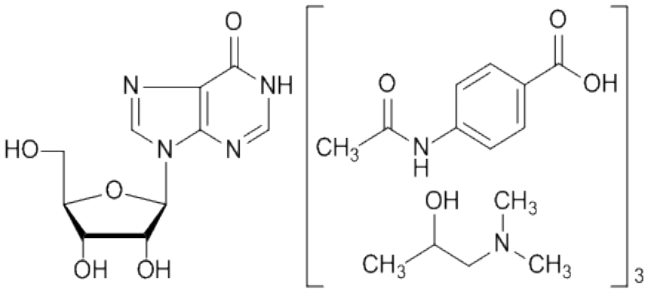
1.4.1 PRESCRIBING INFORMATION (SUMMARY OF PRODUCT CHARACTERISTICS)

1	**Name of the Finished Product:**
1.1	**Product Name:** **Brand Name:** VIRALEX **Generic Name:** Inosine Pranobex 500 mg Tablets
1.2	**Strength :** 500 mg
2	**Qualitative and quantitative compositions:**
	Qualitative Declaration: Active component INN Name: INOSINE DIMEPRANOL ACEDOBEN **Quantitative Declaration:** Each uncoated tablet contains: Inosine Pranobex …. 500 mg

Sr. No.	Content Name	Quality Standard	Qty per Tablet (mg)
DRY MIXING			
A1	(Inosine Pranobex) Inosine Dimepranol Acedoben	IH	500.00 mg
A1	Potato Starch	EP/ BP	75.00 mg
A1	Povidone (K-25)	EP/ BP	35.000 mg
BINDING			
B	Ethanol 96%	EP/ BP	-
LUBRICATION /BLENDING			
C1	Potato Starch	EP/BP	10.000 mg
C2	Magnesium Stearate	EP/BP	10.000 mg
C3	Povidone (K-25)	EP/BP	10.000 mg
	Total		640mg

EP: European Pharmacopoeia
BP: British Pharmacopoeia
IH: Inhouse

3	**Pharmaceutical form:** Oral Tablets **Description:** Inosine pranobex (BAN), also known as Inosine Acedoben Dimepranol (INN), Methisoprinol or Isoprinosine, is a synthetic purine derivative with immunomodulatory and antiviral properties. It is a synthetic compound of p-acetamidobenzoic acid salt of N,N dimethylamino-2-propanol [DIP. PAcBA] and β-inosine in a 3:1 molar ratio. The molecular formula of Inosine Pranobex is $C_{52}H_{78}N_{10}O_{17}$; its molecular weight is 1115.2 g/mol and its structural formula is given below. 
4	**Clinical particulars:**
4.1	**Therapeutic indications:** Viralex (Inosine Pranobex 500mg tablets) is indicated in the management of: • Mild to moderate COVID-19 patients. • Influenza and other acute viral respiratory infections • Mucocutaneous infections due to herpes simplex virus (type 1 and/or type II) • Genital warts as adjunctive therapy to podophyllin or carbon dioxide laser • Subacute sclerosing panencephalitis (SSPE)
4.2	**Posology and method of administration** <u>Posology</u> Adults and the Elderly: The recommended dosage is 50mg/kg bd wt/day, rounded to the nearest multiple of 500mg (usually 3g/day, up to a maximum of 4g/day), administered orally in 3–4 divided doses during waking hours. The recommended duration of therapy is for 10 days. <u>Method of administration</u> For oral use. To make ingestion easier, the tablets may be crushed and dissolved in a small amount of flavored liquid at the time of administration.
4.3	**Contra-indications:** • Hypersensitivity to the active substance. • Acute gout or elevated blood uric acid blood levels.

4.4	**Special warning and precautions for use:** **a.** Inosine Pranobex may cause a transient elevation of baseline serum and urinary uric acid, usually remaining within the normal range (using 8mg % as the upper limit), particularly in males and in the ageing population of both sexes. The elevation of uric acid levels is due to the catabolic metabolism of the Inosine moiety in this product in humans to uric acid. It is not due to a fundamental drug-induced alteration of enzyme or renal clearance function. Therefore, Inosine Pranobex may be administered with caution in patients with a history of gout, hyperuricaemia, urolithiasis, or to patients with impaired renal function. During treatment, uric acid levels in these patients should be monitored closely. **b.** In the case of long term treatment (3 months or longer), the serum and/or urine uric acid levels, liver function, blood count and renal functions should be checked on a regular basis in all patients. There is a possibility that ureteric and biliary calculi may occur when patients receive long term treatment. In some people acute hypersensitivity reactions (urticaria, angioedema, anaphylaxis and anaphylactic shock) may occur. Treatment with Inosine Pranobex should be withdrawn in these cases.
4.5	**Interaction with other drugs, other forms of interactions:** The drug should be used with caution with xanthine oxidase inhibitors (e.g. allopurinol) or uricosuric agents, including diuretics (e.g. hydrochlorothiazide, chlorthalidone, indapamide) and loop diuretics (furosemide, torasemide, ethacrynic acid). Inosine Pranobex may be administered after but not concomitantly with immunosuppressive agents, as there may be a pharmacokinetic influence on the desired therapeutic effects. Concomitant use with zidovudine (AZT) increases AZT nucleotide formation through multiple mechanisms involving increased plasma AZT bioavailability and increased intracellular phosphorylation in human blood monocytes. As a result, Inosine Pranobex increases the effect of AZT.
4.6	**Fertility, Pregnancy & Lactation:** Controlled trials monitoring foetal risk and impairment of fertility in humans are not available. It is not known if Inosine Pranobex is excreted in human milk. Therefore, Inosine Pranobex should not be administered during pregnancy or lactation unless the physician decides the benefits outweigh the potential risk. Although animal tests have shown no teratogenic effect, the use of Inosine Pranobex in women where pregnancy is suspected or confirmed should be avoided.

4.7 Effects on ability to drive and operate machine:

Inosine Pranobex has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects:

Frequency convention – very common: ≥1/10; Common: ≥1/100, <1/10; Uncommon: ≥1/1,000, <1/100; Rare: ≥1/10,000, <1/1,000; Very rare: <1/10,000, including isolated reports; Not Known: Cannot be estimated from the available data.

System Organ Class	Frequency	Adverse Reaction
Immune system disorders:	Not known	Angioedema, Hypersensitivity, Urticaria, Anaphylactic reaction
Psychiatric disorders	Uncommon	Nervousness
Nervous system disorders	Common	Headache, Vertigo
	Uncommon	Somnolence (Drowsiness), Insomnia
	Not Known	Dizziness
Gastrointestinal disorders:	Common	Vomiting, Nausea, Epigastric discomfort, Epigastric pain
	Uncommon	Diarrhoea, Constipation
	Not known	Abdominal pain upper
Skin and subcutaneous tissue disorders	Common	Rash, Pruritus (Itching)
	Not known	Erythema
Musculoskeletal and connective tissue disorders	Common	Arthralgia
Renal and urinary disorders	Uncommon	Polyuria
General disorders and administration site conditions	Common	Fatigue, Malaise
Investigations	Very Common	Blood uric acid increased, Urine uric acid increased
	Common	Blood urea increased, Transaminases increased, Blood alkaline phosphate increased

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation 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 via:

- Email: drugsafety@themismedicare.com
- Link to download form - https://www.themismedicare.com/adverse-events/

4.9	**Overdose:** There has been no experience of overdose with Inosine Pranobex. However, serious adverse effects apart from increased levels of uric acid in the body, seem unlikely in view of the animal toxicity studies. Treatment should be restricted to symptomatic and supportive measures.
5	**Pharmacological Properties:**
5.1	**Pharmacotherapeutic Group (ATC Code):** J05AX05 **Pharmacodynamic Properties:** Inosine Pranobex is a synthetic purine derivative with immunomodulatory and antiviral properties, which result from an apparent in vivo enhancement of host immune responses due to the drug. In clinical studies Inosine Pranobex has been shown to normalise (to the patient's baseline) a deficient or dysfunctional cell-mediated immunity by evoking a Th1 type response which initiates T lymphocyte maturation and differentiation and potentiation of induced lymphoproliferative responses, in mitogen or antigen-activated cells. Similarly, the drug has been shown to modulate T lymphocyte and natural killer cell cytotoxicity, T8 suppressor and T4 helper cell functions and also to increase the number of IgG and complement surface markers. Inosine Pranobex increases cytokine IL-1 production and enhances IL-2 production, up regulating the expression of the IL-2 receptor in vitro. It significantly increases endogenous IFN -γ secretion and decreases the IL-4 production in vivo. It has also been shown to potentiate neutrophil, monocyte and macrophage chemotaxis and phagocytosis. In vivo, Inosine acedoben dimeparanol enhances potentiation of depressed lymphocytic mRNA protein synthesis and translational ability while inhibiting viral RNA synthesis achieved by yet-to-be-clarified degrees of (1) incorporation of Inosine-mediated orotic acid into polyribosomes; (2) inhibition of polyadenylic acid attachment to viral messenger RNA and (3) molecular reorganisation of lymphocyte intramembrane plasma particles (IMP) which take part in emitting signals via specific T cells receptor (TcR) that results in a nearly threefold increase in density. Inosine Pranobex inhibits cGMP phosphodiesterase only at high concentrations in vitro and at levels not involved in the in vivo immunopharmacological effects. In vitro, Inosine Pranobex exhibits inhibitory activity on the replication of herpes virus type 1 (HSV-1).

5.2	**Pharmacokinetic Properties:** Each moiety of the drug exhibits separate pharmacological properties. Absorption: When administered orally in man, Inosine Pranobex is rapidly and completely absorbed (≥ 90%) from the gastrointestinal tract and appears in the blood. Similarly, 94-100% of IV values of DIP [N,N-dimethylamino-2-propanol] and PacBA [p-acetamidobenzoic acid] components are recovered in urine after oral administration in Rhesus monkeys. Distribution: Radiolabelled material was found in the following tissues in order of decreasing specific activity when drug was administered to monkeys: kidneys, lung, liver, heart, spleen, testes, pancreas, brain and skeletal muscle. Metabolism: In human subjects following a 1 g oral dose of Inosine Pranobex, the following plasma levels were found for DIP and PAcBA, respectively: 3.7µg/ml (2 hours) and 9.4µg/ml (1 hour). In human dose tolerance studies, peak post-dose elevation of uric acid levels as a measurement of drug-derived inosine are not linear and can vary±10% between 1-3 hours. Excretion: The 24-hour urinary excretion of PAcBA and its major metabolite under steady-state conditions at 4g per day amounted to approximately 85% of the administered dose. 95% of the DIP-derived radioactivity in urine was recovered as unchanged DIP and DIP N-oxide. The elimination half-life is 3.5 hours for DIP and 50 minutes for PAcBA. The major metabolites in humans are the N-oxide for DIP and the o-acylglucuronide for PAcBA. Because the inosine moiety is degraded by the purine degradation pathway to uric acid, radiolabelled experiments in humans are inappropriate. In animals up to about 70% of the administered inosine can be recovered as urinary uric acid following oral tablet administration and the remainder as the normal metabolites, xanthine and hypoxanthine. Bioavailability/AUC: Urinary recoveries under steady state conditions of the PAcBA moiety and its metabolite were found to be > 90% of the expected value from solution. The recovery of the DIP moiety and its metabolite was >76%. The plasma AUC was >88% for DIP and > 77% for PAcBA.

5.3	**Preclinical Safety Data:** Animal Toxicology/ Pharmacology Inosine pranobex showed a low toxicity profile in multivariate acute, subacute and chronic toxicology in mice, rats, dogs, cats and monkeys in doses up to 1500mg/kg/day and produced the lowest acute oral LD_{50} at 50 times the maximum therapeutic dosage level of 100mg/kg/day. Long-term toxicology studies in mice and rats have shown no indication of carcinogenic potential. Standard mutagenicity assays and in vivo studies in mice and rats and in vitro studies in human peripheral blood lymphocytes revealed no aberrant properties. No evidence of perinatal toxicity, embryotoxicity, teratogenicity or impaired reproductive function in mice, rats and rabbits could be demonstrated in studies with continuous parental dosing of up to 20 times the maximum therapeutically recommended human dose (100 mg/kg/day) (See also Use in special populations (such as pregnant women, lactating women) for usage recommendations in pregnancy).
6	**Pharmaceutical Particulars:**
6.1	**List of Excipients:** Povidone K-25, Potato Starch, Magnesium Stearate
6.2	**Incompatibilities:** Not applicable
6.3	**Shelf life:** 24 Months
6.4	**Special precautions for storage:** Store below 30°C, protected from light.
6.5	**Nature and contents of container:** **6 x 10's:** 10 tablets of **VIRALEX** (Inosine Pranobex 500 mg Tablets) are packed in a blister [Printed Aluminium foil and PVC/ PE/ PVDC clear film]. 6 such blisters are packed in a carton with pack insert. **1 x 10's:** 10 tablets of **VIRALEX** (Inosine Pranobex 500 mg Tablets) are packed in a blister [Printed Aluminium foil and PVC/ PE/ PVDC clear film]. 1 such blister is packed in a carton with pack insert.
6.6	**Special precaution for disposal:** Not applicable

7	**Marketing Authorisation Holder:** THEMIS MEDICARE LIMITED Address : 11/12, Udyog Nagar, S. V. Road, Goregaon (West), Mumbai-400104. Country : India Telephone : 91-22-67607080 E-Mail : info@themismedicare.com **Manufacturer :** THEMIS MEDICARE LIMITED Address : Sector 6A, 16, 17 & 18, IIE, SIDCUL, Haridwar, Uttarakhand-249 403. Country : India Telephone : 91-1334-239322/21 E-Mail : hwdgmtech@themismedicare.com
8	**Marketing Authorization Number:** Not Applicable
9	**Date of First Registration /Renewal of the Authorisation:** Not Applicable
10	**Date of revision of the text:** Not Applicable
11	**Dosimetry (if applicable) :** Not Applicable
12	**Instruction for preparations of Radiopharmaceutical (if applicable) :** Not Applicable