide retention and in those cases is relatively unresponsive to the administration of intravenous fluids. Nevertheless, if severe hypotension does occur, treatment can be attempted with plasma expanders and the "head down" position. Noradrenaline may be of little value when  $\alpha$ -adrenergic receptors are blocked. Adrenaline should not be used since stimulation of  $\beta$ -adrenergic receptors will further decrease blood pressure. If blood pressure has been stabilised by the administration of appropriate fluids the Dibenyline infusion may be restarted under close supervision. The blockage produced is often still exerting an effect 24 hours after administration and even in patients with a favourable response close attention to their cardiovascular status should be administration of Dibenyline within 24 hours and the drug should not be given more than twice during a 48 hour period.

Use with great caution in patients in whom a fall in blood pressure and/or tachycardia may be undesirable, such as the elderly or those with severe ischaemic heart disease, congestive heart failure, extensive arteriosclerosis, cerebrovascular disease or renal damage the adrenergic blocking effect may aggravate symptoms or respiratory infections. Alpha-sympathomimetics may be ineffective if used concomitantly with phenoxybenzamine. Care should be taken if phenoxybenzamine is used concomitantly with myocardial depressants e.g. beta-blockers and anti-arrhythmics.

Extravasation should be avoided, as the diluted solution is an irritant to muscle tissue.

Contamination of the hands should be avoided as reactions may occur in sensitive skins.

Phenoxybenzamine is carcinogenic in the rat and has shown mutagenic activity in the bacterial ames test and mouse lymphoma assay. It should only be used after very careful consideration of the risks, in patients in which alternative treatment is inappropriate.

#### **4.5 Interaction with other medicinal products and other forms of interaction**

In shock, because of the occupation of alpha adrenergic receptors, substances stimulating beta-adrenergic receptors (e.g. adrenaline, isoprenaline) should not be given as a further fall in blood pressure may occur. In the acute situations in which phenoxybenzamine is given as an IV infusion, no significant interaction with other drugs have been reported.

#### **4.6 Pregnancy and lactation**

Evidence of safety during pregnancy and lactation is not available so that phenoxybenzamine should only be used in pregnancy if considered essential.

#### **4.7 Effects on ability to drive and use machines**

None known.

#### **4.8 Undesirable effects**

Dibenyline given intravenously has a sedative effect and patients may become more drowsy or less responsive during infusion. This may occur in spite of an excellent cardiovascular response and should not be confused with the decreased responsiveness associated with the worsening shock syndrome.

Other side effects include orthostatic hypotension with dizziness and compensatory tachycardia, miosis, dry mouth, nasal congestion, decreased sweating and gastrointestinal upset.

Convulsions have been reported after rapid infusion. Some fall in blood pressure is a normal response but an idiosyncratic profound hypotensive effect can occur usually with five minutes of starting the infusion.

The effects of one dose of Dibenyline on sympathetic motor response may last 48 hours or more.

#### **4.9 Overdose**

There may be a precipitous fall in blood pressure even at the recommended dosage. Facilities for rapid infusion of intravenous fluid should therefore be available and in the event of such a severe hypotensive episode the Dibenyline infusion should be slowed or stopped. Treatment can be attempted with plasma expanders and the "head down" position. Noradrenaline may be of little value when alpha adrenergic receptors are blocked and adrenaline is contra-indicated.

## **5 PHARMACOLOGICAL PROPERTIES**

### **5.1 Pharmacodynamic properties**

Phenoxybenzamine is a non competitive long acting  $\alpha$ -adrenergic receptor antagonist.

### **5.2 Pharmacokinetic properties**

Phenoxybenzamine is incompletely absorbed from the gastrointestinal tract. The maximum effect is attained in about 1 hour after an intravenous dose. Following oral administration the onset of action is gradual over several hours and persists for 3-4 days following a single dose. The plasma half-life is about 24 hours. Phenoxybenzamine is metabolised in the liver and excreted in the

urine and bile but small amounts remain in the body for several days. It has prolonged action probably owing to stable covalent bonding.

### **5.3 Preclinical safety data**

Phenoxybenzamine is carcinogenic in the rat and has shown mutagenic activity in the bacterial ames test and mouse lymphoma assay. It should only be used after careful consideration of the risks.

## **6 PHARMACEUTICAL PARTICULARS**

### **6.1 List of excipients**

Absolute ethyl alcohol  
Hydrochloric acid AR  
Propylene glycol

### **6.2 Incompatibilities**

Not applicable

### **6.3 Shelf life**

2 years

### **6.4 Special precautions for storage**

Protect from light.  
Store between 2 – 8°C

### **6.5 Nature and contents of container**

2ml clear, colourless glass ampoules.  
Each pack contains 3, 5 or 10 vials.

## **6.6 Special precautions for disposal**

Contamination of the skin should be avoided as reactions may occur in sensitive skins.

## **7 MARKETING AUTHORISATION HOLDER**

Goldshield Pharmaceuticals Ltd.  
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## **8 MARKETING AUTHORISATION NUMBER(S)**

PL 12762/0225

## **9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION**

22 June 2009

## **10 DATE OF REVISION OF THE TEXT**

10/12/2010