

# *BritLofex*<sup>™</sup> Tablets 0.2mg

## Summary of Product Characteristics

### 1. NAME OF THE MEDICINAL PRODUCT

BritLofex Tablets 0.2mg

### 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Lofexidine hydrochloride 0.2mg

### 3. PHARMACEUTICAL FORM

Film-coated tablet.

Peach coloured, round tablet.

### 4. CLINICAL PARTICULARS

#### 4.1 Therapeutic indication

To relieve symptoms in patients undergoing opiate detoxification.

#### 4.2 Posology and method of administration

The recommended route of administration is by mouth.

##### **Adults:**

The dosage of lofexidine should be titrated according to the patient's response. Initial dosage should be 0.8mg per day in divided doses. The dosage may be increased by increments of 0.4 to 0.8mg per day up to a maximum of 2.4mg daily. Maximum single dose should not exceed 4 x 0.2mg tablets (0.8mg). Each patient should be assessed on an individual basis; those undergoing acute detoxification will usually require the highest recommended dose and dosage increments to provide optimum relief at the time of expected peak withdrawal symptoms.

In cases where no opiate use occurs during detoxification, a duration of treatment of 7-10 days is recommended. In some cases the physician may consider longer treatment is warranted.

Concurrent medication to aid sleeping has been frequently used in withdrawal studies. Chloral hydrate or anti-histamines are preferred, benzodiazepines may also suppress some of the withdrawal symptoms.

##### **Children:**

Safety and effectiveness in children has not been established.

##### **Elderly:**

There is no experience of dosing in the elderly from clinical studies. Should use in the elderly be necessary it is advised that special caution is observed in the presence of heart disease or anti-hypertensive therapy.

### **4.3 Contraindications**

BritLofex tablets are contraindicated in patients who are allergic to lofexidine or to other imidazoline derivatives or to any excipients of BritLofex.

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

As with other hypotensive agents, therapy with lofexidine should not be discontinued abruptly. Dosage should be reduced gradually over a period of 2-4 days or longer, to minimise blood pressure elevation and associated signs and symptoms.

Lofexidine should be used with caution in patients with severe coronary insufficiency, recent myocardial infarction, cerebrovascular disease or chronic renal failure and in patients with marked bradycardia (<55 beats per minute). Pulse rate should be assessed frequently. Patients with a history of depression should be carefully observed during long-term therapy with lofexidine.

There have been reports of asymptomatic QT prolongation during lofexidine treatment. Whilst the nature of the relationship between lofexidine and these ECG changes is not yet clear, it would be prudent to avoid the use of lofexidine in patients with known problems of QT prolongation and in patients taking other drugs known to cause QT prolongation.

This medicine contains lactose. Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

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

Lofexidine may enhance the CNS depressive effects of alcohol, barbiturates and other sedatives.

Lofexidine may enhance the effects of anti-hypertensive drug therapy.

Concomitant use of tricyclic antidepressants may reduce the efficacy of lofexidine.

### **4.6 Pregnancy and lactation**

The safety of lofexidine in pregnant women has not been established. High doses of lofexidine given to pregnant dogs and rabbits caused a reduction in foetal weight and increased abortions. Lofexidine should only be administered during pregnancy if the benefit outweighs the potential risk to mother and foetus. It is not known whether this drug is excreted in human milk and caution should be exercised when it is administered to a nursing woman.

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

Lofexidine may have a sedative effect. If affected, patients should be advised not to drive or operate machines.

#### **4.8 Undesirable effects**

The adverse effects of the drug are primarily related to its central alpha-adrenergic agonist effects and comprise drowsiness and related symptoms and dryness of mucous membranes especially mouth, throat and nose.

Hypotension and bradycardia may occur.

There have been reports of asymptomatic QT prolongation during lofexidine treatment.

#### **4.9 Overdose**

Overdosage may cause hypotension, bradycardia and sedation. Gastric lavage should be carried out where appropriate. In most cases, all that is required are general supportive measures.

### **5. PHARMACOLOGICAL PROPERTIES**

#### **5.1 Pharmacodynamic properties**

Pharmacotherapeutic Group: Drugs used in opioid dependence

ATC Classification: N07BC04

Lofexidine hydrochloride is an orally active imidazoline adrenergic alpha-2-receptor agonist; and is believed to have a high affinity for 2A receptor subtypes resulting in less anti-hypertensive activity than clonidine, a non-selective alpha-2-receptor agonist. Hypotension may occur in susceptible subjects, accompanied by a decrease in heart rate.

Abrupt discontinuation of lofexidine has been, in some cases, associated with a transient increase in blood pressure to higher than pre-treatment levels.

#### **5.2 Pharmacokinetic properties**

Lofexidine is extensively absorbed and achieves peak plasma concentration at 3 hours after administration of a single dose. The elimination half-life is 11 hours with accumulation occurring up to four days with repeat dosing. Lofexidine undergoes extensive metabolism in the liver and excretion is mainly by the kidney.

#### **5.3 Preclinical safety data**

Animal toxicology. Lofexidine was tolerated at high dosage in single dose toxicity studies in animals, the LD<sub>50</sub> being >77 mg/kg. With repeat dosing in mice, rats and dogs symptoms related to the pharmacology of the drug (ataxia, sedation, tremor, unkempt appearance and exhaustion) appeared.

Studies of mutagenicity are incomplete but lofexidine did not display mutagenicity in the Ames test. Long-term studies in rats showed no evidence of carcinogenicity.

High doses of lofexidine given to pregnant rats and rabbits caused a reduction in the foetal weight and increased abortions. No teratogenic effects were found.

## **6. PHARMACEUTICAL PARTICULARS**

### **6.1 List of excipients**

Lactose (monohydrate)  
Citric acid  
Povidone  
Microcrystalline cellulose  
Calcium stearate  
Sodium lauryl sulphate  
Purified water

#### *Film Coat:*

Opadry OY-S-9480 Brown

#### *containing*

Hydroxypropylmethyl cellulose  
Titanium dioxide  
Propylene glycol  
Indigo Carmine (E132)  
Sunset Yellow (E110)

### **6.2 Incompatibilities**

None known

### **6.3 Shelf-life**

36 months

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

Store below 25°C. Store in original package.

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

Aluminium foil/aluminium foil blister strips  
Aluminium foil/PVC foil blister strips

### **6.6 Instructions for use and handling**

No special instructions.

## **7. MARKETING AUTHORISATION HOLDER**

Britannia Pharmaceuticals Limited  
41-51 Brighton Road, Redhill, Surrey RH1 6YS, United Kingdom

## **8. MARKETING AUTHORISATION NUMBER**

PL 4483/0036

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

October 1990

## **10. DATE OF (PARTIAL) REVISION OF THE TEXT**

July 2006