1. NAME OF THE MEDICINAL PRODUCT

Maxipol Paracetamol Suspension

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Maxipol Suspension contains 120mg Paracetamol in each 5ml.

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Oral Suspension

A reddish coloured strawberry flavoured suspension.

4. Clinical particulars

4.1 Therapeutic indications

Maxpol Paracetamol Suspension is indicated for the treatment of mild to moderate pain and as an antipyretic. It can be used in many conditions including headache, toothache, earache, teething, sore throat, colds & influenza, aches and pains and post-immunisation fever.

4.2 Posology and method ofadministration

Posology

For the relief of fever after vaccinations

3 and 4 months: 2.5ml. This dose may be given up to 4 times a day starting at the time of vaccination. Do not give more than 4 doses in any 24 hour period. Leave at least 4 hours between doses. If your baby still needs this medicine two days after receiving the vaccine talk to your doctor or pharmacist.

Pain and other causes of fever

Age 3 – 12 months:2.5ml – 5ml three times daily

Age 2 – 5 years: 5ml – 10ml three times daily

Age 6 – 12 years: 10ml – 20ml three times daily

- Do not give more than 4 doses in any 24 hour period
- Leave at least 4 hours between doses
- If symptoms persist after 3 days, consult your doctor.

S**hake the bottle thoroughly before use.**

The Elderly:

In the elderly, the rate and extent of paracetamol absorption is normal but plasma half-life is longer and paracetamol clearance is lower than in young adults.

Method of administration

Oral use.

4.3 Contraindications

Hypersensitivity to paracetamol or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

Do not exceed the recommended dose. Taking more than the recommended dose (overdose) may cause liver damage. In case of overdose, get medical help straight away. Quick medical attention is critical for adults as well as children even if signs or symptoms are not noticed.

Taking this product with other paracetamol-containing medicines could lead to overdose and should therefore be avoided.

Care is advised in the administration of paracetamol to patients with severe renal or severe hepatic impairment.

The hazards of overdose are greater in those with non-cirrhotic alcoholic liver disease. Chronic alcohol users should consult a doctor before use.

Patients should be informed about the signs of serious skin reactions and use of the drug should be discontinued at the first appearance of skin rash or any other sign of hypersensitivity.

The label contains the following statements:

Contains paracetamol.

Do not give with any other paracetamol containing products.

For oral use only.

Always use the measuring device supplied with the pack.

Do not give to babies less than 3 months of age.

For infants 3 months no more than 2 doses should be given.

Do not give more than 4 doses in any 24 hour period.

Leave at least 4 hours between doses.

Do not give this medicine to your child for more than 3 days without speaking to your doctor or pharmacist.

As with all medicines, if your child is currently taking any other medicine consult your doctor or pharmacist before using this product.

Keep out of the sight and reach of children.

Do not store above 30°C. Keep bottle in the outer carton.

It is important to shake the bottle for at least 10 seconds before use.

The leaflet contains the following statements:

Immediate medical advice should be sought in the event of an overdose even if the child seems well.

This is because too much paracetamol can cause delayed, serious liver damage.

Very rare cases of serious skin reactions have been reported. Symptoms may include:

- Skin reddening

- Blisters

- Rash

If skin reactions occur or existing skin symptoms worsen, stop use and seek medical help right away.

4.5 Interaction with other medicinal products and other forms of interaction

Metabolism of paracetamol possibly accelerated by carbamazepine, fosphenytoin, phenytoin, phenobarbital, primidone (also isolated reports of hepatotoxicity).

The speed of absorption of paracetamol may be increased by metoclopramide or domperidone and

absorption reduced by cholestyramine.

The anticoagulant effect of warfarin and other coumarins may be enhanced by prolonged regular use of paracetamol with increased risk of bleeding; occasional doses have no significant effect.

Chronic alcohol intake can increase the hepatotoxicity of paracetamol overdose and may have contributed to the acute pancreatitis reported in one patient who had taken an overdose of paracetamol. Acute alcohol intake may diminish an individual's ability to metabolise large doses of paracetamol, the plasma half-life of which can be prolonged.

4.6 Pregnancy and Lactation

Pregnancy
A large amount of data on pregnant women indicate neither malformative, nor feto/neonatal toxicity. Epidemiological studies on neurodevelopment in children exposed to paracetamol in utero show inconclusive results. If clinically needed, paracetamol can be used during pregnancy however it should be used at the lowest effective dose for the shortest possible time and at the lowest possible frequency.

When given to the mother in therapeutic doses (1 g single dose), paracetamol crosses the placenta into foetal circulation as early as 30 minutes after ingestion and is metabolised in the foetus by conjugation with sulfate and increasingly with glutathione.

Breast-feeding
Paracetamol is excreted in breast milk but not in a clinically significant amount. Available published data do not contraindicate breast-feeding.

Fertility
There is no information relating to the effects of this medicine on fertility.

4.7 Effects on ability to drive and use machines
None known.

4.8 Undesirable effects
Adverse drug reactions (ADRs) identified during clinical trials and post-marketing experience with paracetamol are listed below by System Organ Class (SOC).

The frequencies are defined according to the following convention:

Very common	≥1/10
Common	≥1/100 to <1/10
Uncommon	≥1/1,000 to <1/100)
Rare	≥1/10,000 to <1/1,000
Very rare	<1/10,000
Not known	(cannot be estimated from available data).

ADRs are presented by frequency category based on 1) incidence in adequately designed clinical trials or epidemiology studies, if available or 2) when incidence is unavailable, frequency category is listed as Not known.

System Organ Class (SOC)	Frequency	Adverse Drug Reaction (Preferred Term)
Blood and lymphatic system disorders	Not known	Blood disorder (including thrombocytopenia and agranulocytosis) [1]
Immune System Disorders	Very rare Very rare	Anaphylactic reaction Hypersensitivity
Hepatobiliary disorders	Not known	Liver injury[2]
Skin and Subcutaneous Tissue disorders	Very rare Not known	Rash Fixed eruption

	Not known Not known	Rash pruritic Urticaria
Renal and urinary disorders	Uncommon Not known	Nephropathy toxic Renal papillary necrosis[3]
Investigations	Not known	Transaminases increased[4]

[1] Reported following paracetamol use, but not necessarily causally related to the drug

[2] Chronic hepatic necrosis has been reported in a patient who took daily therapeutic doses of paracetamol for about a year

[3] Reported after prolonged administration

[4] Low level transaminase elevations may occur in some patients taking therapeutic doses of paracetamol; these elevations are not accompanied with liver failure and usually resolve with continued therapy or discontinuation of paracetamol.

Very rare cases of serious skin reactions have been reported.

Chronic hepatic necrosis has been reported in a patient who took daily therapeutic doses of paracetamol for about a year and liver damage has been reported after daily ingestion of excessive amounts for shorter periods. A review of a group of patients with chronic active hepatitis failed to reveal differences in the abnormalities of liver function in those who were long-term users of paracetamol nor was the control of the disease improved after paracetamol withdrawal.

4.9 Overdose

Liver damage is possible in adults and adolescents (≥12 years of age) who have taken 7.5g or more of paracetamol. It is considered that excess quantities of a toxic metabolite (usually adequately detoxified by glutathione when normal doses of paracetamol are ingested) become irreversibly bound to liver tissue. Ingestion of 5g or more of paracetamol may lead to liver damage if the patient has risk factors (see below)

Risk Factors:

If the patient

a) Is on long term treatment with carbamazepine, phenobarbitone, phenytoin, primidone, rifampicin, St John's Wort or other drugs that induce liver enzymes

OR

b) Regularly consumes ethanol in excess of recommended amounts

OR

c) Is likely to be glutathione deplete e.g, eating disorders, cystic fibrosis, HIV infection, starvation, cachexia

Symptoms

Symptoms of paracetamol overdosage in the first 24 hours are pallor, nausea, hyperhidrosis, malaise, vomiting, anorexia and abdominal pain. Liver damage may become apparent 12 to 48 hours after ingestion. This may include hepatomegaly, liver tenderness, jaundice, acute hepatic failure and hepatic necrosis. Abnormalities of glucose metabolism and metabolic acidosis may occur. Blood bilirubin, hepatic enzymes, INR, prothrombin time, blood phosphate and blood lactate may be increased. In severe poisoning, hepatic failure may progress to encephalopathy, haemorrhage, hypoglycaemia, cerebral oedema and death. Acute renal failure with acute tubular necrosis, strongly suggested by loin pain, haematuria and proteinuria, may develop even in the absence of severe liver damage. Cardiac arrhythmias and pancreatitis have been reported.

Haemolytic anaemia (in patients with glucose-6-phosphate dehydrogenase [G6PD] deficiency): Haemolysis has been reported in patients with G6PD deficiency, with use of paracetamol in overdose.

Management

Immediate treatment is essential in the management of paracetamol overdose. Despite a lack of significant early symptoms, patients should be referred to hospital urgently for immediate medical attention.

Symptoms may be limited to nausea or vomiting and may not reflect the severity of the overdose or the risk of organ damage. Management should be in accordance with established treatment guidelines, see BNF overdose section.

Treatment with activated charcoal should be considered if the overdose has been taken within 1 hour. Plasma paracetamol concentrations should be measured at 4 hours or later after ingestion (earlier concentrations are unreliable). Treatment with N-acetylcysteine may be used up to 24 hours after ingestion of paracetamol, however the maximum protective effect is obtained up to 8 hours post-ingestion. The effectiveness of the antidote declines sharply after this time. If required the patient should be given intravenous N-acetylcysteine, in line with the established dosage schedule. If vomiting is not a problem oral methionine may be a suitable alternative for remote areas, outside hospital. Management of patient who present with serious hepatic dysfunction beyond 24h from ingestion should be discussed with the NPIS or a liver unit.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Other Analgesics and Antipyretics (Anilides)

ATC Code: N02 BE01

Paracetamol has analgesic and antipyretic effects that do not differ significantly from those of aspirin. However it has only weak anti-inflammatory effects. It is only a weak inhibitor of prostaglandin biosynthesis although there is some evidence to suggest it may be more effective against enzymes in the central nervous system than in the periphery. This may in part account for its activity profile.

5.2 Pharmacokinetic properties

Absorption
Paracetamol is rapidly and almost completely absorbed from the gastrointestinal tract with peak plasma concentrations occurring 0.5-2 hours after dosing. The plasma half-life is approximately 2 hours after therapeutic doses in adults but is increased in neonates to about 5 hours.

Distribution
It is widely distributed through the body.

Biotransformation
Metabolism is principally by the hepatic microsomal enzymes and urinary excretion accounts for over 90% of the dose within 1 day. Virtually no paracetamol is excreted unchanged, the bulk being conjugated with glucoronic acid (60%), sulphuric acid (35%) or cysteine (3%).

Children have less capacity for glucuronidation of the drug than adults.

Elimination
Following therapeutic doses 90-100% of the drug is recovered in the urine within 24 hours.

5.3 Preclinical safety data

Preclinical data reveal no special hazard for humans based on conventional studies of single and repeated dose toxicity, genotoxicity, and carcinogenicity.

Conventional studies using the currently accepted standards for the evaluation of toxicity to reproduction and development are not available.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sucrose
Sorbitol Solution 70%
Glycerol
Xanthan Gum
Methyl Hydroxybenzoate
Strawberry Flavour
Allura Red
Deionised Water

6.2 Incompatibilities
None known

6.3 Shelf life
3 years.

6.4 Special precautions for storage
Do not store above 30°C. Keep bottle in the outer carton.

6.5 Nature and contents of container
Amber bottle with Ropp aluminium screw cap, fitted with an inner plastic measuring cap.
Pack size 60 ml.

6.6 Special precautions for disposal
No special requirements for disposal.

7 APPLICANT/MANUFACTURER
Avro Pharma Limited
Daid House Plot 2, Block J, Limca Way,
Isolo Industrial Estate, Oshodi-Apapa Expressway,
Isolo, Lagos State, Nigeria.
Tel: +234(1)2913955
Email: info.avropharma@gmail.com