

# Lasix®

**Indications—Oral:** Edema associated with congestive heart failure, cirrhosis of the liver and renal disease including the nephrotic syndrome and other edematous states. Mild to moderate hypertension or with other antihypertensive agents in more severe cases. **Parenteral:** Acute pulmonary edema, cerebral edema or when oral therapy is precluded. **Contraindications:** Complete renal shutdown. Discontinue if increasing azotemia and oliguria occur during treatment of severe progressive renal disease. In hepatic coma, in states of electrolyte depletion, hypovolemia or hypotension, do not institute therapy until the basic condition is improved or corrected. Do not administer to jaundiced newborn infants or to infants suffering from diseases with the potential of causing hyperbilirubinemia and possibly kernicterus. **Warnings:** Lasix is a potent diuretic requiring careful medical supervision. Dose and dose schedule have to be adjusted to the individual patient's needs. Cases of tinnitus and reversible deafness have been reported. There have also been some reports of cases, the majority in children undergoing renal transplantation, in which permanent deafness has occurred. Hearing impairment is more likely to occur in patients with severely reduced renal function who are given large doses of Lasix parenterally, at a rate exceeding 4 mg/min or in patients also receiving drugs known to be ototoxic. Do not use in pregnant women unless the benefits outweigh the possible risks to the foetus. Sulfonamide diuretics have been reported to decrease arterial responsiveness to pressor amines and to enhance the effects of tubocurarine. Exercise caution in administering curare or its derivatives during Lasix therapy. Discontinue 1 week prior to elective surgery. **Precautions:** Excessive diuresis may result in circulatory collapse or vascular thrombosis. It is essential to maintain fluid and electrolyte balance. During long-term therapy a high-potassium diet is recommended. Potassium supplements should be given when high doses are used over prolonged periods. Particular caution with potassium levels is desirable in patients on digitalis glycosides, potassium-depleting steroids, or in infants and children. Potassium supplementation, diminution in dose, or discontinuation of Lasix may be required. Strict restriction in sodium intake is not advisable. Potassium supplements and aldosterone antagonists may be added when treating hepatic cirrhosis with ascites. Sudden alterations of fluid and electrolyte balance in patients with cirrhosis may precipitate hepatic coma. In edematous hypertensives reduce the dosage of other antihypertensives since Lasix potentiates their effects. Monitor urine and blood glucose as decreased glucose tolerance has been observed. Monitor serum calcium levels particularly in children receiving i.v. Lasix, as rare cases of tetany have been reported. Simultaneous administration with cephaloridine is not advisable. Patients receiving high doses of salicylates with Lasix may experience salicylate toxicity at lower doses. Lasix parenteral in doses up to 100 mg should be injected slowly (1–2 minutes) when the i.v. route is used. **Adverse reactions:** Electrolyte depletion may occur especially with high doses and restricted salt intake; it may manifest itself by weakness, dizziness, lethargy, leg cramps, anorexia, vomiting and/or mental confusion. Asymptomatic hyperuricemia can occur and gout may rarely be precipitated. Transient elevations of BUN may be seen especially in renal insufficiency. Dermatitis, pruritus, paresthesia, blurring of vision, postural hypotension, nausea, vomiting or diarrhea may occur. Anemia, leukopenia, and thrombocytopenia (with purpura) and rare cases of agranulocytosis have occurred. **Overdosage—Symptoms:** Dehydration, electrolyte depletion and hypotension. Hepatic coma may be precipitated in cirrhotic patients. **Treatment:** Discontinue Lasix and apply corrective treatment. **Dosage and administration—Adults:** **Oral—Edema:** Usual initial dosage is 40–80 mg. Adjust according to response. If diuresis has not occurred after 6 hours, increase dosage by increments 20–40 mg. The effective dose can then be repeated 1 to 3 times daily. Maximum daily dose: 200 mg. Maintenance dosage must be adjusted individually. An intermittent dosage schedule of 2–4 consecutive days each week may be utilized. With doses exceeding 120 mg/day, clinical and laboratory observations are advisable. **Hypertension:** Usual dosage is 20–40 mg twice daily. Individualize therapy and adjust dosage of concomitant antihypertensive therapy. **Parenteral:** Usual dosage is 20–40 mg given as a single dose, injected i.m. or i.v. The i.v. injection should be given slowly (1–2 minutes), and should not be added into the tubing of a running infusion solution. Ordinarily, a prompt diuresis ensues. If diuresis is not satisfactory, succeeding doses may be increased by increments of 20 mg 2 hours after the previous dose, until the required diuresis is obtained. Maximum daily dose: 100 mg. Switch to oral therapy as soon as practical. Acute pulmonary edema: Administer 40 mg by slow i.v. injection, followed if necessary by another 40 mg 1–1½ hours later. **Pediatric use:** Institute therapy under close observation in the hospital. Initial oral or parenteral dose is 0.5–1 mg/kg. The total daily dose should not exceed 2 mg/kg orally or 1 mg/kg parenterally, given in divided doses 6–12 hours apart. In newborn and premature, the daily dose should not exceed 1 mg/kg. Particular caution with potassium levels is desirable. Adopt an intermittent dosage schedule as soon as possible. Lasix should not be added into the tubing of a running infusion solution. **Supply:** White, round, 20 mg tablets (Code DLF) in bottles of 30 and 300. Yellow, round, scored 40 mg tablets (Code DL1) in bottles of 50 and 500 and Unit Dose boxes of 100. Amber ampoules of 2 ml (20 mg) in boxes of 5 and 50; 4 ml (40 mg) in boxes of 50. Product monograph on request. 1364/7096 E.

# Lasix® Special

**Composition:** Each tablet contains 500 mg furosemide. Each 25 ml ampoule contains 250 mg furosemide. **Indications—** Exclusively for patients with severely impaired renal function. To be used under strict medical supervision within a hospital setting. May be used as an adjuvant treatment of oliguria and of edema in selected patients with acute renal failure or with chronic renal failure or with the nephrotic syndrome. **Contraindications:** Complete renal shutdown and G.F.R. below 5 ml/min. In patients whose G.F.R. is above 20 ml/min. In patients with hepatic cirrhosis or with renal failure due to poisoning with nephrotoxic or hepatotoxic substances, or with renal failure accompanied by hepatic coma. Severe hypokalemia, hypovolemia or hypotension until serum potassium, fluid balance and blood pressure have been restored to normal. **Warnings:** Cases of tinnitus and reversible deafness have been reported. There have also been some reports of cases, the majority in children undergoing renal transplantation, in which permanent deafness has occurred. Hearing impairment is more likely to occur in patients with severely reduced renal function who are given large doses of Lasix parenterally, at a rate exceeding 4 mg/min or in patients also receiving drugs known to be ototoxic. Do not use in pregnant women unless the benefits outweigh the possible risks to the foetus. Sulfonamide diuretics have been reported to decrease arterial responsiveness to pressor amines and to enhance the effects of tubocurarine. Exercise caution in administering curare or its derivatives during Lasix therapy. Discontinue 1 week prior to elective surgery. Do not administer to jaundiced newborn infants or to infants suffering from diseases with the potential of causing hyperbilirubinemia and possibly kernicterus. **Precautions:** Excessive diuresis may result in circulatory collapse or vascular thrombosis. It is essential to maintain fluid and electrolyte balance. During long-term therapy a high-potassium diet is recommended. Potassium supplements should be given when high doses are used over prolonged periods. Particular caution with potassium levels is desirable in patients on digitalis glycosides, potassium-depleting steroids, or in impending hepatic coma. Potassium supplementation, diminution in dose, or discontinuation of Lasix may be required. Strict restriction in sodium intake is not advisable. In edematous hypertensives reduce the dosage of other antihypertensives since Lasix potentiates their effects. Monitor urine and blood glucose as decreased glucose tolerance has been observed. Monitor serum calcium levels as rare cases of tetany have been reported. The simultaneous administration of Lasix and cephaloridine is not advisable. Patients receiving high doses of salicylates with Lasix may experience salicylate toxicity at lower doses. Rate of infusion should not exceed 4 mg/min. **Adverse reactions:** Electrolyte depletion may occur especially with high doses and restricted salt intake; it may manifest itself by weakness, dizziness, lethargy, leg cramps, anorexia, vomiting and/or mental confusion. Asymptomatic hyperuricemia can occur and gout may rarely be precipitated. Transient elevations of BUN may be seen especially in renal insufficiency. Dermatitis, pruritus, paresthesia, blurring of vision, postural hypotension, nausea, vomiting, or diarrhea may occur. Anemia, leukopenia, and thrombocytopenia (with purpura) and rare cases of agranulocytosis have occurred. **Overdosage—Symptoms:** Dehydration, electrolyte depletion and hypotension. **Treatment:** Discontinue drug and institute appropriate corrective treatment. **Dosage and Administration—Parenteral:** Initial dose of 250 mg are mixed with 250 ml of a suitable infusion solution and given by intravenous drip at a rate not exceeding 4 mg/min. Additional dose of 500 mg should be given if initial dose fails to produce an adequate increase in urinary output after one hour. The effective dose can be repeated every 24 hours. A maximum daily dose of 1000 mg should not be exceeded. Lasix Special 250 mg can be mixed to 250 ml of 5% dextrose in water, isotonic saline or lactated Ringer's injection, immediately before use. Precipitation may occur in solutions with a pH of the mixture less than 5.5. Not to be added into the tubing of a running infusion solution, and not to be mixed with any other drugs in the infusion bottle. If indicated as in case of hypovolemic patients, the i.v. infusion of the undiluted solution must be given with the aid of a motor-driven precision syringe so as to make sure that the upper limit of 4 mg Lasix (0.4 ml) per minute is not exceeded. **Oral:** Effective intravenous dose is used as the initial dose. Additional dose may be raised by 250 to 500 mg should the initial dose fail to produce an adequate urinary output within 4–6 hours. The maximum daily dose of 1000 mg should not be exceeded. **Supply:** Yellow round, quarter-scored 500 mg tablets (Code DLX) in bottles of 20. Amber ampoules of 25 ml (250 mg) in a sterile solution at pH of 9.1. Product Monograph on request. 1368/7106 E.

## Hoechst

Pharmaceutical Division, Canadian Hoechst Ltd., Montreal



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## The bleeding limit

To the editor: There are many objectionable statements in Robert McCaldon's article "Don't bleed on my carpet" (*Can Med Assoc J* 115: 679, 1976). One of the most striking is "those whom seem hell-bent on... [suicide] should not be impeded in the fulfilment of their destiny". The naïve assumption that people are the way they are because they want to be that way is distinctly unprofessional. The good physician should encourage, not discourage, further study into the causes and remedies of conditions that lead to self-destructive behaviour.

In manic-depressive illness the suicide rate used to approach 20%. The disease was so devastating that arguments for allowing patients to destroy themselves might have had marginal acceptance as recently as 1950. The introduction of lithium therapy has laid such arguments to rest. Many conditions that appear hopeless today may not be so within months or years. The good physician should make reasonable efforts to keep people alive in the hope that truly helpful remedies for their problems will appear.

No sensible editor would permit me sufficient space to enlarge on my other objections to "Don't bleed on my carpet". In general, the bombastic, cynical and nihilistic style smacks of rhetoric and polemic and is distinctly lacking in thoughtful consideration of the serious problem of the limits of clinical medicine.

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## Circumcision

To the editor: Some time ago Dr. L.J. Genesove quoted my wartime studies (*Circumcision and venereal disease. Can Med Assoc J* 56: 54, 1947) in defence of circumcision. The reason for my original inquiry was that discussions on circumcision were seldom supported by factual observations.

The situation has not changed much in the last 30 years. Nursery committees still make pronouncements on the subject without examination of the available data.

I would like to see data collected on the frequency of penile pathology — warts, balanitis, chancroid and venereal lesions — in the circumcised v. the uncircumcised. The role of the uncircumcised male as a vector for trichomoniasis, candidiasis or nonspecific urethritis should also be studied. Such studies should be correlated with the social status and sexual habits of the subjects for validity.

Complications are common when circumcision is done without good judgement or surgical skill, so there should be more documentation of the incidence of such complications and the incidence and ill effects of meatal ulcer in circumcised children.

Phimosis still occurs in children with conscientious parents (Fig. 1). I am



FIG. 1—Phimosis in young child.

also told by my colleagues in geriatrics that similar complications occur in the aged, cause much suffering and may require surgery.

This letter is written as a plea for more light and less heat in discussions regarding circumcision.

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### Thrombotic thrombocytopenic purpura

*To the editor:* Gundlach and Tarnasky recently commented on the treatment of thrombocytopenic purpura (TTP) (*Can Med Assoc J* 115: 1194, 1976). It is now apparent that with three forms of therapy a number of patients have recovered from TTP. These forms of therapy were the use of steroids and splenectomy, the administration of platelet suppressant drugs and, more recently emphasized, the use of exchange transfusions<sup>1</sup> or plasmapheresis (I. Cooper: personal communication, 1977). Although it is now generally accepted that disseminated intravascular platelet aggregation occurs in TTP, its mechanism is uncertain. Favourable results with exchange transfusion support the possibility that the trigger for the platelet aggregation in TTP is an intravascular stimulus,<sup>2</sup> perhaps a circulating immune complex.

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### References

1. BUKOWSKI RM, HEWLETT JS, HARRIS JW, et al: Exchange transfusions in the treatment of thrombocytopenic purpura. *Semin Hematol* 13: 219, 1976

2. NEAME PB, LECHAGO J, LING ET, et al: Thrombotic thrombocytopenic purpura: report of a case with disseminated intravascular platelet aggregation. *Blood* 42: 805, 1973

### Hypertension secondary to bilateral hydronephrosis

*To the editor:* Hypertension resulting from hydronephrosis is rare.<sup>1</sup> The following is a case of hypertension secondary to bilateral hydronephrosis of a relatively limited duration.

A 58-year-old man presented in July 1972 with features suggestive of prostatic hypertrophy of approximately 5 years' duration. At that time the blood pressure had been recorded as 142/84 mm Hg, the blood urea nitrogen (BUN) value was 8.2 mg/dl and intravenous pyelography showed findings consistent with prostatic hypertrophy, but indicated normal function of the kidneys.

In January 1975 he complained of lower abdominal discomfort, troublesome frequency of micturition, thirst and frequent headaches. His bladder was palpable but not tender and a large benign prostate was detected. The blood pressure was 200/120 mm Hg in both arms and the BUN concentration was 52.0 mg/dl. Intravenous pyelography on Jan. 9, 1975 showed gross bilateral hydronephrosis secondary to chronic retention of urine (Fig. 1).

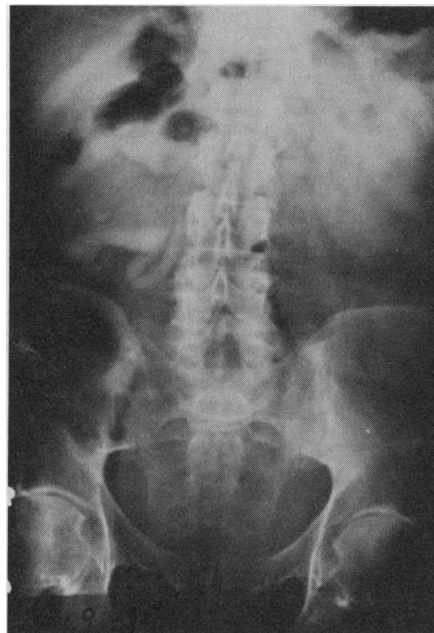


FIG. 1—Gross bilateral hydronephrosis secondary to chronic retention of urine.

Retropubic prostatectomy was performed on Jan. 17, 1975, when 49 g of prostatic tissue was removed. Postoperatively his blood pressure decreased: it was 110/80 mm Hg 24 hours after operation, 140/80 mm Hg on Jan. 22, 1975 and 140/90 mm Hg on Feb. 11, 1975. The BUN value was 12.5 mg/dl on Feb. 11, 1975. Intravenous pyelography on Feb. 19, 1975 showed resolution of hydronephrosis (Fig. 2).

### REGLAN® (metoclopramide hydrochloride)

**Classification:** Reglan® brand of metoclopramide hydrochloride is a modifier of upper gastrointestinal tract motility.

**Indications:** Reglan is indicated as an adjunct in the management of delayed gastric emptying associated with subacute and chronic gastritis and sequelae of surgical operations such as vagotomy and pyloroplasty. In such indications, when there is delayed gastric emptying, Reglan may relieve symptoms such as nausea, vomiting, bloating, and epigastric distress.

**Contraindications:** Reglan should not be administered to patients in combination with MAO inhibitors, tricyclic antidepressants, sympathomimetics, or foods with high tyramine content, since safety of such an association has not been established. As a safety measure, a two-week period should elapse between using any of these drugs and administration of Reglan.

The safety of use of Reglan in pregnancy has not been established. Therefore, Reglan should not be used in women of child-bearing potential unless, in the opinion of the physician, expected benefits to the patient outweigh the potential risks to the fetus.

**Warnings:** Drugs with atropine-like action should not be used simultaneously with Reglan since they have a tendency to antagonize the effects of this drug on gastrointestinal motility. Reglan should not be used in conjunction with potent ganglioplegic or neuroleptic drugs or drugs with acetylcholine-like action, since potentiation of effects may occur. Additive sedative effects may occur when administered concurrently with sedatives, hypnotics, narcotics, or tranquilizers.

**Precautions:** Reglan should not be used in patients with epilepsy and extrapyramidal syndromes unless its expected benefits outweigh the risk of aggravating these symptoms. Reglan does not appear to aggravate the manifestations of Parkinson's disease in patients treated with levodopa. In view of the risk of extrapyramidal manifestations, metoclopramide should not be used in children unless a clear indication has been established.

The recommended dosage of Reglan should not be exceeded, since a further increase in dosage will not produce a corresponding increase in clinical response. The dosage recommended for children should not exceed 0.5 mg/kg daily.

**Adverse Reactions:** Drowsiness, fatigue, and lassitude occur in approximately 10 percent of patients at recommended dosage. Less frequent adverse reactions, occurring in approximately 5 percent of patients, are: insomnia, headache, dizziness, or bowel disturbances.

Parkinsonism and/or other extrapyramidal symptoms have been reported in approximately 1 percent of patients. Such reactions appear to occur more frequently in children and young adults, and particularly at higher-than-recommended dosage. An increase in the frequency and severity of seizures has been reported in conjunction with the administration of Reglan to epileptic patients.

**Dosage and Administration:**  
*Note: Total daily dosage must not exceed 0.5 mg/kg body weight.*

#### Adults:

*Tablets:* ½ to 1 tablet (5-10 mg) three or four times a day before meals and at bedtime

*Syrup:* 5 to 10 ml (5-10 mg) three or four times a day before meals and at bedtime

#### Children (5-14 years):

*Syrup:* 2.5 to 5 ml (2.5-5 mg) three times a day before meals

#### Availability:

*Tablets:* Each blue scored compressed tablet contains 10 mg of metoclopramide hydrochloride. Available in bottles of 100 and 500 tablets. DIN 386014.

*Syrup:* Each ml contains 1 mg of metoclopramide hydrochloride. Available in bottles of 4 fl. oz. DIN 386022.

Product monograph available on request.

ATROBINS

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