

# **Trihexyphenidyl Hydrochloride Tablets I.P. 2 mg**

## **Pacitane<sup>®</sup> Tablets**



### **1. GENERIC NAME**

Trihexyphenidyl Hydrochloride Tablets I.P. 2 mg

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

Each uncoated tablet contains:  
Trihexyphenidyl Hydrochloride I.P. 2 mg

#### List of Excipients:

Lactose I.P., Maize Starch Special Qlty NBS, Magnesium Stearate I.P., Microcrystalline Cellulose I.P. Colloidal Silicon Dioxide I.P.

### **3. DOSAGE FORM AND STRENGTH**

Uncoated tablets 2 mg

### **4. CLINICAL PARTICULARS**

#### **4.1 Therapeutic Indications**

Adjunctive treatment of all forms of Parkinsonism (postencephalitic, arteriosclerotic, and idiopathic)

Adjuvant therapy when treating these forms of Parkinsonism with levodopa.

Control of extrapyramidal disorders caused by central nervous system drugs such as dibenzoxazepines, phenothiazines, thioxanthenes, reserpine and butyrophenones.

#### **4.2 Posology and Method of Administration**

##### **General**

Dosage should be individualized. The initial dose should be low and then increased gradually, especially in patients over 60 years of age.

Postencephalitic patients may require larger doses. These patients, who are usually more prone to excessive salivation, may prefer to take it after meals, and may, in addition require small amounts of atropine, which, under such circumstances, is sometimes an effective adjuvant.

Whether Pacitane may best be given before or after meals should be determined by the way the patient reacts. If Pacitane tends to dry the mouth excessively, it may be better to take it before meals, unless it causes nausea. If taken after meals, mint candies, chewing gum or water can allay the thirst sometimes induced.

Abrupt withdrawal of treatment for Parkinsonism may result in acute exacerbation of Parkinsonism symptoms; therefore, abrupt withdrawal should be avoided. See also section on 'Abrupt withdrawal of treatment for Parkinsonism'.

Abrupt withdrawal of treatment may result in Neuroleptic Malignant Syndrome (NMS). See also section 'Special Warnings and precaution for use'.

The total daily intake of Pacitane tablets is tolerated best if divided into 3 doses and taken at mealtimes. High doses (>10 mg daily) may be divided into 4 parts, with 3 doses administered at mealtimes and the fourth at bedtime.

### **Pacitane in Idiopathic Parkinsonism**

As initial therapy for Parkinsonism, 1 mg of Pacitane may be administered the first day. The dose may then be increased by 2 mg increments at intervals of three to five days, until a total of 6 to 10 mg is given daily. The total daily dose will depend upon what is found to be the optimal level. Many patients derive maximum benefit from this daily total of 6 to 10 mg, but some patients, chiefly those in the postencephalitic group, may require a total daily dose of 12 to 15 mg.

### **Pacitane in Drug-Induced Parkinsonism**

The size and frequency of dose of Pacitane needed to control extrapyramidal reactions to commonly employed tranquilizers, notably the phenothiazines, thioxanthenes, reserpine and butyrophenones, must be determined empirically. The total daily dosage usually ranges between 5 and 15 mg although, in some cases, these reactions have been satisfactorily controlled with as little as 1 mg daily. It may be advisable to commence therapy with a single 1 mg dose. If the extrapyramidal manifestations are not controlled in a few hours, the subsequent doses may be progressively increased until satisfactory control is achieved. Satisfactory control may sometimes be more rapidly achieved by temporarily reducing the dosage of the tranquilizer when instituting Pacitane therapy, and then adjusting dosage of both drugs until the desired ataractic effect is retained without onset of extrapyramidal reactions.

It is sometimes possible to maintain the patient on a reduced Pacitane dosage after the reactions have remained under control for several days. Instances have been reported in which these reactions have remained in remission for long periods after Pacitane therapy was discontinued.

### **Concomitant use with levodopa**

When Pacitane is used concomitantly with levodopa, the usual dose of each may need to be reduced. Careful adjustment is necessary, depending on side effects and degree of symptom control. A Pacitane of 3 to 6 mg daily, in divided doses, is usually adequate.

### **Concomitant use with other parasympathetic inhibitors**

Pacitane may be substituted, in whole or in part, for other parasympathetic inhibitors. The usual technique is partial substitution initially, with progressive reduction in the other medication as the dose of Pacitane is increased.

### **Use in the Elderly**

Sensitivity to the actions of parasympatholytic drugs may increase with age, particularly over the age of 60; therefore, elderly patients generally should be started on low doses of Pacitane and observed closely. See also section 4.4. Special warnings and precaution for use- Geriatric patients

### **Use in Patients with Renal Impairment and Hepatic Impairment**

Patients with impaired renal or hepatic function should be monitored carefully, since side effects may be aggravated or increased by any reduction in the metabolism of Pacitane.

### **Use in Children**

Safety and effectiveness in pediatric patients have not been established. See also section on PEDIATRIC USE.

## **4.3 Contraindications**

Pacitane tablets are contraindicated in patients with:

- hypersensitivity to trihexyphenidyl or any other ingredients of the preparation;
- narrow angle glaucoma. Blindness after long-term use due to narrow angle glaucoma has been reported (see sections 4.4. Special Warnings and Precautions for Use and 4.8. Undesirable Effects).

## **4.4 Special Warnings and Precautions for Use**

Patients to be treated with Pacitane should have a gonioscope evaluation prior to initiation of therapy and close monitoring of intraocular pressures. The use of anticholinergic drugs may precipitate angle closure with an increase in intraocular pressure. If blurring of vision occurs during therapy, the possibility of narrow angle glaucoma should be considered. Blindness has been reported due to aggravation of narrow angle glaucoma (see sections 4.3. Contraindications and 4.8. Undesirable effects).

Pacitane should be administered with caution in the presence of fever, high environmental temperature, and/or during physical exercise, especially when given concomitantly with other atropine like drugs to the chronically ill, alcoholics, the elderly, those who have central nervous system disease, or those who do manual labor in a hot environment. Anhidrosis may occur more

readily when some disturbance of sweating already exists. If there is evidence of anhidrosis, the possibility of hyperthermia should be considered. Dosage should be decreased so that the ability to maintain body heat equilibrium via perspiration is not impaired. Severe anhidrosis and fatal hyperthermia have occurred with the use of anticholinergics under the conditions described above.

### **Neuroleptic Malignant Syndrome (NMS)**

A potentially fatal symptom complex sometimes referred to as Neuroleptic Malignant Syndrome (NMS) has been reported in association with dose reduction or discontinuation of Pacitane. Clinical manifestations of NMS are hyperpyrexia, muscle rigidity, altered mental status, and evidence of autonomic instability (irregular pulse or blood pressure, tachycardia, diaphoresis and cardiac dysrhythmias).

The diagnostic evaluation of patients with this syndrome is complicated. In arriving at a diagnosis, it is important to identify cases where the clinical presentation includes both serious medical illness (e.g., pneumonia, systemic infection, etc) and untreated or inadequately treated extrapyramidal signs and symptoms (EPS). Other important considerations in the differential diagnosis include central anticholinergic toxicity, heat stroke, drug fever, and primary central nervous system (CNS) pathology.

### **Pediatric Use**

Safety and effectiveness in pediatric patients have not been established.

### **Geriatric Patients**

Sensitivity to the actions of parasympatholytic drugs may increase with age, particularly over the age of 60; therefore, elderly patients generally should be started on low doses of Pacitane and observed closely. Pacitane has been shown to cause some cognitive dysfunctions in the elderly, including confusion and memory impairment (see sections 4.2 Posology and method of Administration, section 4.4. Special warnings and precautions for use and section 4.8. Undesirable effects).

### **Cardiac function**

Pacitane has atropinic properties as a result, existing hypertension may be aggravated and tachycardia may occur. Patients at risk (arrhythmia, heart failure, coronary disease, mitral stenosis) should be monitored carefully over a prolonged period.

### **Parasympatholytic properties**

Pacitane has parasympatholytic properties; it should be administered with care to patients presenting glaucoma, or obstructive disorders of the gastrointestinal or urogenital tract (for example prostate hypertrophy). Patients over the age of 60 are often very sensitive to anticholinergic agents; as a result, a very strict control of the dosage is indispensable. Early glaucoma may be precipitated by the administration of parasympatholytic agents(see sections 4.3. Contraindications, 4.4. Special warnings and precautions for use- Geriatric use and 4.8. Undesirable effects).

## **Tardive dyskinesia**

Tardive dyskinesia may appear in some patients on long-term therapy with antipsychotic drugs or may occur after therapy with these drugs has been discontinued. Anti-parkinsonism agents do not alleviate the symptoms of tardive dyskinesia and in some instances may aggravate them. However, parkinsonism and tardive dyskinesia often coexist in patients receiving chronic neuroleptic treatment, and anticholinergic therapy with Pacitane may relieve some of these parkinsonism symptoms. Pacitane is not recommended for use in patients with tardive dyskinesia unless they have concomitant Parkinson's disease.

## **Patients with arteriosclerosis or with a history of idiosyncrasy to other drugs**

Patients with arteriosclerosis or with a history of idiosyncrasy to other drugs may exhibit reactions of mental confusion, agitation, disturbed behavior, or nausea and vomiting. Such patients should be allowed to develop a tolerance through the initial administration of a small dose and gradual increase in dose until an effective level is reached. If a severe reaction should occur, administration of the drug should be discontinued for a few days and then resumed at a lower dosage. Psychiatric disturbances can result from indiscriminate use (leading to overdose) to sustain continued euphoria (see section 4.8. Undesirable effects).

## **Abrupt withdrawal of treatment for Parkinsonism**

Abrupt withdrawal of treatment for Parkinsonism may result in acute exacerbation of Parkinsonism symptoms; therefore, abrupt withdrawal should be avoided (see section 4.2. Posology and method of administration-General).

## **4.5 Drug Interactions**

### **CNS depressants**

Cannabinoids, barbiturates, opiates, and alcohol may have additive effects with Pacitane and thus, an abuse potential exists. Alcohol use should be avoided as increased Pacitane metabolism may occur, which may lead to lower blood concentrations and decreased therapeutic effects.

### **Anticholinergics**

The concomitant use of Pacitane with other anticholinergic drugs may produce increased or additive peripheral anticholinergic effects. Monoamine oxidase inhibitors and tricyclic antidepressants possessing significant anticholinergic activity may intensify the anticholinergic effects of antidyskinetic agents because of the secondary anticholinergic activities of these medications.

### **Neuroleptics**

Prophylactic administration of anticholinergic agents, such as Pacitane, as a prevention of drug induced Parkinsonism during neuroleptic therapy is not recommended. There may be an increased risk for the development of tardive dyskinesia during concomitant administration of anticholinergics and neuroleptics. See also section 'Tardive dyskinesia'.

## **Levodopa**

The usual dose of either Pacitane or levodopa may need to be reduced during concomitant therapy, since concomitant administration may increase drug induced involuntary movements. See also section on ‘Concomitant use with Levodopa’.

## **Anticonvulsants**

Exacerbation of seizures in patients with adequately controlled epilepsy has been suggested during initiation of anticholinergic agents such as Pacitane.

## **Foods**

The use of acidic foods such as citrus and fruit juices may decrease the effect of a Pacitane dose. Large amounts of coffee with Pacitane use may lead to a euphoric effect.

## **4.6 Use in special populations**

### Pregnancy

Animal reproduction studies to evaluate teratogenic and embryotoxic potential have not been conducted with Pacitane. It is also not known whether Pacitane can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. In general, Pacitane should be used during pregnancy only if the potential benefit to the mother justifies the unknown risk to the fetus.

### Lactation

It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when Pacitane is administered to a nursing mother. As with other anticholinergics, Pacitane may cause suppression of lactation. Therefore, Pacitane should only be used if the expected benefit to the mother outweighs the potential risk to the infant.

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

Pacitane may impair mental and/or physical abilities required for performance of hazardous tasks, such as operating machinery or driving a motor vehicle. Patients should be cautioned about operating machinery, including automobiles, until they are reasonably certain that Pacitane therapy does not adversely affect their ability to engage in such activities.

## **4.8 Undesirable Effects**

### **System Organ Class Adverse Reaction**

#### ***Psychiatric disorders***

Frequency undetermined

#### **Hallucinations**

#### ***Nervous system disorders***

Frequency undetermined

**Dizziness, nervousness, impairment of memory or forgetfulness, confusion or delirium, drowsiness or sedation, exacerbation of Parkinsonism with abrupt treatment withdrawal, choreiform movements. Neuroleptic Malignant Syndrome (NMS) with abrupt treatment withdrawal**

#### *Eye disorders*

Frequency undetermined

**Blurred vision, and dilation of pupils, cycloplegia, increased intraocular pressure, narrow angle glaucoma (blindness has been reported in some cases)**

#### *Cardiac disorders*

Frequency undetermined

**Tachycardia, paradoxical sinus bradycardia**

#### *Gastrointestinal disorders*

Frequency undetermined

**Dry mouth, nausea, constipation, vomiting, suppurative parotitis secondary to excessive dryness of mouth, paralytic ileus and dilation of colon**

#### *Skin and subcutaneous tissue disorders*

Frequency undetermined

**Dry skin**

#### *Renal and urinary disorders*

Frequency undetermined

**Urinary hesitancy or retention**

In addition to adverse events seen in adults, the following adverse events have been reported in the literature in pediatric patients: hyperkinesias, psychosis, forgetfulness, weight loss, restlessness, chorea, and sleep alterations.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after registration of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions.

## **4.9 Overdose**

### **Signs and Symptoms**

Overdosage with Pacitane produces typical central symptoms of atropine intoxication (the central anticholinergic syndrome). Correct diagnosis depends upon recognition of the peripheral signs of parasympathetic blockade, including fever. Other reported effects include lip smacking and tasting movements. The condition can progress to stupor, coma, paralysis, cardiac and respiratory arrest, and death.

## **Treatment**

Treatment of acute overdose involves symptomatic and supportive therapy. Gastric lavage or other methods to limit absorption should be instituted. A small dose of diazepam or a short-acting barbiturate may be administered if CNS excitation is observed. Phenothiazines are contraindicated because the toxicity may be intensified due to their antimuscarinic action, causing coma. Respiratory support, artificial respiration or vasopressor agents may be necessary. Hyperpyrexia must be reversed, fluid volume replaced and acid-balance maintained. Urinary catheterization may be necessary. It is not known if Pacitane is dialyzable.

## **5. PHARMACOLOGICAL PROPERTIES**

### **5.1 Mechanism of Action**

Pacitane is a substituted piperidine salt,  $\alpha$ -Cyclohexyl $\alpha$ -phenyl-l-piperidinepropanol hydrochloride. Pacitane is an anticholinergic agent, which exerts a direct inhibitory effect upon the parasympathetic nervous system. It also has a relaxing effect on smooth musculature; exerted both directly upon the muscle tissue itself and indirectly through an inhibitory effect upon the parasympathetic nervous system. Its therapeutic properties are similar to those of atropine although undesirable side effects are ordinarily less frequent and less severe than the latter.

### **5.2 Pharmacodynamic Properties**

No data available

### **5.3 Pharmacokinetic Properties**

No data available

## **6 NONCLINICAL PROPERTIES**

### **6.1 Animal toxicology or Pharmacology**

#### **Carcinogenesis, mutagenesis, impairment of fertility**

No carcinogenicity studies have been conducted for Trihexyphenidyl. Trihexyphenidyl was evaluated for mutagenic potential using five different histidine-requiring mutants (TA 98, TA 100, TA 1535, TA 1537 and TA 1538) of *Salmonella typhimurim*. Studies were conducted with and without activation by rat liver homogenate "S-9" fraction. Under the condition of this assay, trihexyphenidyl was not mutagenic.

In limited studies, prolonged administration of oral daily doses of 20 mg/kg of trihexyphenidyl to dogs for 15 or 27 weeks and up to 100 mg/kg (doses which were in excess of 100 times the human therapeutic dose) to rats for 15 weeks did not modify fertility.

## **7. DESCRIPTION**

Trihexyphenidyl Hydrochloride Tablets I.P. 2 mg - Clean white, round, flat, beveled tablets with break line on one surface and other side plain.



## **8. PHARMACEUTICAL PARTICULARS**

### **8.1 Incompatibilities**

None

### **8.2 Shelf Life**

36 months

### **8.3 Packaging information**

30 tablets are blister packed using rear printed Aluminium foil and front plain clear PVC film.

### **8.4 Storage and handling instructions**

Store protected from moisture, freezing and excessive heat (any temperature above 40°C).  
Keep out of reach of children.

## **9. PATIENT COUNSELLING INFORMATION**

Pacitane may impair mental and/or physical abilities required for performance of hazardous tasks, such as operating machinery or driving a motor vehicle. Patients should be cautioned about operating machinery, including automobiles, until they are reasonably certain that Pacitane treatment does not adversely affect their ability to engage in such activities.

Alcohol use should be avoided as it may lead to increased metabolism of Pacitane which may lead to lower blood concentrations and decreased therapeutic effects (see section 4.5 Interaction with Other Medicinal Products and Other Forms of Interaction).

Pacitane should be used with caution in the presence of fever, high environmental temperature, and/or during physical exercise especially when given concomitantly with other atropine like drugs in patients who are chronically ill, alcoholics, the elderly, those who have central nervous system disease, or those who do manual labor in a hot environment (see section 4.4 special warnings and precautions for use).

Post encephalitic patients who are usually more prone to excessive salivation, may prefer to take it after meals.

Patients should have close monitoring of intraocular pressure (see section 4.4 special warnings and precautions for use).

Abrupt withdrawal of treatment of parkinsonism should be avoided as it may result in acute exacerbation of Parkinsonism symptoms.

**10. DETAILS OF MANUFACTURER**

**Manufactured by:**

Pfizer Limited, Plot No. L-137, Phase III A, Verna Industrial Estate, Verna, Goa 403722

**11. DETAILS OF PERMISSION OR LICENSE NUMBER WITH DATE**

Manufacturing Licence No\*.: 544 dated 01 Dec 2014 (\*The manufacturing license is renewed every 5 years as per Indian regulations).

**12. DATE OF REVISION**

March 2025