

# **PRODUCT MONOGRAPH**

**Pr**  
**NTP-HYDROCHLOROTHIAZIDE**  
(Hydrochlorothiazide Tablets USP)  
25 mg & 50 mg

**DIURETIC - ANTIHYPERTENSIVE**

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**NTP-HYDROCHLOROTHIAZIDE**  
(Hydrochlorothiazide Tablets, USP)

25 mg & 50 mg

Diuretic – Antihypertensive

**PART I: HEALTH PROFESSIONAL INFORMATION SUMMARY PRODUCT INFORMATION**

**SUMMARY PRODUCT INFORMATION**

<b>Route of Administration</b>	<b>Dosage Form/ Strength</b>	<b>Clinically Relevant Nonmedicinal Ingredients</b>
Oral	tablet 25 mg & 50 mg	None. <i>For a complete listing see Dosage Forms, Composition and Packaging section.</i>

**INDICATIONS AND CLINICAL USE**

NTP-HYDROCHLOROTHIAZIDE (Hydrochlorothiazide) is indicated for the treatment of:

- Edema
- Hypertension
- Toxemia of Pregnancy

**Edema**

NTP-HYDROCHLOROTHIAZIDE (hydrochlorothiazide) is indicated in edema associated with congestive heart failure, hepatic cirrhosis, corticosteroid and estrogen therapy, premenstrual tension with edema and in edema of renal origin (i.e. nephrotic syndrome, acute glomerulonephritis and chronic renal disease). In obese patients in whom fluid retention is a complicating factor, it may help to initiate a loss of fluid and, thus of weight.

**Hypertension**

NTP-HYDROCHLOROTHIAZIDE may be used alone or as an adjunct to other antihypertensive drugs. Since it enhances the action of these agents, their dosage must be reduced to avoid an excessive drop in pressure and other unwanted side effects.

**Toxemia of Pregnancy**

NTP-HYDROCHLOROTHIAZIDE may be effective in the treatment of toxemia of pregnancy (including eclampsia).

**Geriatrics (> 65 years of age):** No data is available.

**Pediatrics (0 to 16 years of age):** No data is available.

## **CONTRAINDICATIONS**

- NTP-HYDROCHLOROTHIAZIDE (Hydrochlorothiazide Tablets, USP), as all diuretics, is contraindicated in anuria.
- NTP-HYDROCHLOROTHIAZIDE should be discontinued if increasing azotemia and oliguria occur during treatment of severe progressive renal disease.
- NTP-HYDROCHLOROTHIAZIDE is contraindicated in persons known to be sensitive to hydrochlorothiazide or to other sulfonamide-derived drugs.
- Patients who are hypersensitive to any ingredient in the formulation of NTP-HYDROCHLOROTHIAZIDE or component of the container. For a complete listing, see the **Dosage Forms, Composition and Packaging** section of the product monograph.

## **WARNINGS AND PRECAUTIONS**

### **General**

Patients on long therapy with hydrochlorothiazide are required to be on potassium rich diet. Periodic determinations of serum electrolytes to detect possible electrolyte imbalance should be performed.

The antihypertensive effects of the drug may be enhanced in the postsympathectomy patient.

### **Carcinogenesis and Mutagenesis**

No data available.

### **Cardiovascular**

No data available.

### **Ear/Nose/Throat**

No data available.

### **Endocrine and Metabolism**

**Calcium:** Calcium excretion is decreased by thiazides.

**Chloride:** Chloride deficiency is generally mild and does not require specific treatment except under special conditions such as renal or/and hepatic disease.

**Dilutional Hyponatremia:** Dilutional hyponatremia may occur in edematous patients in hot weather; appropriate therapy is water restriction rather than administration of salt except when hyponatremia is life threatening. In actual salt depletion, appropriate replacement is the therapy of choice.

**Fluid and electrolyte imbalance:** All patients receiving thiazide should be observed for clinical signs of fluid or electrolyte imbalance: namely hyponatremia, hypochloremic alkalosis, and hypokalemia. Serum and urine electrolyte determinations are particularly important when the patient is vomiting excessively, or receiving parenteral fluids. Warning signs of serum electrolyte imbalance, irrespective of cause are: dryness of mouth, thirst, weakness, lethargy, drowsiness, restlessness, muscle pains or cramps, muscular fatigue, hypotension, oliguria, tachycardia, and gastrointestinal disturbances such as nausea and vomiting. Serum electrolytes may also be influenced by medication such as digitalis.

**Hyperuricemia:** Hyperuricemia may occur or frank gout may be precipitated in certain patients receiving thiazide therapy.

**Hypokalemia:** Hypokalemia may develop, especially with rapid diuresis, when severe cirrhosis is present or during concomitant use of corticosteroids or ACTH. Deficient oral electrolyte intake will also contribute to hypokalemia. Hypokalemia may sensitize or exaggerate the response of the heart to the toxic effects of digitalis (e.g. increased ventricular irritability). Hypokalemia may be avoided or treated by the use of potassium supplements.

**Insulin:** Insulin requirements in diabetic patients may be increased, decreased, or remain unchanged. Latent diabetes mellitus may become manifest during thiazide therapy. Concomitant therapy with lithium is not recommended with diuretics because of the reduction of renal clearance of lithium and therefore an added risk of lithium toxicity.

**Parathyroid gland:** Pathological changes in the parathyroid gland with hypercalcemia and hypophosphatemia have been observed in a few patients on prolonged thiazide therapy. The common complications of hyperparathyroidism such as renal lithiasis, bone resorption, and peptic ulceration have not been reported. Use of thiazides should be discontinued before carrying out tests for parathyroid function.

**Protein bound iodine (PBI):** Thiazides may decrease serum PBI levels without signs of thyroid disturbance.

### **Gastrointestinal**

Non-specific small bowel lesions consisting of stenosis with or without ulceration, may occur in association with the administration of enteric coated potassium salts, alone or with oral diuretics. These small bowel lesions have caused obstruction, hemorrhage and perforation. Surgery was frequently required and deaths have occurred. Available information tends to implicate enteric coated potassium salts, although lesions of this type also occur spontaneously. Such preparations should be used only when adequate dietary supplementation is not practical, and should be discontinued immediately if abdominal pain, distention, nausea, vomiting or gastrointestinal bleeding occur.

### **Genitourinary**

No data available.

### **Hematologic**

No data available.

### **Hepatic/biliary/Pancreatic**

Hydrochlorothiazide should be used with caution in patients with impaired hepatic function or progressive liver disease, since minor alterations of fluid and electrolyte balance or of serum ammonia may precipitate hepatic coma.

### **Immune**

The possibility of exacerbation or activation of systemic lupus erythematosus has been reported.

Sensitivity reactions may occur in patients with or without a history of allergy or bronchial asthma.

### **Neurologic**

No data available.

### **Ophthalmologic**

No data available.

### **Peri-Operative Considerations**

No data available.

### **Psychiatric**

No data available.

### **Renal**

In progressive renal impairment, therapy with hydrochlorothiazide should be withheld or discontinued. Hydrochlorothiazide may commence or precipitate azotemia. It should be used with caution in patients with severely impaired renal function to avoid toxic or cumulative effect. If azotemia becomes more severe and oliguria occurs during treatment of patients with severe renal disease, administration of the diuretic must be stopped.

### **Respiratory**

No data available.

### **Sensitivity/Resistance**

No data available.

### **Sexual Function/Reproduction**

No data available.

### **Skin**

No data available.

## **Special Population**

### **Pregnant Women**

Thiazides cross the placental barrier and appear in cord blood. When hydrochlorothiazide is used in pregnancy or in women of child-bearing age, the potential benefits of the drug should be weighed against the possible hazards to the fetus. These hazards include fetal or neonatal jaundice, thrombocytopenia, and possibly other adverse reactions which have occurred in the adult.

The routine use of diuretics in otherwise healthy pregnant women with or without mild edema is not indicated.

### **Nursing Women**

Since thiazides appear in breast milk, hydrochlorothiazide is contraindicated in nursing mothers. If use of the drug is deemed essential, the patient should stop nursing.

### **Pediatrics (0 to 18 years of age)**

Safety and effectiveness in children under 18 years of age have not been established.

### **Geriatrics**

Safety and effectiveness in adults over 65 years of age have not been established.

## **ADVERSE REACTIONS**

Whenever adverse reactions are moderate or severe, thiazide dosage should be reduced or therapy withdrawn.

Cardiovascular: Orthostatic hypotension (may be aggravated by alcohol, barbiturates, or narcotics).

Central nervous system: Dizziness, vertigo, paresthesias, headache, xanthopsia.

Gastrointestinal system: Anorexia, gastric irritation, nausea, vomiting, cramps, diarrhea, constipation, jaundice (intrahepatic cholestatic jaundice), pancreatitis, sialadenitis.

Hematologic: Leukopenia, agranulocytosis, thrombocytopenia, aplastic anemia.

Hypersensitivity: Purpura, photosensitivity, rash, urticaria, necrotizing angitis (vasculitis), fever, respiratory distress including pneumonitis, anaphylactic reactions.

Other: Hyperglycemia, glycosuria, hyperuricemia, muscle spasm, weakness, restlessness, transient blurred vision.

## **DRUG INTERACTIONS**

Hydrochlorothiazide adds to or potentiates the action of other antihypertensive drugs. Potentiation occurs especially with ganglionic or peripheral adrenergic blocking drugs.

### **Drug-Drug Interactions**

**Alcohol, barbiturates or narcotics:** Orthostatic hypotension may occur and may be potentiated by alcohol, barbiturates, or narcotics.

**Lithium:** Concomitant therapy with lithium is not recommended with diuretics because of the reduction of renal clearance of lithium and therefore an added risk of lithium toxicity.

**Norepinephrine:** Thiazides may decrease arterial responsiveness to norepinephrine. This diminution is not sufficient to preclude effectiveness of the pressor agent for therapeutic use.

**Probenecid:** The rate of elimination of hydrochlorothiazide is decreased somewhat by the coadministration of probenecid without, however, an accompanying reduction in diuresis.

**Tubocurarine:** Thiazide drugs may increase the responsiveness to tubocurarine.

### **Drug-Food Interactions**

Interactions with food have not been established.

### **Drug-Herb Interactions**

Interactions with herbal products have not been established.

### **Drug-Laboratory Test Interactions**

There are no known interactions of Hydrochlorothiazide with commonly used laboratory tests.

## **DOSAGE AND ADMINISTRATION**

Therapy should be individualized according to the patients requirement. Use the smallest dosage necessary to achieve the required response.

### **Dosing Considerations**

#### **Adult patients**

- Diuresis
- Toxemia of pregnancy
- Premenstrual tension with edema
- Control of Hypertension

#### **Infants and Children**



## **Adult patients**

### **Diuresis**

The recommended adult dosage is 50 to 100 mg once or twice a day. Many patients respond to intermittent therapy, i.e. administration on alternate days or on three to five days each week.

With an intermittent schedule, excessive response and the resulting undesirable electrolyte imbalance are less likely to occur.

### **Toxemia of pregnancy**

The recommended dosage is 100 mg daily or, in severe cases and for brief periods, 200 mg daily (in divided doses). Frequency of administration may range from once every four days to daily.

### **Premenstrual tension with edema**

The recommended dosage is 25 to 50 mg once or twice a day from the first appearance of symptoms until onset of the menses.

### **Control of Hypertension**

The usual recommended starting dosage is 50 or 100 mg a day as a single or divided dose. Dosage is increased or decreased according to the blood pressure response of the patient. Some patients may require doses of 200 mg a day in divided doses.

Careful observation for changes in blood pressure must be made when NTP-HYDROCHLOROTHIAZIDE (Hydrochlorothiazide Tablets, USP) is used with other antihypertensive drugs, especially during initial therapy. The dosage of other agents must be reduced by at least 50%, as soon as it is added to the regimen, to prevent excessive drop in blood pressure. As the blood pressure falls under the potentiating effect of this agent, a further reduction in dosage, or discontinuation of other antihypertensive drugs may be necessary. A single daily dose as low as 12.5 mg of Hydrochlorothiazide could be used in combination with another antihypertensive.

In the case of hypertension monotherapy, doses as low as a single daily dose 12.5 mg may be effective (especially in the elderly or as a starting dose), as well as a daily dose of 25 mg given in two divided doses.

### **Infants and Children**

The usual recommended pediatric dosage is based on 1.0 mg of NTP-HYDROCHLOROTHIAZIDE per pound of body weight per day in two doses. Infants under 6 months of age may require up to 1.5 mg per pound per day in two doses.

On this basis, infants up to 2 years of age may be given 12.5 to 37.5 mg daily in two doses. Children from 2 to 12 years of age may be given 37.5 to 100 mg daily in two doses. Dosage in both age groups should be based on body weight.

The 25 mg tablet can not be divided into quarters.

## **OVERDOSAGE**

### **Symptoms**

Overdosage of hydrochlorothiazide may produce diuresis accompanied with electrolyte imbalance (hypokalemia, hyponatremia and hypochloremic alkalosis) and dehydration.

The symptoms are as follows: dryness of mouth, thirst, weakness, lethargy, drowsiness, restlessness, muscle pains or cramps, muscular fatigue, hypotension, oliguria, tachycardia, gastrointestinal disturbances, mental confusion, delirium, convulsions, shock, coma.

Hypokalemia can sensitize or exaggerate the response of the heart to the toxic effects of digitalis (e.g. increased ventricular irritability).

Hydrochlorothiazide may precipitate hepatic coma in patients with cirrhosis; increase the effect of other antihypertensive agents and decrease arterial responsiveness to norepinephrine.

### **Treatment**

No specific antidote is available.

Treatment is symptomatic and supportive. Induce emesis or perform gastric lavage. Correct dehydration, electrolyte imbalance, hepatic coma, and hypotension by established procedures. Administer oxygen or artificial respiration for respiratory impairment.

For management of a suspected drug overdose, contact your regional Poison Control Centre.
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## **ACTION AND CLINICAL PHARMACOLOGY**

### **Mechanism of Action**

Hydrochlorothiazide is a diuretic and an antihypertensive agent. The exact mechanism of the antihypertensive effect is unknown. Hydrochlorothiazide has no effect on normal blood pressure.

Hydrochlorothiazide affects the renal tubular mechanism of electrolyte reabsorption. It increases excretion of sodium and chloride in approximately equivalent amounts and reduces the rate of formation of solute-free water. Natriuresis causes a secondary loss of potassium and bicarbonate.

## **Pharmacokinetics**

**Absorption:** Hydrochlorothiazide is rapidly absorbed from the gastrointestinal tract. Onset of action after oral administration occurs in 2 hours and the peak effect at approximately 4 hours. Duration of action persists for approximately 6 to 12 hours.

**Distribution:** The drug is distributed throughout the extracellular space and does not accumulate in tissues other than the kidney. It passes readily through the placental barrier to the fetus.

**Metabolism:** Hydrochlorothiazide is not metabolized.

**Excretion:** Hydrochlorothiazide is eliminated rapidly by the kidney.

## **STORAGE AND STABILITY**

NTP-HYDROCHLOROTHIAZIDE (Hydrochlorothiazide Tablets, USP) Tablets should be stored at controlled room temperature (15°C to 30°C) away from heat and light.

## **DOSAGE FORMS, COMPOSITION AND PACKAGING**

NTP-HYDROCHLOROTHIAZIDE (Hydrochlorothiazide Tablets, USP) tablets are available for oral use in two dosage strengths of 25 mg and 50 mg hydrochlorothiazide, USP.

## **Availability of Dosage Forms**

NTP-HYDROCHLOROTHIAZIDE (Hydrochlorothiazide Tablets, USP) Tablets are supplied as:

25 mg tablets: Small, light orange-colored, round, flat-faced, bevel-edged, and compressed tablets, with engraved bisect on one side and plain on the reverse.  
Supplied in bottles of 100 and 1000 tablets.

50 mg tablets: Light orange-colored, round, flat-faced, bevel-edged, and compressed tablets, engraved novo on one side, 50 on the reverse.  
Supplied in bottles of 100 and 1000 tablets.

## **Composition**

NTP-HYDROCHLOROTHIAZIDE (Hydrochlorothiazide Tablets, USP) 25 mg and 50 mg tablets contain 25 mg, 50 mg of Hydrochlorothiazide, respectively. Non medicinal ingredients (alphabetical): colloidal silicon dioxide, FD&C Yellow #6, lactose, magnesium stearate, microcrystalline cellulose and sodium starch glycolate.

## PART II: SCIENTIFIC INFORMATION

### PHARMACEUTICAL INFORMATION

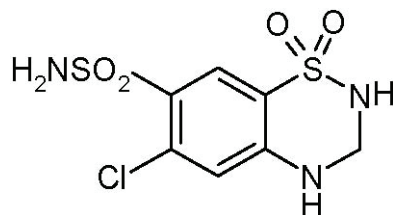
#### Drug Substance

Proper Name: Hydrochlorothiazide

Chemical Name: 6-chloro-3,4-dihydro-2H-1,2,4-benzothiadiazine-7-sulfonamide 1,1-dioxide

Molecular formula and molecular mass:  $C_7H_8ClN_3O_4S_2$ ; 297.72 g/mol

Structural formula:



Physicochemical properties: Hydrochlorothiazide is a white or almost white odourless, crystalline powder with a slightly bitter taste. It is almost insoluble in water, benzene, chloroform, ether and dilute mineral acids, and soluble 1 in 500 of alcohol and 1 in 50 of acetone. It is freely soluble in dimethyl formamide; n-butylamine and solutions of alkali hydroxides.

### DETAILED PHARMACOLOGY

Orally, hydrochlorothiazide is an effective diuretic and antihypertensive agent. Diuresis is affected by inhibition of tubular resorption of electrolytes and an accompanying volume of water. Hydrochlorothiazide increases the excretion of sodium and chloride in approximately equivalent amounts and causes a simultaneous, usually minimal loss of bicarbonate. The excretion of ammonia is reduced slightly as a consequence of which concentrations of ammonia in the blood may be increased. Hydrochlorothiazide slightly increases the excretion of potassium. Calcium excretion is decreased and magnesium excretion is increased.

## TOXICOLOGY

### Acute Toxicity

SPECIES	ROUTE	LD <sub>50</sub> (mg/kg)
MOUSE	ORAL	10,000*
MOUSE	I.V.	884
RAT	ORAL	10,000*
RAT	I.P.	3,130*
RABBIT	I.V.	461
DOG	I.V.	1,000

Dogs tolerated at least 2,000 mg/kg orally without signs of toxicity.

\*Hydrochlorothiazide was administered as a suspension.

### Subacute Toxicity:

#### Rat

Hydrochlorothiazide administered to rats, orally as a suspension at doses of 500, 1,000 and 2,000 mg/kg/day, 5 days/week, for 3 weeks did not produce any toxic symptoms. Three of the ten rats which received 2,000 mg/kg/day of sodium hydrochlorothiazide salt died after the 5<sup>th</sup> day of treatment.

The mortality was attributed to pneumonia.

#### Dog

Hydrochlorothiazide administered to dogs, orally at doses of 250, 500 and 1,000 mg/kg, 7 days/week for 8 weeks did not produce any observable adverse effects or gross signs of drug toxicity except for electrolytic imbalance.

### Chronic Toxicity

#### Rat and Dog

The results of 6-month chronic oral toxicity on hydrochlorothiazide in rats and dogs indicated no toxicity attributable to the drug administered to rats at doses of up to 2 grams/kg/day and to dogs at doses of up to 250 mg/kg/day. On gross examination the following changes were observed in the dog: slight depression of plasma potassium; small amounts of yellow crystalline precipitate in the bladder in two of twelve dogs tested. Histomorphologic studies did not show any drug related changes.

## REFERENCES

1. Applied Pharmacology. The Kidneys, Ch. 310. Classification of Diuretics, pp. 587-589. W.B. Saunders Company, Philadelphia; Toronto, 1976.
2. Physicians' Desk Reference (PDR), 1977, pp. 1090. HydroDiuril (hydrochlorothiazide, MSD) U.S.P.
3. FROHLICH, E.D. Hypertension pp. 208-213. Current Therapy, 1976. Conn, F. Editor. W.B. Saunders Company, Philadelphia, London, Toronto
4. MUDGE, G.H. Diuretics and other agents employed in the mobilization of edema fluid. The Pharmacological Basis of Therapeutics, Ch. 39, pp. 854-858. Goodman & Gilman, 4<sup>th</sup> Edition, 1970.
5. SACKNER, M.A.; WALLACK, A.A. BELLETS, S. The Diuretic Effects of hydrochlorothiazide in Congestive Heart Failure, Cirrhosis, Chronic Renal Disease & Hypertension: Preliminary Report based on a study of 28 cases. Am. J. M. Sc., 237; 575-584, May 1959.
6. ZATUCHNI; J.; KING, W.; RESINSKI, M. Hydrochlorothiazide, A new Saluretic. Am. J. M. Sc., 237; 479, April 1959.
7. FORD, R.V. Comparative Studies of The Newer Diuretics. Annals New York Academy of Sciences, 88, 809-814, 1960.
8. FUCKS, M; MOYER, J.H.; NEWMAN, B.E. Human Clinical Pharmacology of the Newer Diuretics: Benzothiadiazine & Phthalimidine. Annals New York Academy of Sciences, 88, 795-808, October 1960.
9. RENNICK, B. Animal Pharmacology of the New Diuretics: Benzothiadiazines, Spirolactones & Phthalimidines. Annals New York Academy of Sciences, 88, 785-794, October 1960.
10. GROLLMAN, A.; FURNESS, F. Present concept of the Mechanism of Urine Formation and of Diuretic Action. Annals of the New York Academy of Sciences, 88 (4): 771-1020, Oct. 1960.
11. BORHANI, N.O. Chlorothiazide & Hydrochlorothiazide: A Comparative Study of their hypotensive, Saluretic & Hyperuricemic action. Ann Int. Med., 53, 342, 1960.
12. WINER, B.N. The Antihypertensive Actions of Benzothiadiazines. Circulation 23: 211, Feb. 1961.
13. ROSENBLOOM, S.E.; SHAPER, R.P.; GOLDSBLOOM, S.; PINCUS, J.; SHAPIRO, A.P. II. Comparison of Chlorothiazide, Hydrochlorothiazide and a Placebo in the Hypertensive Patient. New England J. Med; 264, 164, Jan. 1961
14. KJELLBO, H.; STAKEBERG, H.; MELLGREN, J. Possibly Thiazide - Induced Renal Necrotising Vasculitis. Lancet; 1, 1034, May 1965.
15. CAFRUNY, E.J. How Diuretics work. Geriatrics; 22, 107, Jan. 1967.
16. BRYANT, J.M. SCHVARTZ, N.; ROQUE, M.; FLETCHER, L.; FERTIG, H.; LAULER, D.P. The Hypotensive Effects of Chlorothiazide and Hydrochlorothiazide. Am. J. Cardiol.; 7, 392, March 1961.
17. WOLF, R.L.; MENDLOWITZ, M.; ROBOZ, J.; GITLOW, S.E. Treatment of Hypertension with

Antihypertensive Diuretic Drugs. Am. Heart H.; 72, 692, Nov. 1966.

18. TANNENBAUM, P.J.; CROSLY, A.P. A Comparison of the Effects of Hydrochlorothiazide and Hydrochlorothiazide on Electrolyte Balance. Clin. Pharmacol. & Therap.: 7, 777, Nov.-Dec. 1966.

19. KOLODNY, A.L. Technic of Drug Evaluation in Hypertension.. New York J. Med., 62, 1585, May 1962.

20. SALERNO, L.J.; STONE, M.L. The Use of Diuretics in the Pregnant Patient. Annals of the New York, Academy of Sciences, 88, 881-889, Oct. 1960.

21. Product Monograph for pms-HYDROCHLOROTHIAZIDE, Biomed 2002 Inc., Montreal, Quesbec, Canada. Date of Revision: December 20, 2005.

22. Product Monograph for TEVA-HYDROCHLOROTHIAZIDE, Teva Canada Limited, Toronto, Ontario, Canada. Date of Revision: November 16, 2011.

## IMPORTANT: PLEASE READ

### PART III: CONSUMER INFORMATION

#### **NTP-HYDROCHLOROTHIAZIDE** Hydrochlorothiazide Tablets USP

This leaflet is part III of a three-part “Product Monograph” published when NTP-HYDROCHLOROTHIAZIDE was approved for sale in Canada and is designed specifically for Consumers. This leaflet is a summary and will not tell you everything about NTP-HYDROCHLOROTHIAZIDE. Contact your doctor or pharmacist if you have any questions about the drug.

#### **ABOUT THIS MEDICATION**

##### What the medication is used for:

NTP-HYDROCHLOROTHIAZIDE has been prescribed to you for edema (swelling) associated with heart failure, cirrhosis of the liver, corticosteroid and estrogen therapy and for edema originating from the kidneys; or hypertension; or toxemia (hypertension) due to pregnancy.

##### What it does:

NTP-HYDROCHLOROTHIAZIDE elevates the rate of urine secretion and lowers blood pressure. Hydrochlorothiazide affects the kidneys ability to reabsorb electrolytes. It increases excretion of sodium and chloride in approximately equivalent amounts and reduces the rate of formation of solute-free water.

##### When it should not be used:

You should not use NTP-HYDROCHLOROTHIAZIDE if you:

- are allergic to Hydrochlorothiazide or to other sulfonamide-derived drugs.
- are allergic to any of the other ingredients in the product (please see “What the nonmedicinal ingredients are”)
- have no production of urine.
- experience an increase of urea or creatinine and a decrease in urine production during treatment of severe progressive kidney disease.

Stop taking the drug and contact your doctor immediately if you experience an allergic reaction or any severe or unusual side effects.

What the medicinal ingredient is:  
Hydrochlorothiazide.

##### What the nonmedicinal ingredients are:

colloidal silicon dioxide, FD&C Yellow #6, lactose, magnesium stearate, microcrystalline cellulose and sodium starch glycolate.

##### What dosage forms it comes in:

**Tablets:** 25 mg & 50 mg

#### **WARNINGS AND PRECAUTIONS**

Before you use NTP-HYDROCHLOROTHIAZIDE talk to your doctor or pharmacists if:

- If you are taking enteric-coated potassium salts
- If you have impaired liver function or progressive liver disease
- If you have impaired kidney function
- If you are taking anti-hypertensive medication or other adrenergic blocking drugs.
- If you have a history of sensitivity reactions or a history of allergic reactions to this or other medications
- If you have lupus

Remember to keep this and other medications away from children.

Tell your physician or pharmacist all medication you are taking, including any non-prescription or herbal medicines.

##### Other precautions:

Do not take NTP-HYDROCHLOROTHIAZIDE if you are:

- pregnant or breast-feeding.
- are allergic to any of its ingredients.

#### **INTERACTIONS WITH THIS MEDICATION**

Drugs that may interact with NTP-HYDROCHLOROTHIAZIDE include:

- Lithium. Concomitant therapy with lithium is not recommended with NTP-HYDROCHLOROTHIAZIDE because of the reduction of kidney clearance of lithium and therefore an added risk of lithium toxicity.
- Orthostatic hypotension (low blood pressure while you are standing) may occur and may be enhanced by alcohol, barbiturates, or narcotics



**IMPORTANT: PLEASE READ**

You should always tell your physician about all drugs you are taking, including those obtained without a prescription.

**PROPER USE OF THIS MEDICATION**

Take this medicine exactly as prescribed by your physician.

**Adult patients**

**Diuresis**

The recommended adult dosage is 50 mg to 100 mg once or twice a day. Many patients respond to intermittent therapy, i.e. administration on alternate days or on three to five days each week.

**Toxemia of pregnancy**

The recommended dosage is 100 mg daily or, in severe cases and for brief periods, 200 mg daily (in divided doses). Frequency of administration may range from once every four days to daily.

**Premenstrual tension with swelling**

The recommended dosage is 25mg to 50 mg once or twice a day from the first appearance of symptoms until onset of the menses.

**Control of Hypertension**

The usual recommended starting dosage is 50 or 100 mg a day as a single or divided dose. Dosage is increased or decreased according to the blood pressure response of the patient. Some patients may require doses of 200 mg a day in divided doses.

**Infants and Children**

The usual recommended pediatric dosage is based on 1.0 mg of NTP-HYDROCHLOROTHIAZIDE per pound of body weight per day in two doses. Infants under 6 months of age may require up to 1.5 mg per pound per day in two doses.

On this basis, infants up to 2 years of age may be given 12.5 to 37.5 mg daily in two doses.

The 25 mg tablet can not be divided into quarters.

**Overdose:**

If you take too many doses, call your physician immediately.

**In case of drug overdose, contact a health care practitioner, hospital emergency department or regional Poison Control Centre immediately, even if there are no symptoms.**

**Missed Dose:**

If you miss a dose, and it is close to the next scheduled dose, take your medicine at the next scheduled time. Do NOT double dose.

**SIDE EFFECTS AND WHAT TO DO ABOUT THEM**

**Gastrointestinal system:** Decreased appetite, gastric irritation, nausea, vomiting, cramps, diarrhea, constipation, jaundice (intrahepatic cholestatic jaundice), inflammation of the pancreas, inflammation or enlargement of salivary glands.

**Central nervous system:** Dizziness, a feeling that you or your surroundings are moving, sensation of tingling or numbness, headache, impaired sense of sight.

**Hematologic:** Leukopenia, agranulocytosis, thrombocytopenia, aplastic anemia.

**Cardiovascular:** postural hypotension (may be aggravated by alcohol, barbiturates, or narcotics).

**Hypersensitivity:** spontaneous bleeding under the skin, sensitivity to light, rash, red patches on the skin, fever, respiratory distress including pneumonitis, anaphylactic reactions.

**Other:** Hyperglycemia, muscle spasm, weakness, restlessness, transient blurred vision.

**SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN, AND WHAT TO DO ABOUT THEM**

	Symptom/effect	Talk with your doctor or pharmacist		Stop taking drug and call your doctor or pharmacist
		If effect persists or becomes bothersome	In all cases	
Common	Allergic reactions (swelling, skin rash, itching)			√
	Chest Pain			√
	Stomach ulcer (burning pain in the gut, vomiting...)		√	
	Blood problems (loss of energy, low blood platelet count...)		√	
	Imbalance of minerals in the blood		√	

*This is not a complete list of side effects. If you have any unexpected effects while taking this drug, contact your doctor or pharmacist.*

## HOW TO STORE IT

- Store at controlled room temperature, 15°- 30°C.
- Keep out of the reach and sight of children.
- Do not use after the expiry date indicated on the package.
- Protect from heat and light.

## REPORTING SUSPECTED SIDE EFFECTS

You can report any suspected adverse reactions associated with the use of health products to the Canada Vigilance Program by one of the following 3 ways:

Report online at [www.healthcanada.gc.ca/medeffect](http://www.healthcanada.gc.ca/medeffect)

Call toll-free at 1-866-234-2345

Complete a Canada Vigilance Reporting Form and:

◦ Fax toll-free to 1-866-678-6789, or

◦ Mail to:

Canada Vigilance Program

Health Canada

Postal Locator 0701E

Ottawa, Ontario

K1A 0K9

Postage paid labels, Canada Vigilance Reporting Form and the adverse reaction reporting guidelines are available on the MedEffect™ Canada Web site at [www.healthcanada.gc.ca/medeffect](http://www.healthcanada.gc.ca/medeffect).

NOTE: Should you require information related to the management of side effects, contact your health professional. The Canada Vigilance Program does not provide medical advice.

## MORE INFORMATION

This document plus the full product monograph, prepared for health professionals can be obtained by contacting,

NT Pharma Canada Limited at:

1-800-268-4127 ext 5005 (English)

1-877-777-9117 (French)

or [druginfo@tevacanada.com](mailto:druginfo@tevacanada.com)

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