PATIENT INFORMATION LEAFLET

NITROGLICERINA BIOINDUSTRIA L.I.M.

50 mg/50 ml concentrate for solution for infusion.
C01DA02 Nitroglycerine - Equivalent medicinal

QUALITATIVE AND QUANTITATIVE COMPOSITION
One vial contains:
Active substance: Nitroglycerin 50 mg
Excipients : glucose-propylene glycol- water for injection

PHARMACEUTICAL FORM
Concentrate for infusion solution -1 vial 50 ml.

PHARMACOTHERAPEUTIC CLASS
Vasodilating agent used in heart diseases.

MARKETING AUTHORIZATION HOLDER
Bioindustria L.I.M. S.p.A. - Via De Ambrosiis, 2 - Novi Ligure (AL) - Italy

MANUFACTURER AND FINAL CONTROLLER
Bioindustria L.I.M. S.p.A. - Via De Ambrosiis, 2 - Novi Ligure (AL) - Italy

THERAPEUTIC INDICATIONS

Unstable angina, variant angina, Prinzmetal's angina. Acute left ventricular failure following or not following acute myocardial infarction, especially with high filling pressure and reduced output per min. Acute pulmonary oedema and pulmonary pre-oedema. Hypertensive crisis.

CONTRAINDICATION
The product must not be used in the following cases:
- Known hypersensitivity to nitroglycerine.
- Closed-angle glaucoma.
- Acute circulatory insufficiency (cardiogenic shock, cardiocirculatory collapse).
- Systemic hypotension (< 100 mm Hg systolic; < 60 mm Hg diastolic).
- Acute myocardial infarction with low filling pressure, except in intensive care units under continuous haemodynamic monitoring.
- Grave hypovolaemia.
- Generally during pregnancy and lactation (see Special warnings).

PRECAUTIONS
The product must be used with great care when treating patients with cranial traumas and cerebral haemorrhage.
Systolic and diastolic pressure, heart rate, plasma volume, systolic pulmonary arterial pressure (right cardiac catheterisation in patients with acute heart failure and myocardial infarct with low filling pressure), left ventricular filling pressure, output/min and EEG must be constantly checked.

INTERACTIONS
Ethanol may enhance the nitroglycerin response.
Vasodilators, antihypertensives and diuretics increase its hypotensive effect. Peripheral dispersion of nitroglycerin is prevented by indometacine administration.

SPECIAL WARNINGS
The solution of nitroglycerin for infusion must not be brought into contact with PVC tubes, since as much as 80% of the nitroglycerin may be lost depending on the flow rate. The literature shows that such losses are reduced when other materials, such as polythene, are used. The compatibility of the tube material with nitroglycerin must always be checked to make sure that the clinical effect desired is obtained.

Pregnancy and lactation
During the first three months of pregnancy and during lactation the drug must only be used when really needed and under the direct supervision of the physician in charge.

Effects on the ability to drive vehicles and use machinery
Some secondary effects (orthostatic hypotension, nausea, vertigo) may attenuate the ability to react, especially at the start of the treatment. Prudence is thus recommended when driving vehicles or using machinery.

KEEP THE PRODUCT OUT OF REACH AND SIGHT OF CHILDREN

POSOLOGY AND METHOD OF ADMINISTRATION

Doses are adjusted to each patient's needs and according to the responses displayed by the parameters that must be monitored. Experience shows that the range is 0.5-6 mg/h by continuous i.v. infusion.

Higher doses are rarely required reaching up to 6 mg/h. The infusion solution is prepared by dilution according to the table below and infused with an automatic device or drop by drop according to the second (infusion) table below (1 ml is equivalent to about 20 drops in a normal infusion).

Dilution table

No. vials (amount of active substance)			1 (50 mg)	2 (100 mg)	3 (150 mg)
Solution-Vials			50 ml	100 ml	150 ml
Diluent solution needed in ml	Dilution	1:10	500	1000	1500
		1:20	1000	2000	3000
		1:40	2000	4000	6000
Final volume of solution (ml)	Dilution	1:10	550	1100	1650
		1:20	1050	2100	3150
		1:40	2050	4100	6150
Final concentration of nitroglycerin (mg/ml)	Dilution	1:10		0,09	
		1:20		0,05	
		1:40		0,02	

Infusion table

Quantity of NTG required per hour	Diluition					
	1:10		1:20		1:40	
	Infusion rate					
	ml/h	drops/min	ml/h	drops/ min	ml/h	drops/min
0.50 mg	5.50	2	10.50	3-4	20.50	6-7
0.75 mg	8.25	3	15.75	5	30.75	10
1.00 mg	11.00	3-4	21.00	7	41.00	13-14
1.25 mg	13.75	4-5	26.25	8-9	51.25	17
1.50 mg	16.50	5-6	31.50	10-11	61.50	20-21
2.00 mg	22.00	6-7	42.00	14	82.00	26-27
2.50 mg	27.50	9	52.50	17	102.50	34
3.00 mg	33.00	11	63.00	21	123.00	41
3.50 mg	38.50	13	73.50	24-25	143.50	47-48
4.00 mg	44.00	12-13	84.00	28	164.00	53
4.50 mg	49.50	14-15	94.50	31-32	184.50	59-60
5.00 mg	55.00	18	105.00	35	205.00	68
5.50 mg	60.50	20	115.50	38-39	225.50	74-75
6.00 mg	66.00	22	126.00	42	246.00	82

INCOMPATIBILITIES

Nitroglycerine is compatible with the usual clinical infusion solutions (physiological, 4-30% glucose, Ringer's, solution containing proteins). No incompatibilities with other infusion solutions have been discovered so far. Dilutions must be made in glass containers for phleboclysis using polyethylene administration sets.
The solution must not be brought into contact with PVC tubes, since as much as 80% of the nitroglycerine may be lost depending on the flow rate. The literature shows that such losses are reduced when other materials, such as polythene, are used. The compatibility of the tube material with nitroglycerine must always be checked to make sure that the clinical effect desired is obtained.

OVERDOSAGE

Accidental overdosage may result in severe hypotension and reflex tachycardia. These reactions can be corrected by slowing or temporarily suspending the infusion until the patient's condition stabilises, and by adopting appropriate supportive measures. Additional corrective measures are not usually needed because the haemodynamic effects of nitroglycerine are transient.
If, however, further treatment is indicated, the i.v. administration of plasma substitutes and/or alpha-adrenergic agonists should be considered.

UNDESIRABLE EFFECTS

Headache, including severe and persistent, caused by cerebral vasodilatation, may occur immediately after administration of nitroglycerin.
Dizziness, confusion, weakness, increased heart rate and other manifestations of hypotension, such as nausea vomiting, diaphoresis, pallor and dizziness are usually related to drug overdose. Only rarely nitroglycerin can induce bradycardia and sign of ipervagotonia.
Furthermore in patients treated with nitrates, it is possible the occurrence of skin rash or exfoliative dermatitis.
Have been rare reports of methemoglobinemia rapidly reversible by reducing the infusion rate and administration of methylene blue.
Undesirable effects such as flushing, headache and postural hypotension may be a limitation to therapy, especially in early on when angina is severe or when patients are hypersensitive to the effects of nitrates. The headache usually disappears during treatment.
Reported adverse events are listed below by class of device.
- Blood and lymphatic system disorders
Rare: Methaemoglobinaemia
- Nervous system disorders: dizziness, headache
- Disorders of the eye: blurred vision
- Cardiac disorders: tachycardia , palpitation,paradoxical bradycardia, syncope
- Vascular disorders: postural hypotension
- Gastrointestinal disorders: nausea,digestive troubles
- Skin and subcutaneous tissue disorders: rash
- General disorders and administration site alterations impairments
General disorders: flushing with erythema, weakness, sweating
Very rare: cyanosis
Alteration of the site of administration
Burning, erithema
Methaemoglobinaemia has been associated with prolonged treatment or with high doses.
Compliance with the instructions in the leaflet reduces the risk of side effects.

SHELF LIFE AND STORAGE

See the expiration date printed on the packaging. This date refers to the product unopened, properly stored.
Warning: do not take this medicine after the expiration date printed on the packaging use.

DATE OF LAST (PARTIAL) REVISION OF THE TEXT

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