PROVAS® Infusion
(Paracetamol)

COMPOSITION:
Each 100ml PROVAS® vial contains 1000mg Paracetamol

DESCRIPTION:
PROVAS® (Paracetamol/Acetaminophen) is an established antipyretic and analgesic

CHEMISTRY:
PROVAS® (Paracetamol/Acetaminophen) is part of the class of drug known as "aniline analgesic". It is the active metabolite of Phenacetin

MECHANISM OF ACTION:
PROVAS® (Paracetamol/Acetaminophen) reduces the production of prostaglandins (Pro-inflammatory chemicals). PROVAS® (Paracetamol/Acetaminophen) reduces the oxidized form of Cyclo-Oxygenase enzyme, preventing from forming pro-inflammatory chemicals. PROVAS® (Paracetamol/Acetaminophen) also modulates the endogenous cannabinoid system. Paracetamol is metabolized to AM404, a compound with several actions; most important, it inhibits the uptake of endogenous cannabinoid/vanilloid anandamide by neuron. Anandamide uptake would result in the activation of main pain receptor of the body. Furthermore, AM404 inhibits sodium channels

PHARMACOKINETICS:
Adults:
Absorption:
Paracetamol pharmacokinetics is linear up to 2 g after single administration and after repeated administration during 24 hours
The maximal plasma concentration (Cmax) of paracetamol observed at the end of 15-minutes intravenous infusion of 1 g of PROVAS® (Paracetamol/Acetaminophen) is 30 µg/ml

Distribution:
The volume of distribution of paracetamol is approximately 1 L/kg
Paracetamol is not extensively bound to plasma proteins
Following infusion of 1 g paracetamol, significant concentrations of paracetamol (about 1.5 µg/mL) were observed in the cerebrospinal fluid at and after the 20 minute following infusion

Metabolism:
Paracetamol is metabolised mainly in the liver following two major hepatic pathways: glucuronic acid conjugation and sulphuric acid conjugation

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

PHARMACODYNAMICS:
PROVAS® 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
PROVAS® reduces fever within 30 minutes after the start of administration with duration of the antipyretic effect of at least 6 hours

INDICATIONS:
PROVAS® 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

DOSAGE AND ADMINISTRATION:

- **Adolescents and adults weighing more than 50 kg:**
  Paracetamol 1g per administration, i.e. one 100 ml vial, up to four times a day
  The minimum interval between each administration must be 4 hours
  The maximum daily dose must not exceed 4g
- **Children weighing more than 33 kg (approximately 11 years old), adolescents and adults weighing less than 50kg:**
  Paracetamol 15mg/kg per administration, i.e. 1.5ml solution per kg up to four times a day
  The minimum interval between each administration must be 4 hours
  The maximum daily dose must not exceed 60 mg/kg (without exceeding 3g)
- **Children weighing more than 10kg (approximately 1 year old) and weighing less than 33kg:**
  Paracetamol 15mg/kg per administration, i.e. 1.5ml solution per kg up to four times a day
  The minimum interval between each administration must be 4 hours
  The maximum daily dose must not exceed 60mg/kg (without exceeding 2g)
- **Term newborn infants, infants, toddlers and children weighing less than 10kg (up to approximately 1 year old):**
  Paracetamol 7.5mg/kg per administration i.e. 0.75ml solution per kg up to four times a day
  The minimum interval between each administration must be 4 hours
  The maximum daily dose must not exceed 30mg/kg
  No safety and efficacy data are available for premature neonates
- **Severe renal insufficiency:** it is recommended, when giving paracetamol to patients with severe renal impairment (creatinine clearance 30 mL/min), to increase the minimum interval between each administration to 6 hours
- **Method of administration:** The paracetamol solution is administered as a 15-minute

Intravenous infusion

CONTRAINDICATIONS:
- Patients with hypersensitivity to paracetamol or to propacetamol hydrochloride (prodrug of paracetamol) or to any of the excipients
- In cases of severe hepatocellular insufficiency

PRECAUTIONS:
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

WARNINGS:
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 no 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

DRUG INTERACTIONS:
- 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 t1/2 of paracetamol
- Caution should be taken with the concomitant intake of enzyme-inducing substances
- Concomitant use of paracetamol (4 g per day for at least 4 days) with oral anticoagulants may lead to slight variations of INR (International Normalized Ratio) 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

UNDESIRABLE EFFECTS:
Very rare cases of hypersensitivity reactions ranging from simple skin rash or urticaria to anaphylactic shock have been reported and require discontinuation of treatment

OVERDOSAGE:
There is a risk of poisoning, particularly in elderly subjects, in young children, in patients with liver disease, in cases of chronic alcoholism, in patients with chronic malnutrition and in patients receiving enzyme inducers. Overdosing may be fatal in these cases

SHELF LIFE:
From a microbiological point of view, unless the method of opening precludes the risk of microbial contamination, the product should be used immediately. If not used immediately, in-use storage times and conditions are the responsibility of the user
If diluted in 0.9% sodium chloride or 5% glucose, the solution should also be used immediately. However, if the solution is not used immediately, do not store for more than 1 hour (infusion time included)

STABILITY: See expiry on the pack

PRESENTATION:
PROVAS® 100ml IV solution for infusion

INSTRUCTIONS:
Dosage as directed by the physician
Keep out of reach of children
Avoid exposure to heat and light
Store at 25ºC or below
Improper storage may deteriorate the medicine
Avoid freezing and injection should not be used if container is leaking, solution is cloudy or it contains undissolved particles

Manufactured by:
SAMI PHARMACEUTICALS (PVT) LTD.
F-95, S.I.T.E., Karachi-Pakistan

پرووَاس انفیوژن
(پیراسیٹامول)
خوراک: ڈاکٹر کی ہدایت کے مطابق استعمال کریں
ہدایات: بچوں کی پہنچ سے دور رکھیں
دوا کو دھوپ اور گرمی سے محفوظ ۲۵ ڈگری سینٹی گریڈ
یا اس سے کم درجہ حرارت پر رکھیں ورنہ دوا خراب ہو جائے گی
تنبیہ: منجمد ہونے سے بچائیں اور انجکشن کے ایک ہونے، دُھندلا ہونے
یا اس میں کوئی غیر حل پزیر شے نظر آنے کی صورت میں ہرگز استعمال نہ کریں

PROVAS® Injection
(Paracetamol)

COMPOSITION:
Each 2ml contains:
Paracetamol BP....300mg

For intramuscular use only

MODE OF ACTION:
Paracetamol inhibits the synthesis of prostaglandin in the central nervous system and peripherally blocks pain impulse generation; produces antipyresis from inhibition of hypothalamic heat-regulating center

INDICATIONS:
For symptomatic relief of fever and pain associated with common infections like tonsillitis, upper respiratory tract infections, post-immunization reactions, after operations, pyrexia of unknown origin and other febrile and painful conditions where patient is unable to take oral medication

PRECAUTIONS:
Hypersensitivity to Paracetamol. Impaired liver or kidney function

CONTRAINDICATIONS:
Renal and Hepatic insufficiency

ADVERSE REACTIONS:
Hematological, skin and other allergic reactions

SIDE EFFECTS:
Nausea, vomiting and urticaria can be reported

DOSAGE AND ADMINISTRATION:
Adults: 2ml, intramuscularly six hourly
Children: ½ - 1ml, intramuscularly six hourly or 6mg/kg of the body weight. Not recommended for children under the age of two years. The dosage can be increased depending upon severity of the condition or as directed by the physician

STABILITY:
See expiry on the pack

PRESENTATION:
Provas® Injection in pack of 5's

INSTRUCTIONS:
Keep out of reach of children
Avoid exposure to heat and light
Store at 25°C or below
Improper storage may deteriorate the medicine

Avoid freezing and Injection should not be used if container is leaking, solution is cloudy or it contains un-dissolved particles

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6th June 2009