1.3 Product information

1.3.1 Summary of Product Characteristics (SmPC)

SUMMARY OF PRODUCT CHARACTERISTICS

PARACETAMOL INFUSION 1.0g/100mL

1 NAME OF THE MEDICINAL PRODUCT

Paracetamol Infusion 1.0 g/100mL

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each bottle contains 1.0g of Paracetamol.

3 PHARMACEUTICAL FORM

Solution for infusion

4 CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS

Paracetamol Infusion is indicated for the short-term treatment of moderate pain, especially following surgery, and for the short-term treatment of fever, when administration by intravenous route is clinically justified by an urgent need to treat pain or hyperthermia and/or when other routes of administration are not possible.

4.2 POSOLOGY AND METHOD OF ADMINISTRATION

Paracetamol may be given by intravenous infusion.

Adults and adolescents weighing over 50 kg may be given single doses of 1 g every 4 hours to a maximum of 4 g in 24 hours.

Those weighing between 33 and 50 kg may be given a dose of 15 mg/kg every 4 hours to a maximum daily dose of 60 mg/kg.

4.3 CONTRAINDICATIONS

-In patients with hypersensitivity to paracetamol or to propacetamol hydrochloride (prodrug of paracetamol) or to any of the excipients.

-In cases of severe hepatocellular insufficiency.

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

It is recommended that a suitable analgesic oral treatment be used as soon as this route of administration is possible. In order to avoid the risk of overdose, check that other medicines administered do not contain paracetamol. Doses higher than those recommended entail the risk of very serious liver damage. Clinical signs and symptoms of liver damage are not usually seen until two days, and up to a maximum of 4-6 days, after administration. Treatment with antidote should be given as soon as possible.

Paracetamol Infusion contains less than 1mmol sodium (23mg) per 100ml of Paracetamol infusion i.e. essentially 'sodium free'.

Paracetamol should be used with caution in cases of: hepatocellular insufficiency, severe

renal insufficiency (creatinine clearance≤30 mL/min), chronic alcoholism, chronic malnutrition (low reserves of hepatic glutathione), and dehydration.

4.5 INTERACTION WITH OTHER MEDICINAL PRODUCTS AND OTHER FORMS OF INTERACTION

• Probenecid causes an almost 2-fold reduction in clearance of paracetamol by inhibiting its conjugation with glucuronic acid. A reduction in the paracetamol dose should be considered if it is to be used concomitantly with probenecid.

• Salicylamide may prolong the elimination t½ of paracetamol.

• Caution should be taken with the concomitant intake of enzyme-inducing substances (see section 4.9 Overdose).

• Concomitant use of paracetamol (4 g per day for at least 4 days) with oral anticoagulants may lead to slight variations of INR values. In this case, increased monitoring of INR values should be conducted during the period of concomitant use as well as for 1 week after paracetamol treatment has been discontinued.

4.6 PREGNANCY AND LACTATION

Pregnancy

Clinical experience of the intravenous administration of paracetamol is limited. However, epidemiological data from the use of oral therapeutic doses of paracetamol indicate no undesirable effects in pregnancy or on the health of the foetus /newborn infant.

Prospective data on pregnancies exposed to overdoses did not show any increase in the risk of malformation.

No reproductive studies with the intravenous form of paracetamol have been performed in animals. However, studies with the oral route did not show any malformation or foetotoxic effects.

Nevertheless, Paracetamol Infusion should only be used during pregnancy after a careful benefit risk assessment. In this case, the recommended posology and duration must be strictly observed.

Lactation

After oral administration, paracetamol is excreted into breast milk in small quantities. No undesirable effects on nursing infants have been reported. Consequently, Paracetamol 10 mg/ml Solution for Infusion may be used in breast-feeding women.

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

Not relevant

4.8 UNDESIRABLE EFFECTS

Organ System	Rare (≥ 1/10,000 to < 1/1,000)	Very rare (< 1/10,000)
General	Malaise	Hypersensitivity reaction
Cardiovascular	Hypotension	/
Liver	Increased levels of hepatic transaminases	/
Skin and subcutaneous tissue disorders	/	Very rare cases of serious skin reactions have been reported.
Platelet/blood	/	Thrombocytopenia Leucopenia, Neutropenia

5 PHARMACOLOGICAL PROPERTIES

5.1 PHARMACODYNAMIC PROPERTIES

Pharmacotherapeutic group : other analgesics and antipyretics

ATC Code : N02BE01

The precise mechanism of the analgesic and antipyretic properties of paracetamol has yet to be established; it may involve central and peripheral actions.

Paracetamol Infusion provides onset of pain relief within 5 to 10 minutes after the start of administration. The peak analgesic effect is obtained in 1 hour and the duration of this effect is usually 4 to 6 hours.

Paracetamol Infusion reduces fever within 30 minutes after the start of administration with a duration of the antipyretic effect of at least 6 hours.

5.2 PHARMACOKINETIC PROPERTIES

Adults

***Absorption*:**

Paracetamol pharmacokinetics is linear up to 2 g after single administration and after repeated administration during 24 hours.

The bioavailability of paracetamol following infusion of 500mg and 1g of Paracetamol Infusion is similar to that observed following infusion of 1g and 2 g propacetamol (containing 500mg and 1 g paracetamol respectively). The maximal plasma concentration (Cmax) of paracetamol observed at the end of 15-minutes intravenous infusion of 500mg and 1g of Paracetamol Infusion is about 15µg/ml and 30 µg/ml respectively.

***Distribution*:**

The volume of distribution of paracetamol is approximately 1 L/kg.

Paracetamol is not extensively bound to plasma proteins.

Following infusion of 1g paracetamol, significant concentrations of paracetamol (about 1.5 µg/mL) were observed in the cerebrospinal fluid at and after the 20th minute following infusion.

***Metabolism*:**

Paracetamol is metabolised mainly in the liver following two major hepatic pathways: glucuronic acid conjugation and sulphuric acid conjugation. The latter route is rapidly saturable at doses that exceed the therapeutic doses. A small fraction (less than 4%) is metabolised by cytochrome P450 to a reactive intermediate (N-acetyl benzoquinone imine) which, under normal conditions of use, is rapidly detoxified by reduced glutathione and eliminated in the urine after conjugation with cysteine and mercapturic acid. However, during massive overdosing, the quantity of this toxic metabolite is increased.

***Elimination*:**

The metabolites of paracetamol are mainly excreted in the urine. 90% of the dose administered is excreted within 24 hours, mainly as glucuronide (60-80%) and sulphate

(20-30%) conjugates. Less than 5% is eliminated unchanged. Plasma half-life is 2.7 hours and total body clearance is 18 L/h.

Neonates, infants and children:

The pharmacokinetic parameters of paracetamol observed in infants and children are similar to those observed in adults, except for the plasma half-life that is slightly shorter (1.5 to 2 h) than in adults. In neonates, the plasma half-life is longer than in infants i.e. around 3.5 hours. Neonates, infants and children up to 10 years excrete significantly less glucuronide and more sulphate conjugates than adults.

Table - Age related pharmacokinetic values (standardised clearance, *CLstd/Foral (L.h-1 70kg-1)

Age	Weight (kg)	CLstd /Foral (L.h-1 70kg-1)
40 weeks PCA	3.3	5.9
3 months PNA	6	8.8
6 months PNA	7.5	11.1
1 year PNA	10	13.6
2 years PNA	12	15.6
5 years PNA	20	16.3
8 years PNA	25	16.3

*CLstd is the population estimate for CL

5.3 PRECLINICAL SAFETY DATA

Preclinical data reveal no special hazard for humans beyond the information included in other sections of the SmPC.

Studies on local tolerance of Paracetamol Infusion in rats and rabbits showed good tolerability.

Absence of delayed contact hypersensitivity has been tested in guinea pigs.

6 PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS

Mannitol

Cysteine hydrochloride, monohydrate

Anhydrous disodium hydrogen phosphate

Hydrochloric acid/ Sodium hydroxide

Water for Injection

6.2 INCOMPATIBILITIES

This medicinal product must not be mixed with other medicinal products except for dilution with 0.9% sodium chloride or 5% glucose solution.

6.3 SHELF LIFE

24 months

6.4 SPECIAL PRECAUTIONS FOR STORAGE

Store below 25℃. Protect from light and heat.

6.5 NATURE AND CONTENTS OF CONTAINER

100ml colorless glass bottle with bromobutyl stopper and an aluminum cap.

6.6 SPECIAL PRECAUTIONS FOR DISPOSAL

Before administration, the product should be visually inspected for any particulate matter and discolouration. For single use only. Any unused solution should be discarded.

7 MARKETING AUTHORISATION HOLDER

Not applicable

8 MARKETING AUTHORISATION NUMBER(S)

Not applicable

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Not applicable

1.3.2 Labelling (outer & inner labels)

Please refer to labels on the specimens. Enclosed

1.3.3 Package Insert (also known as patient information PIL)

100ml colorless glass bottle with bromobutyl stopper and an aluminum cap.

6.6 SPECIAL PRECAUTIONS FOR DISPOSAL

Before administration, the product should be visually inspected for any particulate matter and discolouration. For single use only. Any unused solution should be discarded.

7 MARKETING AUTHORISATION HOLDER

Not applicable

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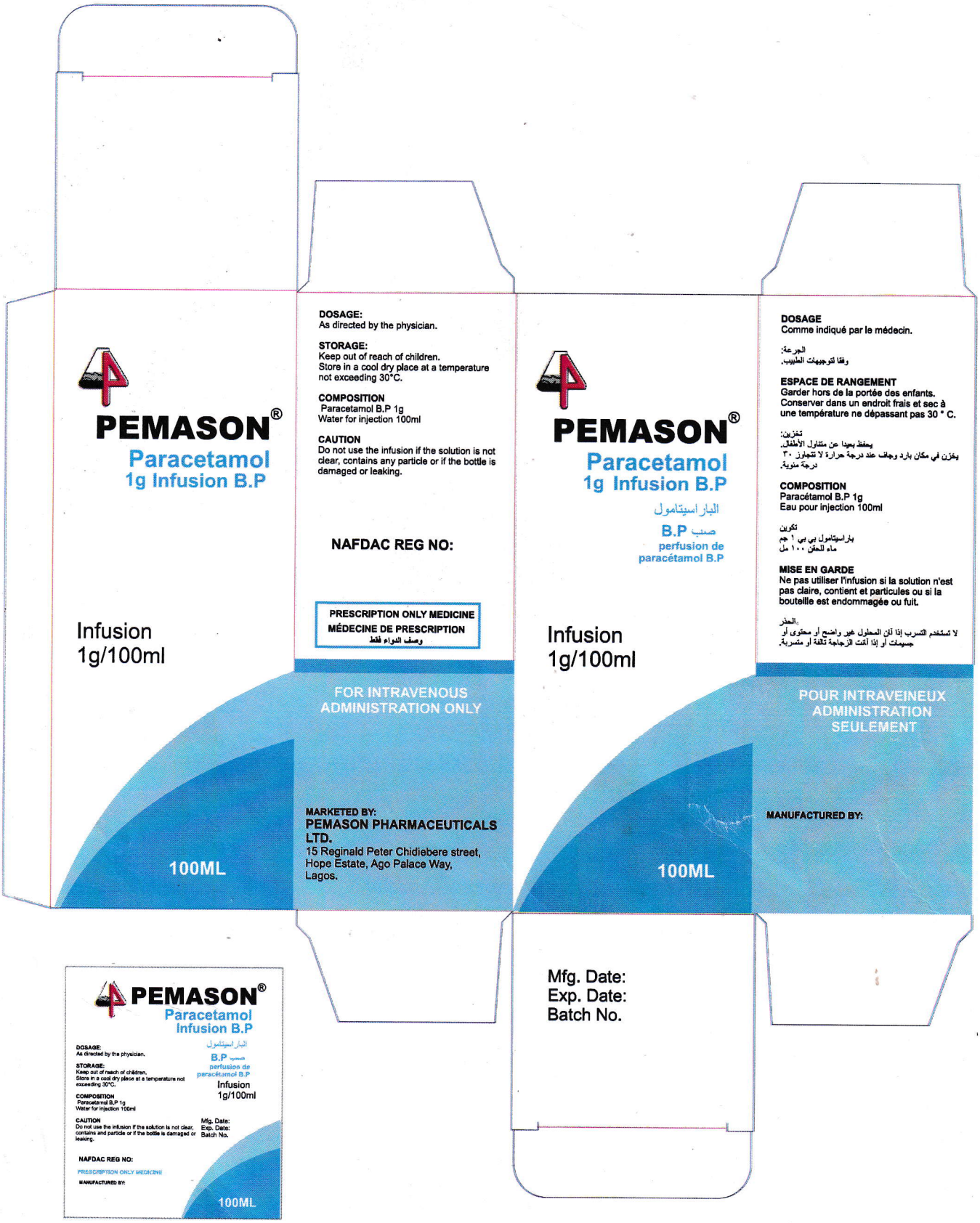
1.3.3 Package Insert (also known as patient information PIL)


PEMASON®
Paracetamol
1g Infusion B.P
Infusion
1g/100ml
100ML
DOSAGE:
As directed by the physician.
STORAGE:
Keep out of reach of children.
Store in a cool dry place at a temperature not exceeding 30°C.
COMPOSITION
Paracetamol B.P 1g
Water for injection 100ml
CAUTION
Do not use the infusion if the solution is not clear, contains any particle or if the bottle is damaged or leaking.
NAFDAC REG NO:
PRESCRIPTION ONLY MEDICINE
MÉDECINE DE PRESCRIPTION
وصف الدواء فقط
FOR INTRAVENOUS ADMINISTRATION ONLY
MARKETED BY:
PEMASON PHARMACEUTICALS LTD.
15 Reginald Peter Chidiebere street,
Hope Estate, Ago Palace Way,
Lagos.
PEMASON®
Paracetamol
1g Infusion B.P
البارا سيتامول
B.P صب
perfusion de paracétamol B.P
Infusion
1g/100ml
100ML
DOSAGE
Comme indiqué par le médecin.
الجرعة:
وفقا لتوجيهات الطبيب.
ESPACE DE RANGEMENT
Garder hors de la portée des enfants.
Conserver dans un endroit frais et sec à une température ne dépassant pas 30 ° C.
تخزين:
يحفظ بعيدا عن متناول الأطفال.
يخزن في مكان بارد وجاف عند درجة حرارة لا تتجاوز ٣٠ درجة مئوية.
COMPOSITION
Paracétamol B.P 1g
Eau pour injection 100ml
تكوين
باراسيتامول بي بي ١ جم
ماء للحقن ١٠٠ مل
MISE EN GARDE
Ne pas utiliser l'infusion si la solution n'est pas claire, contient et particules ou si la bouteille est endommagée ou fuit.
الحذر.
لا تستخدم التسرب إذا كان المحلول غير واضح أو محتوى أو جسيمات أو إذا كانت الزجاجة تالفة أو متسربة.
POUR INTRAVEINEUX ADMINISTRATION SEULEMENT
MANUFACTURED BY:
Mfg. Date:
Exp. Date:
Batch No.
PEMASON®
Paracetamol
Infusion B.P
البارا سيتامول
B.P صب
perfusion de paracétamol B.P
Infusion
1g/100ml
DOSAGE:
As directed by the physician.
STORAGE:
Keep out of reach of children.
Store in a cool dry place at a temperature not exceeding 30°C.
COMPOSITION
Paracetamol B.P 1g
Water for injection 100ml
CAUTION
Do not use the infusion if the solution is not clear, contains and particle or if the bottle is damaged or leaking.
Mfg. Date:
Exp. Date:
Batch No.
NAFDAC REG NO:
PRESCRIPTION ONLY MEDICINE
MANUFACTURED BY:
100ML

100ml colorless glass bottle with bromobutyl stopper and an aluminum cap.

6.6 SPECIAL PRECAUTIONS FOR DISPOSAL

Before administration, the product should be visually inspected for any particulate matter and discolouration. For single use only. Any unused solution should be discarded.

7 MARKETING AUTHORISATION HOLDER

Not applicable

8 MARKETING AUTHORISATION NUMBER(S)

Not applicable

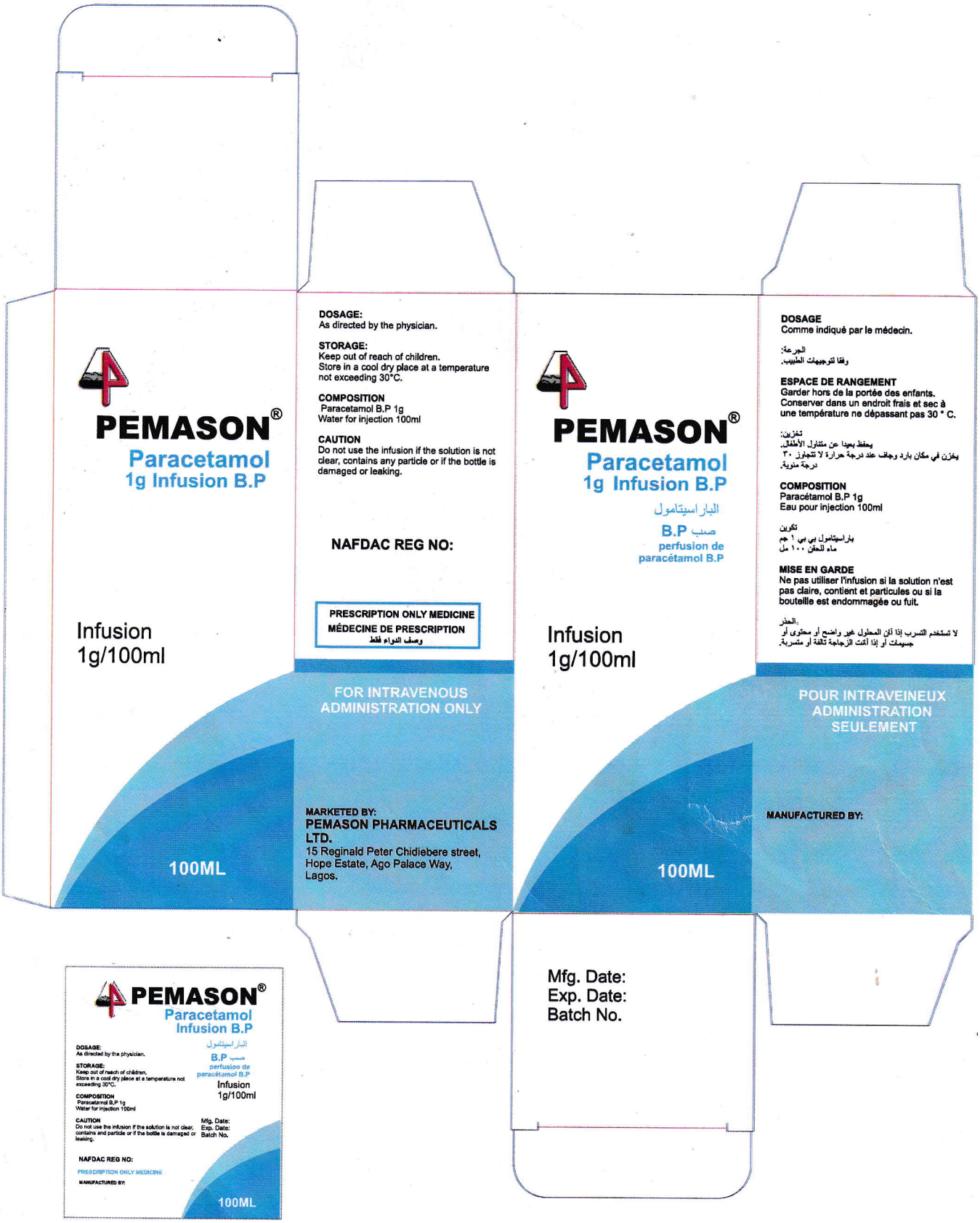
9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Not applicable

1.3.2 Labelling (outer & inner labels)

Please refer to labels on the specimens. Enclosed

1.3.3 Package Insert (also known as patient information PIL)


PEMASON®
Paracetamol
1g Infusion B.P
Infusion
1g/100ml
100ML
DOSAGE:
As directed by the physician.
STORAGE:
Keep out of reach of children.
Store in a cool dry place at a temperature not exceeding 30°C.
COMPOSITION
Paracetamol B.P 1g
Water for injection 100ml
CAUTION
Do not use the infusion if the solution is not clear, contains any particle or if the bottle is damaged or leaking.
NAFDAC REG NO:
PRESCRIPTION ONLY MEDICINE
MÉDECINE DE PRESCRIPTION
وصف الدواء فقط
FOR INTRAVENOUS ADMINISTRATION ONLY
MARKETED BY:
PEMASON PHARMACEUTICALS LTD.
15 Reginald Peter Chidiebere street,
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PEMASON®
Paracetamol
1g Infusion B.P
البارا سيتامول
B.P صب
perfusion de paracétamol B.P
Infusion
1g/100ml
100ML
DOSAGE
Comme indiqué par le médecin.
الجرعة:
وفقا لتوجيهات الطبيب.
ESPACE DE RANGEMENT
Garder hors de la portée des enfants.
Conserver dans un endroit frais et sec à une température ne dépassant pas 30 ° C.
تخزين:
يحفظ بعيدا عن متناول الأطفال.
يخزن في مكان بارد وجاف عند درجة حرارة لا تتجاوز ٣٠ درجة مئوية.
COMPOSITION
Paracétamol B.P 1g
Eau pour injection 100ml
تكوين
باراسيتامول بي بي ١ جم
ماء للحقن ١٠٠ مل
MISE EN GARDE
Ne pas utiliser l'infusion si la solution n'est pas claire, contient et particules ou si la bouteille est endommagée ou fuit.
الحذر.
لا تستخدم التسرب إذا كان المحلول غير واضح أو محتوى أو جسيمات أو إذا كانت الزجاجة تالفة أو متسربة.
POUR INTRAVEINEUX ADMINISTRATION SEULEMENT
MANUFACTURED BY:
Mfg. Date:
Exp. Date:
Batch No.
PEMASON®
Paracetamol
Infusion B.P
البارا سيتامول
B.P صب
perfusion de paracétamol B.P
Infusion
1g/100ml
DOSAGE:
As directed by the physician.
STORAGE:
Keep out of reach of children.
Store in a cool dry place at a temperature not exceeding 30°C.
COMPOSITION
Paracetamol B.P 1g
Water for injection 100ml
CAUTION
Do not use the infusion if the solution is not clear, contains and particle or if the bottle is damaged or leaking.
Mfg. Date:
Exp. Date:
Batch No.
NAFDAC REG NO:
PRESCRIPTION ONLY MEDICINE
MANUFACTURED BY:
100ML

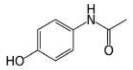
128*214mm

PEMASON

PARACETAMOL INFUSION

NAFDAC REG.NO.:

-COMPOSITION/ACTIVE INGREDIENTS:
-Each 100ml glass bottle contains Paracetamol 1000mg
-CHEMICAL NAME:
Paracetamol: N-(4-Hydroxyphenyl)acetamide.
-STRUCTURAL FORMULAR :



-MOLECULAR FORMULAR :
Paracetamol: $C_8H_9NO_2$

-MOLECULAR WEIGHT:
Paracetamol: 151.16 g/mol.

-PHARMACOLOGY:
PEMASON Paracetamol infusion belongs to the group of drug products classified as Analgesics and anti-pyretics. It does not have marked anti-inflammatory activity though some people use it for such. Mechanism of action of Paracetamol is not fully understood. Paracetamol does not appear to inhibit the cyclooxygenase (COX) system outside the central nervous system, but does so selectively only in the brain where it is believed to achieve this, not by active site blockade, but by reducing COX which must be oxidized to function. Paracetamol also reduces fever and pain by its other actions on the endogenous cannabinoid system in the brain.
Following the administration of 500mg and 1 g dose, onset of action is about 8 minutes, the maximal plasma concentration (Cmax) of paracetamol observed at the end of 15minutes is about 15microgram/ml and 30microgram respectively.
Paracetamol is 10-25% bound to protein with a bio-availability of 63-89%. Volume of distribution is approximately 1L/kg.
It is predominantly metabolized in the liver by two major hepatic pathways: glucuronic acid conjugation and sulphuric acid conjugation, and a small fraction (<4%) by cytochrome P450. The major metabolites (APAP glucuronide and APAP sulfate) with an elimination T1/2 of 1-4 hours are excreted 85-90% in urine within 24hours.
Neonates, infants and children: The pharmacokinetic parameters of paracetamol observed in infants and children are similar to those of adults, except for the plasma half-life that is slightly shorter (1.5-2 h) than in adults. In Neonates, the plasma half-life is longer than in infants i.e. 3.5 hours. Neonates, infants and children up to 10 years excrete significantly less glucuronide and more sulphate conjugates than adults.

-INDICATION:
PEMASON Paracetamol infusion is indicated for the short-term treatment and management of mild to moderate pain especially after surgery, fever and hyperthermia especially when other routes of administration are not possible.

-DOSAGE:
PEMASON Paracetamol infusion is given by intravenous infusion.
Adults 50kg and over: 1g given every 4-6 hours but not exceeding 4g in 24 hours.
Children, Pediatric patients and Neonates: Will use fractions of the adult dose calculated using the following table every 4-6 hours: The maximum dose for each group should never be exceeded.

Patient weight	Dose per administration	Volume per administration	Maximum volume of paracetamol	Maximum daily dose
< 10kg	7.5mg/kg	0.75ml/kg	7.5ml	30mg/kg
>10kg--- < 33kg	15mg/kg	1.5ml/kg	49.5ml	60mg/kg not exceeding 2g
>33kg– <50kg	15mg/kg	1.5ml/kg	75ml	60mg/kg not exceeding 3g

Patients weighing less than 10 kg will require smaller doses/volumes.
There is no safety and efficacy data available for preterm new infants. The maximum daily doses as presented in the chart above are for those not receiving other paracetamol-containing products.

-CONTRA-INDICATION:
PEMASON Paracetamol infusion is contra-indicated to patients sensitive to paracetamol, its prodrug (propacetamol) or any of the other excipients.
Use with caution in hepatocellular insufficiency, severe renal insufficiency (creatinine clearance <30ml/min), chronic alcoholism, chronic malnutrition, (low reserves of hepatic glutathione), and dehydration.

-PREGNANCY/LACTATION:
Experimental studies in animals and humans so far, have shown no congenital malformations when paracetamol is used during pregnancy. It also does not affect closure of fetal ductus arteriosus like other NSAIDS, however, drug use in pregnancy/lactation should be under supervision of healthcare practitioners who will be able to weigh the benefits against the possible risks to the fetus.
Paracetamol for now remains the first-line recommended drug for pain and fever even in pregnancy.

-SIDE-EFFECTS:
The side effects of Paracetamol are rare and are usually mild, although hematological reactions including thrombocytopenia, leucopenia, pancytopenia, neutropenia and agranulocytosis have been reported. Skin rashes and other hypersensitivity reactions asthma, occur occasionally. Rare but severe adverse effects especially in overdosage include Stevens-johnson's syndrome, toxic epidermal necrosis and liver damage (acute liver failure).

-PRECAUTIONS/WARNINGS:
Evaluate kidney/renal status before use and reduce dose in renal insufficiency. In cases of severe renal impairment (creatinine clearance 10-30ml/min), the elimination of paracetamol is slightly delayed, the elimination half-life ranging from 2-5.3 hours. For the glucuronide and sulphate conjugates, the elimination rate is 3 times slower in subjects with severe renal impairment than in healthy subjects. So patients with severe renal impairment (creatinine clearance <30ml/min) the interval between administration should be increased to 6 hours.

-INTERACTIONS:
The concurrent use of paracetamol with other medications may affect the activity of either paracetamol or the other product.
-Use with Metoclopamide may increase the absorption of paracetamol making it more available in the body.
-Prolonged use with Warfarin may possibly increase the anti-coagulant effect of warfarin.

-SHELF-LIFE:
2 years.

-STORAGE:
Store below 25°C.
Protect from light and heat.
Keep out of reach of children.

-PACKAGING:
PEMASON Paracetamol infusion is packed in: 100ml glass bottles.

-MANUFACTURED BY:
SICHUAN KELUN PHARMACEUTICAL CO., LTD.
South of No.2 Road, Xindu Satellite City Industrial Development Zone, Chengdu, Sichuan, P. R. China.

-MARKETED BY:
PEMASON PHARMACEUTICALS LTD.
15 Reginald Peter Chidiebere Street, Hope Estate, Ago Palace Way, Lagos.