PRODUCT MONOGRAPH

PrMYLAN-INDAPAMIDE

Indapamide Tablets

USP

1.25 mg and 2.5 mg

Diuretic/Antihypertensive Agent

MYLAN PHARMACEUTICALS ULC
85 Advance Road
Etobicoke, Ontario
Canada M8Z 2S6

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Control No.: 283896

PRODUCT MONOGRAPH

PrMYLAN-INDAPAMIDE

(Indapamide Tablets, USP)

1.25 mg and 2.5 mg

THERAPEUTIC CLASSIFICATION

Diuretic/Antihypertensive agent

ACTION AND CLINICAL PHARMACOLOGY

MYLAN-INDAPAMIDE (indapamide) is a diuretic anti-hypertensive agent. The mechanism whereby indapamide exerts its action in the control of hypertension is not completely elucidated: both renal and extrarenal actions may be involved. The renal site of action is the proximal part of the distal tubule and the ascending part of Henle's loop. Sodium and chloride ions are excreted in approximately equivalent amounts. The increased delivery of sodium to the distal tubular exchange site results in increased potassium excretion and hypokalaemia.

Indapamide is rapidly and completely absorbed after oral administration. Peak blood levels are obtained after 1 to 2 hours. Indapamide is concentrated in the erythrocytes and is 79% bound to plasma proteins and to erythrocytes.

It is taken up by the vascular wall in smooth vascular muscle according to its high lipid solubility. Seventy per cent of a single oral dose is eliminated by the kidneys and 23 per cent by the gastrointestinal tract. Indapamide is metabolized to a marked degree, the unchanged product representing approximately 5 per cent of the total dose found in the urine during 48 hours following administration. Elimination of indapamide from the plasma is biphasic with half-lives of 14 and 25 hours respectively.

Clinical Pharmacology:

Comparative Bioavailability Studies
A comparative two-way, single-dose bioavailability study was performed on MYLAN-INDAPAMIDE 2.5 mg Tablets and a marketed brand of indapamide 2.5 mg tablets. The pharmacokinetic data (geometric means, C.V.) for both formulations is tabulated below:

MYLAN-INDAPAMIDE TABLETS
(1 x 2.5 mg)
From Measured Data

Geometric Mean
Arithmetic Mean (CV%)

Parameter	Mylan-Indapamide 2.5 mg Tablet (Mylan Pharmaceuticals ULC)	*Lozide® 2.5 mg Tablets	Ratio of Geometric Means (%)	(90% CI)***
AUC_{0-t} (ng hr/mL)	3592.2 (34)	3361.3 (33)	107	102.1 – 111.7
AUC_{inf} (ng hr/mL)	4085.9 (33)	3760.4 (30)	109	103.3 – 113.6
C_{max} (ng/mL)	217.1 (28)	212.0 (23)	103	96.2 – 108.6
** T_{max} (h)	2.1 (43)	2.1 (42)		
** $T_{½}$ (h)	12.9	12.4		

*Lozide® is manufactured by Servier Canada Inc. and purchased in Canada.
**For T_{max} and $T_{1/2}$, arithmetic means (CV%) are presented.
***90% Confidence Intervals for the ratio of geometric means

INDICATIONS AND CLINICAL USE

MYLAN-INDAPAMIDE (indapamide) is indicated in the management of essential hypertension. It may be tried as a sole therapeutic agent in the treatment of mild to moderate hypertension. Normally indapamide, as other diuretics, is used as the initial agent in multiple drug regimens.

CONTRAINDICATIONS

Hypersensitivity to indapamide, to other sulfonamides or to any of the excipients,
Severe renal failure (creatinine clearance below 30 ml/min),
Hepatic encephalopathy or severe impairment of liver function,
Hypokalaemia,
Combinations with anti-arrhythmic agents causing torsade de pointes,
Pregnancy,

Lactation,
Hereditary problems of galactose intolerance, glucose-galactose malabsorption, or total lactase deficiency as MYLAN-INDAPAMIDE contains lactose.

WARNINGS

Electrolyte changes observed with MYLAN-INDAPAMIDE (indapamide) may be severe. The recommended maximum daily dose of 2.5 mg/day should not be exceeded.

Hypokalaemia may occur at all doses with consequent weakness, cramps and cardiac dysrhythmias. Hypokalaemia is a particular hazard in digitalized patients; dangerous or fatal cardiac arrhythmias may be precipitated.

Hypokalaemia occurs commonly with diuretics; electrolyte monitoring is essential particularly in patients who would be at increased risk from hypokalaemia, such as patients with cardiac arrhythmias or those who are receiving concomitant cardiac glycosides.

Patients with renal insufficiency receiving MYLAN-INDAPAMIDE (indapamide) should be carefully monitored. If an increase of azotemia and oliguria occur during treatment, the diuretic should be discontinued.

Hyperuricemia may occur during administration of MYLAN-INDAPAMIDE (indapamide). Rarely gout has been reported. Blood uric acid levels should be monitored, particularly in patients with a history of gout who should continue to receive appropriate treatment.

When liver function is impaired, thiazide-related diuretics may cause, particularly in case of electrolyte imbalance, hepatic encephalopathy which can progress to hepatic coma. Administration of the diuretic should be stopped immediately if this occurs.

Cases of photosensitivity reactions have been reported with thiazides and thiazide-related diuretics (see **Adverse Reactions**). If photosensitivity reaction occurs during treatment, it is recommended to stop the treatment. If a re-administration of the diuretic is deemed necessary, it is recommended to protect exposed areas to the sun or to artificial UVA.

PRECAUTIONS

Patients receiving indapamide should be carefully observed and serum electrolytes monitored for signs and symptoms of fluid or electrolyte imbalance; namely hyponatremia, hypochloremia and hypokalaemia. Blood urea nitrogen, uric acid, and glucose levels should also be assessed during therapy. Hypokalaemia, an ever present hazard with most diuretics, will be more common in association with concomitant steroid or ACTH therapy and with inadequate electrolyte intake. The serum potassium should be determined at regular intervals and potassium supplementation instituted when indicated. (See **Warnings**).

The signs of electrolyte imbalance are: dryness of the mouth, thirst, weakness, lethargy, drowsiness, restlessness, muscle pains or cramps, muscle fatigue, hypotension, oliguria, gastrointestinal disturbances such as nausea and vomiting, tachycardia and ECG changes.

Potassium depletion with hypokalaemia is the major risk of thiazide and related diuretics. Hypokalaemia may cause muscle disorders. Cases of Rhabdomyolysis have been reported, mainly in the context of severe hypokalaemia. The risk of onset of hypokalaemia (< 3.4 mmol/l) must be prevented in certain high risk populations, i.e. the elderly, malnourished and/or polymedicated, cirrhotic patients with oedema and ascites, coronary artery disease and cardiac failure patients. In this situation, hypokalaemia increases the cardiac toxicity of digitalis preparations and the risks of arrhythmias.

Individuals with a long QT interval are also at risk, whether the origin is congenital or iatrogenic. Hypokalaemia and bradycardia are both predisposing factors to the onset of severe arrhythmias, in particular, potentially fatal *torsades de pointes* among those individuals with long QT interval.

More frequent monitoring of plasma potassium is required in all the situations indicated above. The first measurement of plasma potassium should be obtained during the first week following the start of treatment. Detection of hypokalaemia requires its correction.

Plasma sodium must be measured before starting treatment, then at regular intervals subsequently. Any diuretic treatment may cause hyponatraemia, sometimes with very serious consequences. The fall in plasma sodium may be asymptomatic initially and regular monitoring is therefore essential, and should be even more frequent in the elderly and cirrhotic patients.

Calcium excretion is decreased by diuretics pharmacologically related to indapamide. However, after six to eight weeks of indapamide 1.25 mg treatment and in long-term studies of hypertensive patients with higher doses of indapamide, serum concentrations of calcium increased only slightly with indapamide.

Prolonged treatment with drugs pharmacologically related to indapamide may in rare instances be associated with hypercalcemia and hypophosphatemia secondary to physiologic changes in the parathyroid gland; however, the common complications of hyperparathyroidism, such as renal lithiasis, bone resorption, and peptic ulcer, have not been seen. Frank hypercalcaemia may be due to previously unrecognised hyperparathyroidism.

Treatment should be discontinued before tests for parathyroid function are performed. Like the thiazides, indapamide may decrease serum PBI levels without signs of thyroid disturbance.

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

Thiazide and related diuretics are fully effective only when renal function is normal or only minimally impaired (plasma creatinine below levels of the order of 25 mg/l, *i.e.* 220 µmol/l in an adult) but are ineffective when the creatinine clearance is less than 30 mL/min.

In the elderly, this plasma creatinine must be adjusted in relation to age, weight and gender.

Hypovolaemia, secondary to the loss of water and sodium induced by the diuretic at the start of treatment causes a reduction in glomerular filtration. This may lead to an increase in blood urea and plasma creatinine. This transitory functional renal insufficiency is of no consequence in individuals with normal renal function but may worsen preexisting renal insufficiency.

MYLAN-INDAPAMIDE (indapamide) is contraindicated in patients with severe hepatic impairment since diuretics may induce metabolic alkalosis in cases of potassium depletion which may precipitate episodes of hepatic encephalopathy. (See **Contraindications**)

Orthostatic hypotension may occur and may be potentiated by alcohol, barbiturates, narcotics or concurrent therapy with other antihypertensives.

When MYLAN-INDAPAMIDE (indapamide) is given with other non-diuretic antihypertensive agents, the effects on blood pressure are additive.

Sulfonamide derivatives have been reported to exacerbate or activate systemic lupus erythematosus. These possibilities should be kept in mind with the use of indapamide although no case has been reported to date.

Severe dermatological adverse reactions, some accompanied by systemic manifestations, have been rarely reported with the use of indapamide. In the majority of cases, the condition subsided within 14 days following discontinuation of indapamide therapy (See **Adverse Reactions**).

Although indapamide exerts minimal effect on glucose metabolism, insulin requirements may be affected in diabetics. Monitoring of blood glucose is important in diabetics, in particular in the presence of hypokalaemia. Hyperglycemia and glycosuria may occur in patients with latent diabetes.

Athletes should note that this product contains an active substance which may cause a positive reaction in doping tests.

Choroidal effusion, acute myopia and secondary angle-closure glaucoma
Sulfonamide or sulfonamide derivative drugs can cause an idiosyncratic reaction resulting in choroidal effusion with visual field defect, transient myopia and acute angle-closure glaucoma. Symptoms include acute onset of decreased visual acuity or ocular pain and typically occur within hours to weeks of drug initiation. Untreated acute angle-closure glaucoma can lead to permanent vision loss. The primary treatment is to discontinue drug intake as rapidly as possible. Prompt medical or surgical treatments may need to be considered if the intraocular pressure remains uncontrolled. Risk factors for developing acute angle-closure glaucoma may include a history of sulfonamide or penicillin allergy.

Use in Pregnancy
As a general rule, the administration of diuretics **should not be used by pregnant women nor used** to treat physiological oedema of pregnancy. Diuretics can cause foetoplacental ischaemia, with a risk of impaired foetal growth (See **Contraindications**).

Use in Nursing Mothers
Breast-feeding is inadvisable (Indapamide is excreted in human milk). (See **Contraindications**)

Use in Children
The safety and effectiveness of indapamide in children have not been established. Its use in this age group, therefore, is not recommended.

Use in Elderly
In the elderly, the plasma creatinine must be adjusted in relation to age, weight and gender. Elderly patients can be treated with indapamide 1.25 mg when renal function is normal or only minimally impaired.

Indapamide does not affect vigilance but different reactions in relation with the decrease in blood pressure may occur in individual cases, especially at the start of the treatment or when another antihypertensive agent is added. As a result the ability to drive vehicles or to operate machinery may be impaired.

Interactions with other medicinal products and other forms of interactions

Combinations that are not recommended:

Lithium:
Increased plasma lithium with signs of overdosage, as with a salt-free diet (decreased urinary lithium excretion). However, if the use of diuretics is necessary, careful monitoring of plasma lithium and dose adjustment are required.

Combinations requiring precautions for use:

Torsades de pointes-inducing drugs such as but not limited to:
- class Ia antiarrhythmic agents(e.g. quinidine, hydroquinidine, disopyramide) and class Ic (e.g. flecainide),
- class III antiarrhythmic agents (e.g. amiodarone, sotalol, dofetilide, ibutilide),
- some antipsychotics:
    phenothiazines (e.g. chlorpromazine, levomepromazine, trifluoperazine),
benzamides (e.g. amisulpride)
butyrophenones (e.g. haloperidol)
other antipsychotics (e.g. pimozide),
- psychoanaleptic (e.g. donepezil),
- SSRIs (e.g. citalopram, escitalopram),

- antimicrobial agents: fluoroquinolones (e.g. moxifloxacin, ciprofloxacin), macrolides (e.g. erythromycin IV, clarithromycin), azole antifungals (e.g. fluconazole),
- antiparasitics (e.g. chloroquine, pentamidine)
- antihistamines
- antiemetics (e.g. ondansetron, domperidone),
- antineoplastic and immunomodulating agents (e.g. vandetanib, oxaliplatin, anagrelide),
- anaesthetics (e.g. propofol, sevoflurane)
- other substances such as: bepridil, methadone, papaverine.

Increased risk of ventricular arrhythmias, particularly *torsades de pointes* (hypokalaemia is a risk factor). Monitor for hypokalaemia and correct, if required, before introducing this combination. Clinical, plasma electrolytes and ECG monitoring.

Use substances which do not have the disadvantage of causing torsades de pointes in the presence of hypokalaemia.

N.S.A.I.Ds. (systemic route) including COX-2 selective inhibitors, high dose salicylic acid (≥ 3 g/day):
Possible reduction in the antihypertensive effect of indapamide.
Risk of acute renal failure in dehydrated patients (decreased glomerular filtration).
Hydrate the patient; monitor renal function at the start of treatment.

Antihypertensive medications (e.g. Angiotensin converting enzyme (A.C.E.) inhibitors):
Risk of sudden hypotension and/or acute renal failure when treatment with an A.C.E. inhibitor is initiated in the presence of preexisting sodium depletion (particularly in patients with renal artery stenosis).

In hypertension, when prior diuretic treatment may have caused sodium depletion, it is necessary:
- either to stop the diuretic 3 days before starting treatment with the A.C.E. inhibitor, and restart a hypokalaemic diuretic if necessary;
- or give low initial doses of the A.C.E. inhibitor and increase the dose gradually.

In congestive heart failure, start with a very low dose of A.C.E. inhibitor, possibly after a reduction in the dose of the concomitant hypokalaemic diuretic.

In all cases, monitor renal function (plasma creatinine) during the first weeks of treatment with an A.C.E. inhibitor.

Other compounds causing hypokalaemia (e.g. amphotericin B (IV), corticosteroids (e.g. gluco and mineralo corticoids), ACTH (e.g. tetracosactide) and stimulant laxatives:
Increased risk of hypokalaemia (additive effect).
Monitoring of plasma potassium and correction if required. Use non-stimulant laxatives.

Skeletal muscle relaxants (e.g. Baclofen):
Increased antihypertensive effect.
Hydrate the patient; monitor renal function at the start of treatment.

Digitalis preparations (e.g. Digoxin):
Hypokalaemia predisposing to the toxic effects of digitalis.
Monitoring of plasma potassium and ECG and, if necessary, adjust the treatment.

Citalopram:
Increased risk of hyponatraemia.

Allopurinol:
Concomitant treatment with indapamide may increase the incidence of hypersensitivity reactions to allopurinol.

Combinations to be taken into consideration:

Potassium-sparing diuretics (amiloride, spironolactone, triamterene):
Whilst rational combinations are useful in some patients, hypokalaemia or hyperkalaemia (particularly in patients with renal failure or diabetes) may still occur. Plasma potassium and ECG should be monitored and, if necessary, treatment reviewed.

Antihyperglycemic medications (e.g. Metformin):
Increased risk of metformin induced lactic acidosis due to the possibility of functional renal failure associated with diuretics and more particularly with loop diuretics. Do not use metformin when plasma creatinine exceeds 15 mg/l (135 μmol/l) in men and 12 mg/l (110 μmol/l) in women.

Iodinated contrast media:
In the presence of dehydration caused by diuretics, increased risk of acute renal failure, in particular when large doses of iodinated contrast media are used.
Rehydration before administration of the iodinated compound.

Anticholinergic and adrenergic antagonists (e.g. Imipramine-like antidepressants, neuroleptics in particular pimozide):
Antihypertensive effect and risk of orthostatic hypotension increased (additive effect).

Calcium (salts):
Risk of hypercalcaemia resulting from decreased urinary elimination of calcium.

Ciclosporin, tacrolimus:
Risk of increased plasma creatinine without any change in circulating cyclosporine levels, even in the absence of water/sodium depletion.

Corticosteroids:
Decreased antihypertensive effect (water/sodium retention due to corticosteroids).

ADVERSE REACTIONS

The safety data presented under this section involves two different databases and was obtained at two different time periods. For the earliest database (indapamide 2.5 mg), consisting mainly of European studies performed before 1980, adverse events were collected with respect to a possible causal relationship to treatment, whereas for the most recent database (indapamide 1.25 mg), consisting exclusively of North-American studies, adverse events were collected irrespective of such a causal relationship. This explains why the overall incidence of adverse events at the 2.5 mg dose appears to be lower than at the 1.25 mg dose (see below).

Most adverse events for both dosages, 1.25 mg and 2.5 mg, have been mild or moderate.

The adverse reactions represent data from clinical studies involving a total of 992 patients given indapamide 2.5 mg: 349 patients from 4 placebo controlled studies treated for 8 to 12 weeks; 356 patients from 6 active controlled studies treated for 6 up to more than 52 weeks; 287 patients from 4 uncontrolled studies treated for 6 up to 40 weeks.

The overall rate of adverse events, with respect to a possible causal relationship to the drug, was 29% and discontinuation of therapy due to adverse events was required in 5.6% of patients.

The most severe and common adverse event is the electrolyte imbalance. Electrolyte changes reported include hypokalaemia (14.2%; requiring potassium supplementation 6%; with clinical symptoms 1.2%), hypochloremia (9.4%) and hyponatremia (3.1%) (See **Precautions**).

The other changes observed in laboratory parameters are minor and infrequent: elevation in blood uric acid (8.6%), blood glucose (6.0%), BUN (5.7%) and blood creatinine (3.6%).

The most frequent adverse events (incidence ≥ 1%) reported for patients treated with indapamide 2.5 mg were: headache (3.4%), vertigo (2.2%), dizziness (1.9%), asthenia (1.7%) and muscle cramps (1.2%).

All other adverse events occurred at an incidence of less than 1% and included by body system:

Central Nervous: drowsiness, sleepiness, insomnia, weakness, lethargy and visual disturbance.

Gastrointestinal: nausea, anorexia, dryness of mouth, gastralgia, vomiting, diarrhoea and constipation.

Musculoskeletal: joint pain, back pain and weakness of legs.

Cardiovascular: orthostatic hypotension, tachycardia and ECG changes (non specific ST-T change, U waves, left ventricular strain).

Urogenital: impotence, modification of libido and polyuria.

Dermatological: rash and pruritus.

Endocrine**:** gout.

Other: tinnitus, malaise, fainting and sweat.

In placebo-controlled studies involving 306 patients given indapamide 1.25 mg and 319 given placebo for up to eight weeks, the overall incidence of adverse events, irrespective of causal relationship, was about 50% in both indapamide and placebo groups. In the indapamide 1.25 mg group, 4.2% of patients discontinued treatment because of adverse events.

In these studies 20% of patients treated with indapamide 1.25 mg had at least one potassium value below 3.4 mEq/L.

The most frequently reported adverse events (incidence ≥ 1%) in the indapamide 1.25 mg group were: headache (17%), infection (12%), pain (8%), dizziness (7%), back pain (5%), rhinitis (5%), asthenia (4%), dyspepsia (4%), flu syndrome (3%), hypertonia (3%), sinusitis (3%), chest pain (2%), constipation (2%), cough (2%), diarrhoea (2%), edema (2%), nausea (2%), pharyngitis (2%), conjunctivitis (1%), nervousness (1%) and ECG abnormalities (non-specific ST-T changes (7%), sinus bradycardia (3%), arrhythmia (2%) or tachycardia (2%)).

All other clinical adverse events occurred at an incidence of less than 1%. These are the following:

Central Nervous: agitation, amnesia, anxiety, ataxia, coordination abnormality, depression, dream abnormality, hyperesthesia, insomnia, migraine, paresthesia, somnolence, twitching and vertigo.

Gastrointestinal: increased appetite, dry mouth, GI carcinoma, GI disorders, duodenitis, dysphagia, esophagitis, flatulence, gastritis, gastroenteritis, oral moniliasis, proctitis, rectal disorders, rectal hemorroïds, stomatitis, tooth disorders and vomiting.

Musculoskeletal: arthralgia, arthritis, bone disorders, joint disorders, bone fracture, bone pain, chondrodystrophy, myalgia, myasthenia and myopathy.

Cardiovascular: angina pectoris, bundle branch block, ventricular extrasystoles, atrial fibrillation, atrial flutter, hypertension, postural hypotension, palpitations, syncope, supraventricular tachycardia and vasodilation.

Urogenital: dysmenorrhea, dysuria, impotence, urinary tract infection, nocturia, oliguria, urinary frequency or urgency, renal pain or calculus, prostate disorders and vaginitis.

Respiratory: bronchitis, dyspnea, laryngitis, lung disorder and sputum increase.

Dermatological: acne, application site reaction, exfoliative dermatitis, nail disorder, skin nodule, rash, bullous eruption and sweat.

Metabolic and nutritional: diabetes mellitus and gout.

Special senses: amblyopia, ear disorders, ear pain, otitis, photophobia, taste perversion, tinnitus and vision abnormality.

Other: thyroid disorder, ecchymosis, allergic reaction, edema face, fever, hernia, malaise and monilia.

Postmarketing experience:
The most commonly reported adverse reactions are hypersensitivity reactions, mainly dermatological, in subjects with a predisposition to allergic and asthmatic reactions and maculopapular rashes.
Spontaneously reported adverse reactions, presented below, were reported voluntarily, and thus it is not always possible to reliably establish their frequency. Causal relationships of drug exposure to the adverse reactions are suspected, but have not been definitely established in all cases.

Nervous system disorders: fatigue

Cardiac disorders: electrocardiogram QT prolonged, torsade de pointes (potentially fatal)

Hepato-biliary disorders: hepatitis

Investigations: elevated liver enzyme levels

Metabolism and nutrition disorders:
Hypercalcaemia.
Hyponatraemia with hypovolaemia responsible for dehydration and orthostatic hypotension.
Concomitant loss of chloride ions may lead to secondary compensatory metabolic alkalosis: the incidence and degree of this effect are slight.

Musculoskeletal and connective tissue disorders: myalgia, muscle spasms, muscular weakness

Eye disorders: blurred vision, visual impairment

Among the less common suspected adverse reactions reported in post-marketing experience, the following have been published in the medical literature and/or are classified as serious or potentially serious:

Blood and the lymphatic system disorders: agranulocytosis, aplastic and haemolytic anemia, leucopenia, thrombocytopenia

Cardiac disorders: ventricular arrhythmia

Eye disorders: acute myopia, cataract, optic neuritis, acute angle-closure glaucoma, choroidal effusion

Gastrointestinal disorders: pancreatitis

Hepato-biliary disorders: abnormal hepatic function, possibility of onset of hepatic encephalopathy in case of hepatic insufficiency

Metabolism and nutrition disorders: hyperosmolar coma

Musculoskeletal and connective tissue disorders: rhabdomyolysis

Nervous system disorders: stroke

Renal and urinary disorders: acute hypersensitivity reaction leading to interstitial nephritis and renal failure

Skin and subcutaneous tissue disorders: angioedema, epidermal necrolysis, erythema multiforme, erythroderma, photosensitivity with bullae, possible worsening of pre-existing acute disseminated lupus Erythematosus, purpura, Stevens-Johnson syndrome, urticaria

Vascular disorders: vasculitis

One case of synergetic effect of clofibrate with indapamide leading to hyponatremia, hypokalaemia, hypoosmolarity, nausea and progressive loss of consciousness.

Relationship with the administration of indapamide has not been proved in all cases.

SYMPTOMS AND TREATMENT OF OVERDOSAGE

Symptoms
There have been no reports of overdosage. Based on the pharmacological activities of MYLAN-INDAPAMIDE (indapamide), overdosage may lead to excessive diuresis with electrolyte depletion. In cirrhotic patients, overdosage might precipitate hepatic coma.

Treatment
There is no specific antidote. Treatment is symptomatic and supportive. Discontinue drug. Induce emesis or perform gastric lavage. Correct dehydration, electrolyte imbalance, hepatic coma and hypotension by established procedures.

If you think you, or a person you are caring for, have taken too much MYLAN-INDAPAMIDE, contact a healthcare professional, hospital emergency department, or regional poison control centre immediately, even if there are no symptoms.

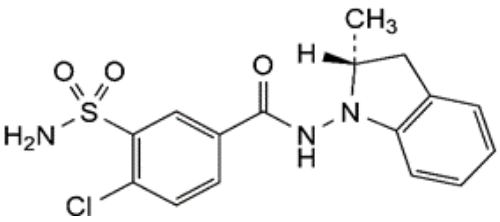
DOSAGE AND ADMINISTRATION

One 1.25 mg tablet per day taken in the morning as a single dose. If the response is not satisfactory after 4 to 8 weeks, the dose may be increased to a maximum of 2.5 mg as a single dose taken in the morning. If the antihypertensive response to MYLAN-INDAPAMIDE (indapamide) is insufficient, an increase in dosage is not recommended (see **Warnings**).

Instead, a non-diuretic antihypertensive agent should be added to the drug regimen. Alternatively if in the opinion of the physician, an important diuretic effect is desirable for the patient's control, a different diuretic which allows for dose titration could be tried instead of indapamide.

PHARMACEUTICAL INFORMATION

Drug Substance
Proper Name: Indapamide



and enantiomer

Molecular Formula
$C_{16}H_{16}ClN_3O_3S$

Molecular Weight
365.83 g/mol

Chemical Name
4-Chloro-*N*-[(2*RS*)-2-methyl-2,3-dihydro-1*H*-indol-1-yl]-3-sulfamoylbenzamide.

Description
White or almost white powder, practically insoluble in water, soluble in ethanol (96 per cent).

Composition
Each MYLAN-INDAPAMIDE 1.25 mg tablet contains indapamide 1.25 mg, and non-medicinal ingredients: lactose, microcrystalline cellulose, povidone, starch, talc, sodium starch glycollate, magnesium stearate, hydroxypropyl methylcellulose, polydextrose, polyethylene glycol, titanium dioxide, triacetin, FD&C yellow #6 Aluminum Lake, and D&C yellow #10 Aluminum Lake.

Each MYLAN-INDAPAMIDE 2.5 mg tablet contains indapamide 2.5 mg, and non-medicinal ingredients: lactose, microcrystalline cellulose, povidone, starch, talc, sodium starch glycollate, magnesium stearate, hydroxypropyl methylcellulose, polydextrose, polyethylene glycol, titanium dioxide, triacetin, FD&C red #40 Aluminum Lake, and FD&C blue #2 Aluminum Lake.

Stability and Storage Recommendations
Store at room temperature (15-30°C).

AVAILABILITY OF DOSAGE FORMS

MYLAN-INDAPAMIDE (indapamide) Tablets 1.25 mg are available in blister packs containing 30 tablets and bottles of 100 tablets. Each 6.5 mm, biconvex, orange, round, film-coated tablet marked "IE 1.25" on one side and "G" on the other contains: 1.25 mg indapamide.

MYLAN-INDAPAMIDE (indapamide) Tablets 2.5 mg are available in blister packs containing 30 and 100 tablets and bottles of 100 and 500 tablets. Each 6.5 mm biconvex, pink, round, film-coated tablet marked "IE 2.5" on one side and "G" on the other contains: 2.5 mg indapamide. MYLAN-INDAPAMIDE is tartrazine free.

PHARMACOLOGY

Indapamide is a non-thiazide sulfonamide derivative with an indole ring, possessing antihypertensive and diuretic properties.

Antihypertensive Action

In normal rats, cats and dogs, intravenous administration of 30 μg to 30 mg/kg failed to change blood pressure or heart rate. No change in cardiac output, heart rate, peripheral or pulmonary resistance was seen. In rats, oral doses of up to 100 mg/kg did not change blood pressure over a 96-hour measurement period.

In hypertensive animals, single doses of 1 to 10 mg/kg, p.o., of indapamide elicited antihypertensive activity as follows:

- in desoxycorticosterone acetate (DOCA)/saline, hypertensive rats with unilateral nephrectomy, a single dose of 10 mg/kg indapamide produced a maximal fall in systolic blood pressure of 25 mmHg after 24 hours and the antihypertensive action lasted for 72 hours.
- similar results were observed in DOCA/saline rats without nephrectomy.
- higher doses up to 100 mg/kg produced only small increases in activity but the blood pressure reduction continued for longer than 1 day.

Following repeated oral administration of indapamide (1 mg/kg) or trichlormethiazide (3 mg/kg) to DOCA/saline nephrectomized rats for 14 days, mean systolic blood pressure fell more with indapamide (33 mmHg) than with trichlormethiazide (23 mmHg). One week after indapamide treatment, the blood pressure had only partially returned towards pre-treatment value.

In the renal hypertensive dog, indapamide 5 mg/kg p.o., produces a maximal reduction (37 mmHg) in systolic blood pressure after 48 hours and an antihypertensive effect was still evident after 4 days.

Repeated administration of 0.5 mg/kg/day p.o. for 11 weeks prevented the onset of hypertension of DOCA/ saline hypertensive rats with unilateral nephrectomy, the effect was still apparent 5 weeks after interrupting treatment.

Hypertensive response induced by norepinephrine, tyramine or sympathetic stimulation were markedly reduced by indapamide (10 mg/kg p.o.) in amyelinated or DOCA/saline hypertensive rats.

Indapamide (10^{-5} and 10^{-4}M) diminished vascular hyper-reactivity to epinephrine, norepinephrine and angiotensin in isolated organ preparations. Indapamide (10^{-6} g/mL) inhibited vascular smooth muscle cell contractility.

In renal hypertensive dogs, blood pressure was reduced at a dose of 1 mg/kg i.v. and cardiac output showed an increase after 2 hours and a slight decrease over 24 hours.

Action on the Kidney

Diuretic activity has been studied in rats and dogs. The parameters were modified differently depending on the dose: the natriuretic and chloruretic activity was observed after doses of 0.1 to 0.3 mg/kg p.o. or i.v., while increased urinary output was seen at 1 mg/kg p.o. or i.v.; and significant increases in urinary potassium excretion were reported after doses of 3 to 10 mg/kg p.o.

Indapamide did not alter glomerular filtration rate or renal haemodynamics in dogs, suggesting that it acts directly on renal tubules. Studies of positive and negative free water clearance suggested that diuresis may have resulted from inhibition of water, sodium and chloride reabsorption in the proximal portion of the distal tubule of the nephron.

TOXICOLOGY

Acute Toxicology (LD_{50})

Route	Animals	No. Animals	LD50 (mg/kg) 48 hours	LD50 (mg/kg) 10 days
PO	mice	10M 10F	))	
	rats	10M 10F	)>3000 (48 hr and 10d.))	
	guinea pigs	4M 4F	))	
IV	mice	10M 10F	577 (538-618) 635 (589-684)	idem 48 hr 611 (575-648)
	rats	10M 10F	440 (412-470) 394 (368-421)	433 (404-463) idem 48 hr
	guinea pigs	4M 4F	358 (312-409) 315 (249-397)	272 (176-421) 285 (239-341)

Signs of Toxicity

Piloerection, bradypnea, hypotonia, diminished motor activity, hypersensitivity, mydriasis, and vasodilation at parenteral doses greater than 400 mg/kg.

Indapamide administered with hydralazine, methyldopa or propranolol did not modify the oral LD50 of the other antihypertensive agents.

Subacute Toxicity

4-Week Oral Toxicity Study in Rats (SPF/CFY Strain)

Rats (5 M, 5 F/group) received indapamide once daily, 7 days a week for 4 weeks at 50, 100 and 200 mg/kg, the findings were: dose-related increase in food consumption by females at 100 and 200 mg/kg; reduced body weight gain in males on high dose during the first two weeks and slight reduction in females at 200 mg/kg; increased number and prominence of foci of dystrophic mineralization at cortico-medullary function in 5/5 F at 200 mg/kg, considered to be due to increased urinary output.

Chronic Toxicity

6-Month Oral Toxicity Study in Beagle Dogs

Dogs (3 M, 3 F/ group) were treated with 0, 2, 20, 200 mg/kg doses, once daily, 7 days a week for 6 months. The drug-related findings were: food intake significantly reduced in males at 20 and 200 mg/kg and in females at 200 mg/kg; weight gain significantly reduced in males at 200 mg/kg dose.

At 200 mg/kg, hypothermia, increased susceptibility to injuries and infections, and increased urinary output were observed.

High neutrophil and low lymphocyte count in all drug-treated females at week 13, persisting in the 200 mg/kg group. High reticulocyte count was also noted.

Elevation of cholesterol and blood glucose, reduction of Na, K, Cl and Mg at week 13 in high dose group with persistence of the glucose abnormalities.

Significantly increased weight of liver and kidneys at 200 mg/kg and of adrenals at 20 and 200 mg/kg were seen. Sinusoidal congestion with central zone degeneration in the liver of one male of the 200 mg/kg group was noted. Slight congestion of adrenals in 3 dosed animals.

52-Week Oral Toxicity Study in Rats (SD/CR Strain)

Groups of 40 males and 40 females received indapamide at doses of 0, 1, 10 or 100 mg/kg once daily, 7 days a week for 52 weeks. The findings were:

Growth rates of treated males declined significantly during the first 6 weeks but terminal weights were comparable with controls.

Significant increases of plasma urea levels (still within the normal range) and of serum uric acid levels in males receiving the highest dose.

In females at high dose, significant weight increase of liver, kidneys and uterus and slight increase of adrenals were noted. Dose-related dystrophic mineralization at the cortico-medullary

junction of kidneys of all drug-treated groups, particularly in females. Six females (2 at each dose) showing these changes died before the termination of the study. Calculi in the bladder of 3 females and bladder papilloma in one at 100 mg/kg dose.

56-Week Oral Toxicity Study in Beagle Dogs

Groups of 4 males and 4 females treated once daily, 7 days a week with 0, 1, 10 and 100 mg/kg of indapamide (the highest dose was reduced to 50 mg/kg on day 86). The findings were:

Excessive diuresis in all dosed animals. Reduction of body weight gain marked at 100 mg/kg; slight at 10 mg/kg. Reduction of food consumption in high dose group. ECG changes (alteration of ventricular repolarization) in 4 animals of the high dose group, 3 at week 11 and 1 at week 26. One of the 2 surviving females in the high dose group had a serum potassium of 2.6 mmol/L.

Hemoconcentration during the first half period of treatment. Abnormally low serum K levels after week 6 at middle and high doses and after week 17 in some low dose animals. High serum cholesterol levels at week 26 in the high dose group.

In high dose groups, about 50% weight reduction of uterus or prostate and ovaries, and weight increase of kidney and adrenals were seen. Replacement of cardiac muscle by adipose tissue in 4/8 animals at high dose. Apparent enlargement of adrenal cortex in 3/4 dogs in the high dose group. Flex dystrophic mineralization observed in renal medulla in all groups, including controls.

Carcinogenicity Studies

Indapamide was administered to 3 groups of 60 males and 60 females Charles River CDI rats and mice at dietary levels of 10, 30 and 100 mg/kg/day for 104 and 91 weeks respectively. A fourth group served as the negative control group. Both strains are susceptible to known carcinogens.

In both species, the incidence of nodules and masses observed at necropsy was comparable between the treated and control groups. Drug-related changes in the kidney (tubular nephrosis and mineralization of parenchyma) were seen in rats. Increased liver cytoplasmic vacuolization was seen in mice.

Under the conditions of testing, indapamide was not tumorigenic.

Teratogenicity Studies

The teratogenicity potential of indapamide was investigated in 3 animal species: mice, rats and rabbits.

- In mice CD/SPF (groups of 30 females), indapamide administered at doses of 0, 5 and 20 mg/kg/day p.o., 6 days a week, from the day of mating and throughout pregnancy did not induce abortions or increase percentage of deaths of the litters. No apparent teratogenic effect was noted.

• In rats SD/SPF: no embryo toxicity was noted in the foetuses of 3 females receiving a daily dose of 250 mg/kg p.o. from the 9th to the 16th day of gestation.

• In rats SD/SPF (groups of 60 females) receiving from the day of mating until the end of pregnancy 0, 10 and 30 mg/kg/day p.o., 6 days a week, indapamide had no effect on the abortion rate, the mean number of foetuses per litter or the incidence of abnormalities.

• In rats CR/CD (groups of 20 females) receiving 0, 1, 25 or 125 mg/kg, once daily from days 6 to 15 of gestation, no adverse effects were reported on abortion rate, implantation rate, mean litter size or fetal weight or fetal mortality. Slightly higher incidence of visceral abnormalities (thin walled heart, hydronephrosis) in treated animals (19-26% vs. 17% in controls).

• In the domestic rabbit (groups of 15 females) receiving 0, 1, 5, 10 and 50 mg/kg/day p.o., once daily, 6 days a week, from the 6th to the 18th day of gestation, increased resorption rate was seen at 50 mg/kg. No apparent teratogenic effect was noted.

• In the New Zealand white rabbit (groups of 13 females) receiving 0, 5, 30 and 180 mg/kg/day p.o., once daily from days 6 to 18 of gestation showed reduction in food consumption and weight gain at 180 mg/kg during the first 4 days of dosing. Total loss of litters occurred in 2 animals at high dose. In the other animals, abortion rate and litter size were unchanged. Incidence of major malformations and minor abnormalities were comparable for all groups and considered to be within the Laboratory standard range.

Fertility and Reproduction Study

Three generation tests, Wistar rats (SPF Strain).

Indapamide was administered at 0, 0.5, 2.5 and 25 mg/kg p.o., once daily to 20 males/group for 70 days before mating and 15 days after, and to 10 females/ group for 8 days before mating up to 30 days post-mating. Findings were as follows:

Reproductive performance was not changed. No changes in mean weight, mean number of foetuses, the incidence of malformations or death rate among neonates were observed.

Behavior and reproductive performance of off-spring were unaffected, but the death rate of neonates (F2 generations) was adversely affected: 35% at low dose and 47% at the high dose vs. 16% in controls (the lack of milk formation in the mothers may have been the cause).

No adverse effects of the F3 generation pups were observed.

REFERENCES

1. Acchiardo SR, Skoutakis VA. Clinical efficacy, safety and pharmacokinetics of indapamide in renal impairment. Am Heart J 1983; 106(Suppl.): 239-44.

2. Ames RP, Griffing E, Marbury T, et al. Effectiveness of indapamide versus enalapril as second-step therapy of systemic hypertension. Am J Cardiol 1992; 69: 267-70.

3. Brennan L, Wu MJ, Laquer UJ. A multicenter study of indapamide in hypertensive patients with impaired renal function. Clin Ther 1982; 5: 121-8.

4. Clarke RJ. Indapamide: a diuretic of choice for the treatment of hypertension? Am J Med Sci 1991; 301(3): 215-20.

5. Ferdinand K, Flamenbaum W, Hall WD et al. Lower dose indapamide therapy in the treatment of patients with mild to moderate hypertension. Am J Hypertens 1993; 6(5 part 2): 121A.

6. Harrower ADB, McFarlane G, Donnelly T, Gray CE. Effect of indapamide on blood pressure and glucose tolerance in non-insulin-dependent diabetes. Hypertension 1985; 7(Suppl II): 161-3.

7. Kocijancic M, Dimkovic S. Antihypertensive effect of indapamide given in conjunction with captopril in severe hypertension. Curr Med Res Opin 1986; 10: 313-8.

8. Leenen FHH, Smith DL, Boer WH, Marquez-Julio A. Diuretic and cardiovascular effects of indapamide in hypertensive subjects: A dose-response curve. Curr Med Res Opin 1983; 8(Suppl 3): 47-52.

9. Leenen FHH, Smith DL, Farkas RM et al. Cardiovascular effects of indapamide in hypertensive patients with or without renal failure. Am J Med 1988; 84(Suppl 1B): 76-85.

10. Leonetti G, Rappelli A, Salvetti A et al. Long-term effects of indapamide: final results of a two-year Italian multicenter study in systemic hypertension. Am J Cardiol 1990; 65: 67H-71H.

11. Levine B. Treatment of hypertension in the elderly. Clin Ther 1994; 16(5): 732-51.

12. Newstead CG, Moore RH, Barnes AJ. Interstitial nephritis associated with indapamide. Br Med J 1990; 300: 1344.

13. Ocon J, Mora J. Twenty-four-hour blood pressure monitoring and effects of indapamide. Am J Cardiol 1990; 65: 58H-61H.

14. Plante GE, Dessurault DL. Hypertension in elderly patients. A comparative study between indapamide and hydrochlorothiazide. Am J Med 1988; 84(Suppl 1B): 98-103.

15. Plante GE, Massry SG, et al. Comparison between the effects of indapamide and hydrochlorothiazide on creatinine clearance in patients with impaired renal function and hypertension. Am J Nephrol 1995; 15: 251-5.

16. Raggi U, Palumbo P, Bevilacqua M et al. Indapamide in the treatment of hypertension in non-insulin-dependent diabetes. Hypertension 1985; 7(Suppl II): 157-60.

17. Soltero I, Fuenmayor I, Colmenares A, et al. Comparative study of indapamide, beta-blockers, and diet. Curr Ther Res 1989; 46(2): 327-35.

18. Stricker BHCh, Biriell C. Skin reactions and fever with indapamide. Br Med J 1987; 295: 1313-14.

19. Van Hee W, Thomas J, Brems H. Indapamide in the treatment of essential arterial hypertension in the elderly. Postgrad Med J 1981; 57(Suppl 2): 29-33.

20. Waal-Manning HJ, Doesburg RMN, Spears GFS. Indapamide in hypertension. N Z Med J 1987; 100: 251-2.

21. Weiss R, Toth P, Miller E, et al. Clinical efficacy and safety of lower-dose indapamide therapy in the treatment of patients with mild to moderate hypertension. Am J Ther 1994; 1: 58-64.

22. Product Monograph - Lozide® (indapamide) 1.25 and 2.5 mg Tablets. Servier Canada Inc. Date of Revision: June 11, 2020. Control # 236979.

PART III: CONSUMER INFORMATION

PrMYLAN-INDAPAMIDE
(Indapamide Tablets, USP)

1.25 mg and 2.5 mg

Read this carefully before you start taking MYLAN-INDAPAMIDE and each time you get a refill. This leaflet is a summary and will not tell you everything about MYLAN-INDAPAMIDE. Talk to your doctor, nurse, or pharmacist about your medical condition and treatment and ask if there is any new information about MYLAN-INDAPAMIDE.

ABOUT THIS MEDICATION

What the medication is used for:
MYLAN-INDAPAMIDE is used to treat mild to moderate high blood pressure.
MYLAN-INDAPAMIDE can be used by itself or with other medicines to treat that condition.

What it does:
MYLAN-INDAPAMIDE is a diuretic often called a "water pill". It increases urination. This lowers blood pressure.
MYLAN-INDAPAMIDE affects the kidney's ability to reabsorb electrolytes.
This medicine does not cure high blood pressure. It helps to control it. Therefore, it is important to continue taking MYLAN-INDAPAMIDE regularly even if you feel fine.

When it should not be used:
Do not take MYLAN-INDAPAMIDE if you:

- Are allergic to indapamide or any other sulfonamide or to any non-medicinal ingredient in the formulation
- Have severe kidney disease
- Have severe liver disease or suffer from a condition called hepatic encephalopathy (a degenerative disease of the brain)
- Have low potassium levels in your blood
- Are taking drugs to treat heart rhythm disturbances (antiarrhythmics) that might cause severe cardiac arrhythmias
- Are breastfeeding. MYLAN-INDAPAMIDE passes into breast milk
- Are pregnant. MYLAN-INDAPAMIDE should not be used during pregnancy. If you become pregnant, discontinue use immediately and discuss with your doctor
- Have lactose intolerance or have hereditary galactose intolerance, glucose-galactose malabsorption or total lactase deficiency because MYLAN-INDAPAMIDE contains lactose

What the medicinal ingredient is:
Indapamide

What the non-medicinal ingredients are:
Each MYLAN-INDAPAMIDE 1.25 mg tablets:
lactose, microcrystalline cellulose, povidone, starch, talc, sodium starch glycollate, magnesium stearate, hydroxypropyl methylcellulose, polydextrose, polyethylene glycol, titanium dioxide, triacetin, FD&C yellow #6 Aluminium Lake, and D&C yellow #10 Aluminium Lake.

Each MYLAN-INDAPAMIDE 2.5 mg tablets:
lactose, microcrystalline cellulose, povidone, starch, talc, sodium starch glycollate, magnesium stearate, hydroxypropyl methylcellulose, polydextrose, polyethylene glycol, titanium dioxide, triacetin, FD&C red #40 Aluminum Lake, and FD&C blue #2 Aluminum Lake.

What dosage forms it comes in:
Tablets of 1.25 mg or 2.5 mg.

WARNINGS AND PRECAUTIONS

BEFORE you use MYLAN-INDAPAMIDE talk to your doctor, nurse, or pharmacist if you:

- Are dehydrated or suffer from excessive vomiting, diarrhoea, or sweating
- Have diabetes, liver or kidney disease
- Have any congenital or a family history of heart rhythm problems
- Suffer from hyperparathyroidism (dysfunctioning of the parathyroid gland)
- Have systemic lupus erythematosus (SLE)
- Are malnourished
- Are elderly
- Have coronary artery disease, heart disease or heart failure
- Had a surgery called a Sympathectomy
- Suffer from gout
- have muscle disorders including muscle pain, tenderness, weakness or cramps,

A decrease in vision or eye pain could indicate the presence of fluid accumulation in the vascular layer of the eye or an increase of pressure in your eye. These manifestations typically occur suddenly within hours to weeks following the taking of MYLAN-INDAPAMIDE. This can lead to permanent vision loss, if not treated. If you have a history of penicillin or sulfonamide allergies, you can be at higher risk of developing these manifestations.

MYLAN-INDAPAMIDE is not recommended for use in children.

You may become sensitive to the sun while taking

MYLAN-INDAPAMIDE. Exposure to sunlight should be minimized.

Athletes should be aware that MYLAN-INDAPAMIDE contains an active ingredient, which may give a positive reaction in doping tests.

Driving and using machines: Before you perform tasks which may require special attention, wait until you know how you respond to MYLAN-INDAPAMIDE. Dizziness, lightheadedness, or fainting can especially occur after the first dose or when another antihypertensive agent is added.

INTERACTIONS WITH THIS MEDICATION

As with most medicines, interactions with other drugs are possible. Tell your doctor, nurse, or pharmacist about all the medicines you take, including drugs prescribed by other doctors, vitamins, minerals, natural supplements, or alternative medicines.

The following may interact with MYLAN-INDAPAMIDE:

- ACTH (e.g. tetracosactide) for treatment of arthritis or inflammatory bowel disease
- Alcohol, barbiturates (sleeping pills), or narcotics (strong pain medications). They may cause low blood pressure and dizziness when you go from lying or sitting to standing up.
- Allopurinol (to treat gout)
- Antibiotics such as moxifloxacin, erythromycin IV, ciprofloxacine, clarithromycin
- Antifungal medications such as amphotericin B (IV), fluconazole
- Antimicrobial medications such as pentamidine
- Baclofen, a skeletal muscle relaxant
- Calcium tablets or other calcium supplements
- Ciclosporin, tacrolimus or other medications to depress the immune system after organ transplantation
- Drugs to treat heart rhythm disturbances (e.g. digoxin, quinidine, hydroquinidine, disopyramide, amiodarone, sotalol, ibutilide, dofetilide, flecainide)
- Drugs to treat high blood pressure, including angiotensin converting enzyme (ACE) inhibitors
- Drugs used to treat mental disorders such as anxiety and schizophrenia (e.g. clozapine, risperidone, pimozide, amisulpride, haloperidol, donepezil)
- Drugs used to treat depression, in particular selective serotonin reuptake inhibitors (SSRIs e.g. paroxetine, sertraline, citalopram, escitalopram) and tricyclic antidepressants (imipramine)
- Iodinated contrast media
- Lithium used to treat bipolar disease
- Metformin, an oral medication for diabetes
- Nonsteroidal anti-inflammatory drugs (NSAIDs), such as ibuprofen, naproxen or celecoxib or high doses of acetylsalicylic acid (more than 3 g/day)
- Oral corticosteroids for treatment of asthma
- Potassium-sparing diuretics (e.g. amiloride, spironolactone, triamterene)
- Stimulant laxatives such as bisacodyl and senna
- Medicines for the treatment of cancer (e.g. vandetanib, oxaliplatin)
- Anaesthetics (e.g. propofol, sevoflurane)
- Anagrelide (used to reduce elevated platelet counts)
- Medicines used to treat nausea and vomiting (e.g. ondansetron, domperidone)
- Papaverine (used to treat gastro-intestinal problems)
- Antiparasitic medicines used to treat certain types of malaria (e.g. chloroquine)
- Antihistamines used to treat allergic reactions , such as hay fever
- Methadone (used to treat addiction)

PROPER USE OF THIS MEDICATION

Take MYLAN-INDAPAMIDE exactly as prescribed. It is recommended to take your dose at about the same time every day in the morning. MYLAN-INDAPAMIDE is for oral use: swallow the tablet whole with water.

Usual Adult dose:
1.25 mg tablet a day.

Maximum dose:
2.5 mg a day
Your doctor may increase the dose to a maximum of 2.5 mg daily depending on your response to treatment after 4 to 8 weeks.
Recommended dose for the elderly: 1.25 mg tablet a day.
This dose may be adjusted depending on your kidney function.

Overdose:

If you think you, or a person you are caring for, have taken too much MYLAN-INDAPAMIDE, contact a healthcare professional, hospital emergency department, or regional poison control centre immediately, even if there are no symptoms.

Missed Dose:
If you have forgotten to take your dose during the day, carry on with the next one at the usual time. Do not double dose.

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

Side effects may include:

- **Headache**
- **Pains in the stomach, back, chest**
- **Dizziness**
- **Fatigue, weakness**
- **Burning or prickling feeling in hands, arms, legs or feet**
- **Muscle cramps**
- **Vertigo**
- **Constipation, diarrhea, nausea, vomiting**
- **Cough, dry mouth**
- **Swelling**
- **Rash, itching**

If any of these symptoms affects you severely, tell your doctor, nurse or pharmacist.

MYLAN-INDAPAMIDE can cause abnormal blood test results. Your doctor will decide when to perform blood tests and will interpret the results.

SERIOUS SIDE EFFECTS AND WHAT TO DO ABOUT THEM

Symptom / effect		Talk to your healthcare professional		Stop taking drug and get immediate medical help
		Only if severe	In all cases	
Common	**Electrolyte disturbances (low levels of sodium, potassium and/or chloride):** muscle weakness, pain or cramps, irregular heartbeat, weakness, generally feeling unwell.		✓	
	Changes in heart rate: faster, slower or irregular heart beat		✓	

SERIOUS SIDE EFFECTS AND WHAT TO DO ABOUT THEM

Symptom / effect		Talk to your healthcare professional		Stop taking drug and get immediate medical help
		Only if severe	In all cases	
	Hyperuricaemia: high uric acid levels in the blood, which may cause gout: pain, swelling and redness in the joints		✓	
	Increased Blood sugar: frequent urination, thirst, hunger.		✓	
Uncommon	**Low blood pressure:** dizziness, fainting, lightheadedness. May occur when you move from lying down or sitting to standing up.		✓	
Unknown	**Decreased White Blood Cells:** infections, fatigue, fever, aches, pains and flu-like symptoms.		✓	

SERIOUS SIDE EFFECTS AND WHAT TO DO ABOUT THEM				
Symptom / effect		Talk to your healthcare professional		Stop taking drug and get immediate medical help
		Only if severe	In all cases	
	Eye Disorders: -Acute Myopia: sudden near sightedness or blurred vision. **-Visual impairment - Decrease in vision or pain in your eyes due to high pressure** (possible signs of fluid accumulation in the vascular layer of the eye or acute angle-closure glaucoma)			✓
	Rhabdomyolysis: muscle pain that you cannot explain, muscle tenderness or weakness, dark brown urine.			✓
	Decreased Platelets: Bruising or unusual bleeding from the skin or other areas, fatigue, weakness.		✓	

SERIOUS SIDE EFFECTS AND WHAT TO DO ABOUT THEM				
Symptom / effect		Talk to your healthcare professional		Stop taking drug and get immediate medical help
		Only if severe	In all cases	
	Decreased Red Blood Cells (anemia): fatigue, shortness of breath, irregular heart rate, dizziness, headache, pale skin.		✓	
	Liver disorder yellowing of the skin or eyes, dark urine, abdominal pain, nausea, vomiting, loss of appetite.		✓	
	Kidney disorder: change in frequency of urination, nausea, vomiting, swelling of extremities, fatigue.		✓	
	Inflammation of the pancreas: severe upper stomach pain that gets worse when you lie down, often with nausea and vomiting.			✓

SERIOUS SIDE EFFECTS AND WHAT TO DO ABOUT THEM				
Symptom / effect		Talk to your healthcare professional		Stop taking drug and get immediate medical help
		Only if severe	In all cases	
	Allergic Reaction/ Angioedema (swelling of the face, lips, mouth, tongue or throat) which may cause difficulty in swallowing or breathing.			✓
	Hypercalcaemia: high calcium levels in the blood, may cause loss of appetite, nausea, vomiting, constipation, stomach pain.			✓
	Torsade de pointes: life-threatening irregular heart beat Record of the electrical activity of the heart (electrocardiogram (ECG)) showing a prolonged QT interval			✓
	Possible worsening of pre-existing lupus: a disease affecting the skin, joints and kidneys			✓

SERIOUS SIDE EFFECTS AND WHAT TO DO ABOUT THEM				
Symptom / effect		Talk to your healthcare professional		Stop taking drug and get immediate medical help
		Only if severe	In all cases	
	Hepatitis a liver disease which may cause nausea, vomiting, loss of appetite, feeling generally unwell, fever, itching, yellowing of the skin and eyes, light colored bowel motions, dark coloured urine			✓
	Severe skin reactions: Stevens Johnson Syndrome, Toxic epidermic necrolysis: skin rash, redness of the skin, blistering of the lips, eyes or mouth, skin peeling, accompanied by fever, chills, headache, cough, body aches and generally feeling unwell			✓

This is not a complete list of side effects. For any unexpected effects while taking MYLAN-INDAPAMIDE, contact your doctor, nurse, or pharmacist.

HOW TO STORE IT

Keep out of reach and sight of children.
Store MYLAN-INDAPAMIDE between 15ºC to 30ºC.
Do not use after the expiry date stated on the carton or blister.

Reporting Side Effects

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada/adverse-reaction-reporting.html) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

MORE INFORMATION

If you want more information about MYLAN-INDAPAMIDE:

- Talk to your healthcare professional.
- Find the full product monograph that is prepared for healthcare professionals and includes this Consumer Information by visiting the Health Canada website: (https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/drug-product-database.html); the manufacturer's website www.mylan.ca, or by calling 1-844-596-9526.

This leaflet was prepared by Mylan Pharmaceuticals ULC
Etobicoke, Ontario M8Z 2S6

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Mylan

Mylan Pharmaceuticals ULC
Etobicoke, ON M8Z 2S6
1-844-596-9526
www.mylan.ca