SCHEDULING STATUS: S6

PROPRIETARY NAME (AND DOSAGE FORM):

VALORON® DROPS

COMPOSITION:

The active constituent of VALORON is tilidine hydrochloride hemihydrate.

Each ml of drops contains:

Tilidine hydrochloride		100 mg
Alcohol		18,7 % v/v
Preservatives:	Sodium methylparaben	0,07 % m/v
	Sodium propylparaben	0,03 % m/v

[twenty drops = 0,5 ml = 50 mg]

PHARMACOLOGICAL CLASSIFICATION:

A 2.9 Other analgesics.

PHARMACOLOGICAL ACTION:

Tilidine is an orally-absorbed synthetic narcotic analgesic.

Pharmacokinetics and Metabolism:

Tilidine is a prodrug, which, following oral administration, is converted to the active analgesic metabolite, nortilidine. The oral bioavailability of tilidine itself is of the order of 6 %. The half-life of elimination of nortilidine is of the order of 3½ hours; peak plasma levels of nortilidine are achieved approximately 45 minutes following oral administration.

Only 3 % of the oral dose is eliminated via the renal route in the form of nortilidine, and less than 0,1 % as unchanged tilidine. The active metabolite nortilidine is eliminated by the hepatic route.

INDICATIONS:

VALORON is indicated for the relief of acute, moderate to severe pain, and chronic cancer-related pain.

CONTRAINDICATIONS:

VALORON is contraindicated in patients with a history of hypersensitivity to this drug.

It should not be used in conditions in which an increase in intracranial pressure may be dangerous.

VALORON should not be used in the management of head injuries, acute alcoholism, after operations on the biliary tract, and in the presence of cyanosis or other significant disturbances of respiratory function.

VALORON should not be used in the presence of myocardial ischaemia.

Contraindicated in porphyria.

Contraindicated in patients being treated with monoamine oxidase inhibitors or within 14 days of discontinuing such treatment.

Safety in pregnancy and lactation has not been established.

WARNINGS:

The potential for significant respiratory depression must always be considered.

DOSAGE AND DIRECTIONS FOR USE:

Adult dosage: 20 drops undiluted 3 to 4 times daily. May be taken with sugar. Use undiluted perilingually or sublingually. If required, the indicated daily dosage may be increased at the discretion of the physician to 100 mg followed by the same dosage 2 hours later, followed by 100 mg 4 to 5 hours later. Thereafter 20 drops 6 to 8 hourly.

Children's dosage: VALORON should not be administered to infants under 1 year of age.

1 mg/kg per single dose should not be exceeded.

The following tabulation indicates the recommended dosage according to body mass and age.

1 drop = 2,5 mg

Mass (kg)	No of drops 3 to 4 times daily	mg	Average mass for age
5 - 7,4	2	5	
7,5 - 9,9	3	7,5	10,5 kg = 1 yr
10 - 12,4	4	10	12,5 kg = 2 yrs
12,5 - 14,9	5	12,5	14,8 kg = 3 yrs
15 - 17,4	6	15	17 kg = 4 yrs
17,5 - 19,9	7	17,5	19 kg = 5 yrs
20 - 22,4	8	20	21 kg = 6 yrs
22,5 - 24,9	9	22,5	23 kg = 7 yrs
25 - 27,4	10	25	26 kg = 8 yrs
27,5 - 29,9	11	27,5	29 kg = 9 yrs
30 - 32,4	12	30	32 kg = 10 yrs
32,5 - 34,9	13	32,5	36 kg = 11 yrs
35 - 37,4	14	35	40 kg = 12 yrs
37,5 - 40	15	37,5	46 kg = 13 yrs

SIDE EFFECTS AND SPECIAL PRECAUTIONS:

Tilidine hydrochloride may cause nausea, vomiting, constipation, drowsiness, confusion, dry mouth, sweating, facial flushing, vertigo, bradycardia, palpitations, orthostatic hypotension, hypothermia, restlessness, changes of mood and miosis. Micturition may be difficult and there may be ureteric or biliary spasm. Raised intracranial pressure may occur. Reactions such as urticaria and pruritus may occur.

Tilidine hydrochloride should be given with caution to patients with hypothyroidism, adrenocortical

insufficiency, impaired liver function, prostatic hypertrophy or shock. It should be used with caution in patients with inflammatory or obstructive bowel disorders. The dosage should be reduced in elderly and debilitated patients.

The administration of tilidine hydrochloride during labour may cause respiratory depression in the new-born infant.

The depressant effects of tilidine hydrochloride are enhanced by depressants of the central nervous system such as alcohol, anaesthetics, hypnotics and sedatives, and neuroleptics such as phenothiazines. Tilidine hydrochloride is subject to abuse and drug dependence may develop especially after repeated administration. Contact dermatitis has been reported.

Patients taking tilidine should not drive motor vehicles, operate machinery or drink alcoholic beverages.

In patients with impaired kidney function it might be advisable to reduce the tilidine dose.

Interactions:

Monoamine oxidase inhibitors may intensify the effects of opioids and can cause confusion, anxiety, respiratory depression, hypertension and coma.

Sedatives, hypnotics, neuroleptics and antidepressants may potentiate the central nervous system-depressant effects of the opioids, and may aggravate hypotension.

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT:

Respiratory depression and depression of other vital functions may occur. Convulsions may occur, particularly in children.

Treatment of overdosage is symptomatic and supportive and may include the antidotal use of repeated doses of naloxone, gastric lavage, or emesis.

IDENTIFICATION:

Clear, colourless liquid in amber glass bottles.

PRESENTATION:

Amber glass bottles of 10 ml. A dropper is attached to the neck of the bottle.

STORAGE INSTRUCTIONS:

Store at or below 25 ^{o}C in a cool, dry place.

KEEP OUT OF REACH OF CHILDREN.

REGISTRATION NUMBER:

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NAME AND BUSINESS ADDRESS OF APPLICANT:

Pfizer Laboratories (Pty) Ltd

85 Bute Lane

Sandton

2196

South Africa

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