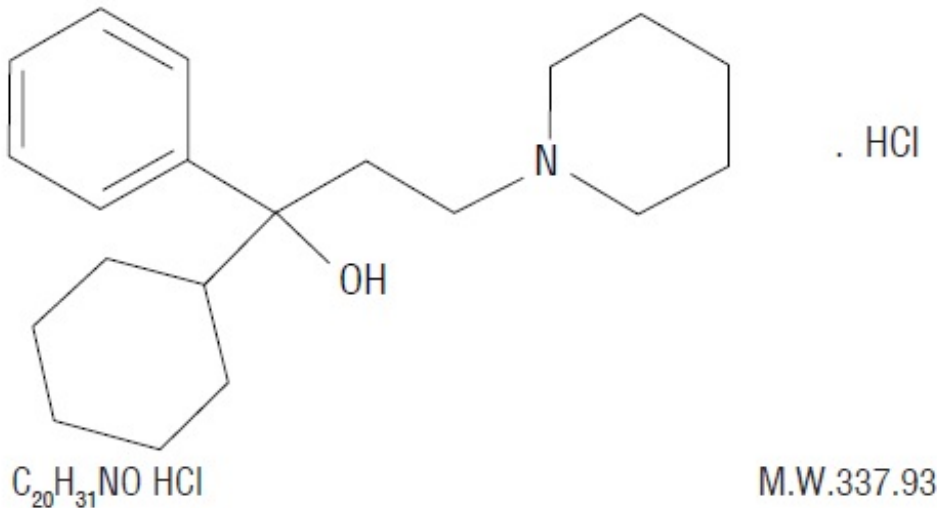


TRIHXYPHENIDYL HYDROCHLORIDE - trihexyphenidyl hydrochloride tablet
Bionpharma Inc.

Rx Only

DESCRIPTION

Trihexyphenidyl HCl is a synthetic antispasmodic drug. It is designated chemically as α -Cyclohexyl α -phenyl-1-piperidinepropanol hydrochloride and its structural formula is as follows:



Trihexyphenidyl HCl occurs as a white or creamy-white, almost odorless, crystalline powder. It is very slightly soluble in ether and benzene, slightly soluble in water and soluble in methanol.

Trihexyphenidyl Hydrochloride Tablets USP 2 mg and 5 mg contain the following inactive ingredients: magnesium stearate, microcrystalline cellulose and sodium starch glycolate.

CLINICAL PHARMACOLOGY

Trihexyphenidyl HCl 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 severe than with the latter.

INDICATIONS AND USAGE

Trihexyphenidyl HCl is indicated as an adjunct in the treatment of all forms of parkinsonism (postencephalitic, arteriosclerotic, and idiopathic). It is often useful as adjuvant therapy when treating these forms of parkinsonism with levodopa. Additionally, it is indicated for the control of extrapyramidal disorders caused by central nervous system drugs such as the dibenzoxazepines, phenothiazines, thioxanthenes, and butyrophenones.

CONTRAINDICATIONS

Trihexyphenidyl HCl is contraindicated in patients with hypersensitivity to trihexyphenidyl HCl or to any of the tablet ingredients. Trihexyphenidyl HCl is also contraindicated in patients with narrow angle glaucoma. Blindness after long-term use due to narrow angle glaucoma has been reported.

WARNINGS

Patients to be treated with trihexyphenidyl HCl 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 **CONTRAINDICATIONS** and **ADVERSE REACTIONS**).

Trihexyphenidyl HCl should be administered with caution in hot weather, especially when given concomitantly with other atropine-like drugs to the chronically ill, alcoholics, 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

A potentially fatal symptom complex sometimes referred to as Neuroleptic Malignant Syndrome (NMS) has been reported in association with dose reduction or Discontinuation of trihexyphenidyl. 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 (eg, 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.

PRECAUTIONS

General

Patients with cardiac, liver, or kidney disorders, or with hypertension, should be closely monitored.

Since trihexyphenidyl HCl has atropine-like properties, patients on long-term treatment should be carefully monitored for untoward reactions.

Since trihexyphenidyl HCl has parasympatholytic activity, it should be used with caution in patients with glaucoma, obstructive disease of the gastrointestinal or genitourinary tracts, and in elderly males with possible prostatic hypertrophy. Incipient glaucoma may be precipitated by parasympatholytic drugs such as trihexyphenidyl HCl.

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. Antiparkinsonism 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 trihexyphenidyl HCl may relieve some of these parkinsonism symptoms. Trihexyphenidyl HCl 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 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 **DRUG ABUSE AND DEPENDENCE**.)

Abrupt withdrawal of treatment for parkinsonism may result in acute exacerbation of parkinsonism symptoms; therefore, abrupt withdrawal should be avoided (see **DOSAGE AND ADMINISTRATION**).

Information for Patients

Trihexyphenidyl HCl 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 trihexyphenidyl HCl therapy does not adversely affect their ability to engage in such activities.

Because of increased sedative effects, patients should be cautioned to avoid the use of alcohol or other CNS depressants while taking trihexyphenidyl HCl.

Since this medication may increase the susceptibility to heat stroke (gastrointestinal (GI) problems, fever, heat intolerance), use with caution during hot weather. (See **WARNINGS**.)

Patients should be advised to report the occurrence of GI problems, fever, or heat intolerance promptly since paralytic ileus, hyperthermia, or heat stroke may occur.

If GI upset occurs, trihexyphenidyl HCl may be taken with food.

Patients should have close monitoring of intraocular pressure. (See **WARNINGS**.)

Drug Interactions

Cannabinoids, barbiturates, opiates, and alcohol may have additive effects with trihexyphenidyl HCl, and thus, an abuse potential exists.

Concurrent use of alcohol or other CNS depressants with trihexyphenidyl HCl may cause increased sedative 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.

Prophylactic administration of anticholinergic agents, such as trihexyphenidyl, 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 **PRECAUTIONS, General**).

The usual dose of either trihexyphenidyl or levodopa may need to be reduced during concomitant therapy, since concomitant administration may increase drug-induced involuntary movements (see **DOSAGE AND ADMINISTRATION**).

Carcinogenesis, Mutagenesis, Impairment of Fertility

No carcinogenicity studies or adequate genotoxicity or fertility studies have been conducted for

trihexyphenidyl HCl.

Pregnancy

TERATOGENIC EFFECTS PREGNANCY CATEGORY C

Animal reproduction studies to evaluate teratogenic and embryotoxic potential have not been conducted with trihexyphenidyl HCl. It is also not known whether trihexyphenidyl HCl can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Trihexyphenidyl HCl should be given to a pregnant woman only if clearly needed.

Nursing Mothers

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 trihexyphenidyl HCl is administered to a nursing woman.

As with other anticholinergics, trihexyphenidyl may cause suppression of lactation. Therefore, trihexyphenidyl should only be used if the expected benefit to the mother outweighs the potential risk to the infant.

Pediatric Use

Safety and effectiveness in pediatric patients have not been established. (See also **ADVERSE REACTIONS.**)

Geriatric Use

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 trihexyphenidyl HCl and observed closely. Trihexyphenidyl HCl has been shown to cause some cognitive dysfunctions in the elderly, including confusion and memory impairment. (See **ADVERSE REACTIONS** and **DOSAGE AND ADMINISTRATION.**)

ADVERSE REACTIONS

Minor side effects, such as dryness of the mouth, blurred vision, dizziness, mild nausea or nervousness, will be experienced by 30 to 50 percent of all patients. These sensations, however, are much less troublesome with trihexyphenidyl HCl than with belladonna alkaloids and are usually less disturbing than unalleviated parkinsonism. Such reactions tend to become less pronounced, and even to disappear, as treatment continues. Even before these reactions have remitted spontaneously, they may often be controlled by careful adjustment of dosage form, amount of drug, or interval between doses.

Isolated instances of suppurative parotitis secondary to excessive dryness of the mouth, skin rashes, dilatation of the colon, paralytic ileus, and certain psychiatric manifestations such as delusions, hallucinations, and paranoia, all of which may occur with any of the atropine-like drugs, have been reported rarely with trihexyphenidyl HCl.

Potential side effects associated with the use of any atropine-like drugs, including trihexyphenidyl HCl, include cognitive dysfunctions, including confusion and memory impairment; constipation, drowsiness, urinary hesitancy or retention, tachycardia, dilation of the pupil, increased intraocular pressure, choreiform movements, weakness, vomiting, and headache. Exacerbation of parkinsonism with abrupt treatment withdrawal has been reported. Neuroleptic malignant syndrome with abrupt treatment withdrawal has been reported (see **WARNINGS, Neuroleptic Malignant Syndrome**).

The occurrence of angle-closure glaucoma in patients receiving trihexyphenidyl HCl has been reported (blindness has been reported in some cases). Paradoxical sinus bradycardia, dry skin, and cycloplegia have been reported.

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

To report SUSPECTED ADVERSE REACTIONS, contact Bionpharma Inc. at 1-888-235-BION or 1-888-235-2466 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch

DRUG ABUSE AND DEPENDENCE

Although trihexyphenidyl HCl is not classified as a controlled substance, the possibility of abuse should be borne in mind due to its stimulant and euphoriant properties.

OVERDOSAGE

The mean oral LD₅₀ of trihexyphenidyl HCl has been reported to be 365 mg/kg (range, 325 to 410 mg/kg) in mice and 1660 mg/kg (1420 to 1940 mg/kg) in rats. At a dose of 40 mg/kg, dogs have exhibited emesis, restlessness followed by drowsiness, equilibrium disturbances, and mydriasis.

In humans, doses up to 300 mg (5 mg/kg) have been ingested without fatalities or sequelae. However, rare cases of death associated with trihexyphenidyl overdoses taken in conjunction with other CNS-depressant agents have been reported or in patients with a compromised respiratory condition. Trihexyphenidyl blood concentrations associated with the fatalities ranged from 0.03 to 0.80 mg/l.

Signs and Symptoms

Overdosage with trihexyphenidyl HCl produces typical central symptoms of atropine intoxication (the central anticholinergic syndrome). Correct diagnosis depends upon recognition of the peripheral signs of parasympathetic blockade, including dilated and sluggish pupils; warm, dry skin; facial flushing; decreased secretions of the mouth, pharynx, nose, and bronchi; foul-smelling breath; elevated temperature; tachycardia, cardiac arrhythmias; decreased bowel sounds; and urinary retention. Neuropsychiatric signs such as delirium, disorientation, anxiety, hallucinations, illusions, confusion, incoherence, agitation, hyperactivity, ataxia, lip smacking and tasting movements, loss of memory, paranoia, combativeness, and seizures may be present. 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 trihexyphenidyl HCl is dialyzable.

DOSAGE AND ADMINISTRATION

Dosage should be individualized. The initial dose should be low and then increased gradually, especially in patients over 60 years of age. Whether trihexyphenidyl HCl may best be given before or after meals should be determined by the way the patient reacts. Postencephalitic 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. If trihexyphenidyl HCl tends to dry the mouth excessively, it may be better to take it before meals, unless it causes nausea. If taken after meals, the thirst sometimes induced can be allayed by mint candies, chewing gum or water.

Abrupt withdrawal of treatment for parkinsonism may result in acute exacerbation of parkinsonism symptoms; therefore, abrupt withdrawal should be avoided. Abrupt withdrawal of treatment may result in neuroleptic malignant syndrome (NMS) (see **WARNINGS**).

Idiopathic Parkinsonism

As initial therapy for parkinsonism, 1 mg of trihexyphenidyl HCl in tablet form 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.

Drug-Induced Parkinsonism

The size and frequency of the trihexyphenidyl HCl dose needed to control extrapyramidal reactions to commonly employed tranquilizers, notably the phenothiazines, thioxanthenes, 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 trihexyphenidyl HCl therapy and then adjusting the 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 trihexyphenidyl HCl 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 trihexyphenidyl HCl therapy was discontinued.

Concomitant Use with Levodopa

When trihexyphenidyl HCl 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. An trihexyphenidyl HCl dosage of 3 to 6 mg daily, in divided doses, is usually adequate.

Concomitant Use with Other Parasympathetic Inhibitors

Trihexyphenidyl HCl 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 trihexyphenidyl HCl is increased.

Trihexyphenidyl HCl tablets - The total daily intake of trihexyphenidyl HCl 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.

HOW SUPPLIED

Trihexyphenidyl Hydrochloride Tablets, USP 2 mg are white colored, round debossed with N, T on either side of the score line and '2' on the other side.

Trihexyphenidyl Hydrochloride Tablets, USP 2 mg are available in

Bottle of 100 tablets (NDC 69452-241-20)

Bottle of 1000 tablets (NDC 69452-241-32)

Trihexyphenidyl Hydrochloride Tablets, USP 5 mg are white colored, round debossed with N, T on

either side of the score line and '5' on other side.

Trihexyphenidyl Hydrochloride Tablets, USP 5 mg are available in

Bottle of 100 tablets (NDC 69452-242-20)

Bottle of 1000 tablets (NDC 69452-242-32)

Dispense in a tight container with child-resistant closure.

Store at 20°-25°C (68°- 77°F). [See USP controlled room temperature.]

Manufactured by:
NATCO PHARMA LIMITED
Kothur-509 228,
Telangana, India.

Distributed by:
Bionpharma Inc.
600 Alexander Road,
Princeton,
NJ 08540
USA

Trihexyphenidyl Hydrochloride Tablets USP 2 mg-Bottle of 100

NDC 69452-241-20

Each tablet contains Trihexyphenidyl hydrochloride USP 2 mg

Dispense in tight container with child-resistant closure.

BIONPHARMA
NDC 69452-241-20
Trihexyphenidyl Hydrochloride Tablets, USP
2 mg
Rx Only 100 Tablets

Distributed by:
Bionpharma Inc.
600 Alexander Road,
Princeton, NJ 08540 USA

Manufactured by:
Natco Pharma Limited
Kothur-509 228,
Telangana, INDIA

M.L.: 164/MN/AP/95/F/R 1018

345353

Each tablet contains: Trihexyphenidyl Hydrochloride USP, 2 mg.

Dosage: See package insert for dosage and full prescribing information.

Dispense in a tight container with child-resistant closure.

Store at 20°C - 25°C (68°-77°F);
[See USP controlled room temperature].

20 Barcode

Unvarnish Area

GTIN 00351991322900
SN 012345678901234
EXP. 00/0000
LOT 123456L

Trihexyphenidyl Hydrochloride Tablets USP 2 mg-Bottle of 1000

NDC 69452-241-32

Each tablet contains Trihexyphenidyl hydrochloride USP 5 mg

Dispense in tight container with child-resistant closure.

345354

3 N 6 9 4 5 2 2 4 1 3 2 5

Distributed by:
Bionpharma Inc.
600 Alexander Road,
Princeton, NJ 08540 USA

Manufactured by:
Natco Pharma Limited
Kothur-509 228,
Telangana, INDIA
1018

M.L.: 164/MN/AP/95/F/R

BIONPHARMA
NDC 69452-241-32

Trihexyphenidyl Hydrochloride Tablets, USP

2 mg

Rx Only **1000 Tablets**

Each tablet contains: Trihexyphenidyl Hydrochloride USP, 2 mg.

Dosage: See package insert for dosage and full prescribing information.

Dispense in a tight container with child-resistant closure.

Store at 20°C - 25°C (68° - 77°F); [See USP controlled room temperature].

2D Barcode

GTIN 00351991322900
SN 012345678901234
EXP. 00/0000
LOT 123456L

Unvarnish area

Trihexyphenidyl Hydrochloride Tablets USP 5 mg-Bottle of 100

NDC 69452-242-20

Each tablet contains Trihexyphenidyl hydrochloride USP 5 mg

Dispense in tight container with child-resistant closure.

345355

3 N 6 9 4 5 2 2 4 2 2 0 9

Distributed by:
Bionpharma Inc.
600 Alexander Road,
Princeton, NJ 08540 USA

Manufactured by:
Natco Pharma Limited
Kothur-509 228,
Telangana, INDIA
1018

M.L.: 164/MN/AP/95/F/R

BIONPHARMA
NDC 69452-242-20

Trihexyphenidyl Hydrochloride Tablets, USP

5 mg

Rx Only **100 Tablets**

Each tablet contains: Trihexyphenidyl Hydrochloride USP, 5 mg.

Dosage: See package insert for dosage and full prescribing information.

Dispense in a tight container with child-resistant closure.

Store at 20°C - 25°C (68° - 77°F); [See USP controlled room temperature].

2D Barcode

GTIN 00351991322900
SN 012345678901234
EXP. 00/0000
LOT 123456L

Unvarnish area

Trihexyphenidyl Hydrochloride Tablets USP 5 mg-Bottle of 1000

DC 69452-242-32

Each tablet contains Trihexyphenidyl hydrochloride USP 5 mg
Dispense in tight container with child-resistant closure.

TRIHEXYPHENIDYL HYDROCHLORIDE

trihexyphenidyl hydrochloride tablet

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	Item Code (Source)	NDC:69452-241
Route of Administration	ORAL		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
TRIHEXYPHENIDYL HYDROCHLORIDE (UNII: AO61G82577) (TRIHEXYPHENIDYL - UNII:6RC5V8B7PO)	TRIHEXYPHENIDYL HYDROCHLORIDE	2 mg

Inactive Ingredients

Ingredient Name	Strength
CELLULOSE, MICROCRYSTALLINE (UNII: OP1R32D61U)	
MAGNESIUM STEARATE (UNII: 70097M6I30)	
SODIUM STARCH GLYCOLATE TYPE A POTATO (UNII: 5856J3G2A2)	

Product Characteristics

Color	WHITE	Score	2 pieces
Shape	ROUND	Size	8mm
Flavor		Imprint Code	N;T;2
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:69452-241-20	100 in 1 BOTTLE; Type 0: Not a Combination Product	12/15/2018	
2	NDC:69452-241-32	1000 in 1 BOTTLE; Type 0: Not a Combination Product	12/15/2018	

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA091630	12/15/2018	

TRIHEXYPHENIDYL HYDROCHLORIDE

trihexyphenidyl hydrochloride tablet

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	Item Code (Source)	NDC:69452-242
Route of Administration	ORAL		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
TRIHEXYPHENIDYL HYDROCHLORIDE (UNII: AO61G82577) (TRIHEXYPHENIDYL - UNII:6RC5V8B7PO)	TRIHEXYPHENIDYL HYDROCHLORIDE	5 mg

Inactive Ingredients

Ingredient Name	Strength
CELLULOSE, MICROCRYSTALLINE (UNII: OP1R32D61U)	
MAGNESIUM STEARATE (UNII: 70097M6I30)	
SODIUM STARCH GLYCOLATE TYPE A POTATO (UNII: 5856J3G2A2)	

Product Characteristics

Color	WHITE	Score	2 pieces
Shape	ROUND	Size	11mm
Flavor		Imprint Code	N;T;5
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:69452-242-20	100 in 1 BOTTLE; Type 0: Not a Combination Product	12/15/2018	
2	NDC:69452-242-32	1000 in 1 BOTTLE; Type 0: Not a Combination Product	12/15/2018	

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA091630	12/15/2018	

Labeler - Bionpharma Inc. (079637826)

Registrant - NATCO PHARMA LIMITED (650224736)

Establishment

Name	Address	ID/FEI	Business Operations
Natco Pharma Limited-Pharma Division		918588174	MANUFACTURE(69452-241, 69452-242)

Revised: 12/2018

Bionpharma Inc.