1. NAME OF THE MEDICINAL PRODUCT

BENZHEXOL TABLETS BP 5 mg

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2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each uncoated tablet contains:

- Benzhexol Hydrochloride BP (5 mg)
- Excipients (-- QS)

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3. PHARMACEUTICAL FORM

White coloured, circular, flat, beveled uncoated tablet having embossing HEXOL/5 on one side and plain on other sides.

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4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Parkinsonism (Postencephalitic, arteriosclerotic, idiopathic) adjunct with levodopa certain extrapyramidal disorders.

4.2 Posology and method of administration

Elderly: patient over 65 years of age tend to the relatively more sensitive and require smaller amount of drug

Children: Not recommended

Method of Administration: Route of administration is oral.

4.3 Contraindications

Hypersensitivity to Benzhexol or to any of the excipients.

4.4 Special warnings and precautions for use

Include risk of the tardive dyskinesia, caution in elderly, patient with glaucoma prostatic hypertrophy, myasthenia gravis psychiatric condition; avoid abrupt withdrawal.

4.5 Interaction with other medicinal products

Interaction with phenothiazine, clozapine, antihistamines, antidepressants, levodopa, metoclopramide domperidone, parasympathomimetics.

4.6 Pregnancy and Lactation

Pregnancy: There is inadequate information regarding the use of benzhexol in Pregnancy. Benzhexol should not be used during pregnancy unless clearly necessary.

Lactation: Benzhexol should not be used during breast-feed.

Fertility: There are no human data on the effect of benzhexol on fertility.

4.7 Effects on ability to drive and use machines

Can cause blurring of vision dizziness and mild nausea. Also mental confusion in some cases.

4.8 Undesirable effects

Modern clinical data required to determine the frequency of undesirable effect are lacking for trihexyphenidyl, minor side effect such as dryness of mouth, constipation, blurring of vision dizziness, mild nausea or nervousness will be experienced by 30-50% of all patients.

4.9 Overdose

Symptoms: dry mouth and tongue, tachycardia, rapid respiration, hyperpyrexia.

Treatment: An adequate An adequate airway should be maintained. Diazepam may be administered to control excitement and convulsions but the risk of central nervous system depression should be considered.

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5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamics properties

Pharmacotherapeutic Group

- **Pharmacotherapeutic Group**: Anticholinergic (antimuscarinic) agent, specifically an antispasmodic.
- **ATC Code**: N04AA01

A) Mechanism of Action

- Trihexyphenidyl antagonizes muscarinic acetylcholine receptors (M_1–M_5), with higher affinity for M_1 and M_4, especially in the CNS
- It directly inhibits parasympathetic efferent impulses, affecting salivary glands, smooth muscles, and ocular structures even at low doses. At higher doses, it may suppress central cerebral motor centers

B) Pharmacodynamic Effects

- **Peripheral Effects**: Diminishes salivation, dilates pupils (mydriasis), elevates heart rate, relaxes smooth muscles (reducing spasms), decreases bronchial secretions, and reduces sweating.
- **Central Effects**: Improves dopaminergic–cholinergic imbalance in basal ganglia, alleviating tremor and rigidity typical in Parkinsonism and drug-induced extrapyramidal symptoms. Some blockade of dopamine reuptake prolongs dopaminergic activity.

C) Clinical Efficacy & Safety

In Parkinsonism / EPS

- Effective for symptomatic management of Parkinson's disease (mono or combination therapy) and extrapyramidal side effects from antipsychotic therapy. Approximately 50–75% of patients experience 20–30% symptomatic improvement Greater impact on tremor; less effective for bradykinesia or rigidity.

In Pediatric Dystonia and Sialorrhea

- Retrospective studies in children with cerebral palsy (CP):
  - In a group of 31 children, most showed motor improvement (arm, hand, oromotor), especially those without spasticity and higher cognitive levels. Side effects were typically transient
  - Another review of 101 pediatric cases (mean age ~7 years): 91% tolerated well over ~3.5 years; benefits were reported in dystonia (upper limbs in ~59%, lower limbs in ~38%), sialorrhea (~60%), and speech (~25%)
- Prospective pilot trial (23 children, 4–15 years old) with secondary dystonia:
  - Doses up to 0.75 mg/kg/day over 9 weeks then tapered over 5 weeks. Significant improvement noted in upper limb function at 15 weeks but not at 9 weeks. Some children with hyperkinetic dystonia initially worsened.
- Clinical guidelines (e.g., for children with CP and generalized dystonia): Routine use is not recommended (conditional, very low-certainty evidence). A carefully monitored trial may be reasonable in selected cases, especially with isolated dystonia or coexisting sialorrhea.

C. Safety & Efficacy

- **Common Adverse Effects**: Dry mouth, blurred vision, constipation, tachycardia, dizziness, mild nausea; more severe: confusion, agitation, hallucinations, especially in elderly or psychiatric patients. Tolerance often develops over time.
- **Overdose**: Presents with anticholinergic toxicity—flushing, hyperthermia, delirium, seizures, possibly fatal. Treatment is supportive; physostigmine may be used as a specific antagonist.
- **Precautions / Contraindications**: Avoid in narrow-angle glaucoma, myasthenia gravis; use caution in elderly males with prostatic hypertrophy, glaucoma, cardiac or hepatic/renal disease. Gradual discontinuation to avoid withdrawal phenomena.
- **Abuse Potential**: Noted in high doses due to hallucinogenic and euphoriant effects.

D. Resistance / Tolerance

- **Tolerance**: Over prolonged use, patients may develop reduced response, necessitating dose adjustment.

E. Pediatric Population

- Not routinely recommended; safety and efficacy in adolescents and children are not well established
- Nonetheless, off-label use exists for dystonia and sialorrhea in CP children, with some positive outcomes from retrospective and pilot studies, albeit with cautious monitoring

5.2 Pharmacokinetic properties

Benzhexol hydrochloride is well absorbed from the gastrointestinal tract. It disappears rapidly from the plasma and tissues and does not accumulate in the body during continued administration of conventional doses.

A. Absorption

- **Route**: Oral
- **Bioavailability**: Trihexyphenidyl is rapidly and well absorbed from the gastrointestinal (GI) tract.
- **Onset of Action**: Usually within 1 hour after oral administration.
- **Peak Plasma Levels**: Occur approximately 2 to 3 hours after ingestion.

Note: Absolute bioavailability has not been fully quantified in humans due to lack of intravenous formulations for comparison.

B. Distribution

- Widely distributed throughout the body, including central nervous system (CNS) tissues.
- Protein Binding: Not extensively documented, but likely low to moderate, as is typical for small, lipophilic compounds.
- Volume of Distribution (Vd)**:** Not precisely established in the literature, but CNS penetration is clinically evident due to central anticholinergic effects.

C. Metabolism

- Hepatic (Liver) metabolism is the primary route.
- Likely metabolized by cytochrome P450 enzymes, although the exact isoforms involved are not well documented.

D. Elimination

- Renal excretion of both parent drug and metabolites.
- A portion of the drug is excreted unchanged in urine.
- Elimination Half-life: Estimated at 3 to 8 hours, though this can vary depending on the dose and individual patient characteristics.
- No significant accumulation in plasma or tissues with prolonged administration at standard doses.

E. Special Populations

Elderly:

- May experience increased sensitivity to both central and peripheral effects (e.g. confusion, hallucinations).
- Slower clearance is possible due to reduced hepatic or renal function.

Renal/Hepatic Impairment:

- Pharmacokinetics not thoroughly studied.
- Use with caution due to potential for altered metabolism and clearance.

Paediatric Population:

- Data limited.
- Pharmacokinetics in children are not well established, though clinical responses (and adverse effects) suggest significant CNS distribution.

5.3 Preclinical safety data

Across multiple available dosage tablets, syrup, and pharmacy sources—the following is consistently stated:

- "None stated."
- Or similar wording such as: "There are no preclinical data of relevance to the prescriber which are additional to that already included in other sections of the SPC."
- Or: "No preclinical data of relevance to the prescriber which are additional to that already included in other sections of the SPC."

This means no specific animal or preclinical toxicity findings—such as studies on carcinogenicity, reproduction, teratogenicity, genotoxicity, target organ toxicity

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6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

- Micro Crystalline Cellolose Powder
- Maize Starch
- Dibasic Calcium Phosphate
- Sodium Lauryl Sulfate
- Methyl Paraben
- Propyl Paraben
- PVPK- 30
- Purified Talcum
- Magnesium Stearate

- Sodium Starch Glycolate
- Colloidal Silicon Dioxide

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

48 months

6.4 Special precautions for storage

Store at a temperature below 30°C. Keep all medicine out of reach of children.

6.5 Nature and contents of container

500 Tablets are packed in Jar pack.

6.6 Special precautions for disposal and other handling

No special disposal requirements.

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7. APPLICANT INFORMATION

M/s. CHRIS NELB PHARMA CO. LTD.

ASHGBON STREET, IDUMOTA, LAGOS

LAGOS ISLAND, LAGOS

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8. MANUFACTURER

M/s. MCCOY PHARMA PVT. LTD.

S-12 & S-13, M.I.D.C., TARAPUR, BOISAR

DIST.: PALGHAR (MH) - 401506