SUMMARY OF PRODUCT CHARACTERISTICS (SMPC)

1. Name of the medicinal product

Vadimol Syrup

2. Qualitative and quantitative composition

Each 5 ml contains

Paracetamol BP 125 mg

3. Pharmaceutical form

Liquid Syrup

4. Clinical particulars

4.1 Therapeutic indications

For the treatment of mild to moderate pain, including headache, migraine, neuralgia, toothache, sore throat, period pains, aches and pains.

For the reduction of fever and to be used as an adjunctive treatment to relieve symptoms of cold and flu.

4.2 Posology and method of administration

Posology

<table>
<tr><td colspan="2">For the relief of fever after vaccinations at 2, 3 and 4 months
One 2.5 mL spoonful (small end). 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.</td></tr>
<tr><td>Age: 2 – 3 months</td><td>Dose</td></tr>
<tr><td>Pain and other causes of fever - if your baby weighs over 4 kg and was born after 37 weeks</td><td>One 2.5 mL spoonful (small end).
If necessary, after 4-6 hours, give a second 2.5 mL dose</td></tr>
<tr><td colspan="2">• Do not give to babies less than 2 months of age
• Leave at least 4 hours between doses</td></tr>
</table>

• Do not give more than 2 doses. This is to ensure that fever that may be due to a serious infection is quickly diagnosed. If your child is still feverish after two doses, talk to your doctor or pharmacist.		
Child's Age	**How Much**	**How often (in 24 hours)**
3 – 6 months	One 2.5 mL spoonful (small end)	4 times
6 – 24 months	One 5 mL spoonful (large end)	4 times
2 – 4 years	One 5.0 mL spoonful (large end) and one 2.5 mL spoonful (small end)	4 times
4 – 8 years	Two 5 mL spoonfuls (large end)	4 times
8 – 10 years	Three 5 mL spoonfuls (large end)	4 times
10 - 12 years	Four 5 mL spoonfuls (large end)	4 times
• 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		

Method of administration

For oral administration only

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

4.3 Contraindications

Hypersensitivity to paracetamol or to any of the excipients, Patients with severe hepatic dysfunction.

4.4 Special warnings and precautions for use

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.

• Contains paracetamol.

• Do not give with any other paracetamol-containing products.

• For oral use only.
• Never give more medicine than shown in the table.
• Always use the spoon supplied with the pack. Do not overfill the spoon.
• Do not give to babies less than 2 months of age.
• For infants 2-3 months not 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 medicine consult your doctor or pharmacist before taking this product.
• Do not store above 25°C. Protect from light. Store in the original package.
• Immediate medical advice should be sought in the event of an overdose, even if the child seems well, because of the risk of delayed serious liver damage.
• If symptoms persist consult your doctor.
• Keep out of the sight and reach of children.

Excipient Warnings:
Sucrose: Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrose-isomaltase insufficiency should not take this medicine.

4.5 Interaction with other medicinal products and other forms of interaction

The hepatotoxicity of Paracetamol, particularly after overdosage, may be increased by drugs which induce liver microsomal enzymes such as barbiturates, tricyclic antidepressants, and alcohol.

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.

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

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.

Antivirals: Regular use of Paracetamol possibly reduces metabolism of Zidovudine (increased risk of neutropenia).

The use of drugs that induce hepatic microsomal enzymes such as anticonvulsants and oral contraceptives may increase the extent of metabolism of paracetamol resulting in reduced plasma concentrations of the drug and a faster elimination rate.

4.6 Fertility, pregnancy and lactation

Pregnancy

A large amount of data on pregnant women indicates 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.

Breast-feeding

Paracetamol is excreted in breast milk but not in clinically significant quantities. Available published data do not contraindicate breast feeding.

4.7 Effects on ability to drive and use machines

None.

4.8 Undesirable effects

Adverse effects of paracetamol are rare but hypersensitivity including skin rash may occur. There have been reports of blood dyscrasias including thrombocytopenia and agranulocytosis, but these were not necessarily causality related to paracetamol.

Very rare cases of serious skin reactions have been reported.

Cases of acute pancreatitis have been reported. Paracetamol has been widely used and reports of adverse reactions are rare, and are generally associated with overdosage.

Allergic reactions occur occasionally.

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.

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

Nephrotoxic effects are uncommon and have not been reported in association with therapeutic doses, except after prolonged administration.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

4.9 Overdose

Liver damage is possible in adults who have taken 10g or more of paracetamol. 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, phenobarbital, 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 depleted e.g. eating disorders, cystic fibrosis, HIV infection, starvation, cachexia.

Symptoms

Symptoms of paracetamol overdosage in the first 24 hours are pallor, nausea, vomiting, anorexia and abdominal pain. Liver damage may become apparent 12 to 48 hours after ingestion. Abnormalities of glucose metabolism and metabolic acidosis may occur. 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.

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 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 concentration 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 patients 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.

The mechanism of analgesic action has not been fully determined. Paracetamol may act predominantly by inhibiting prostaglandin synthesis in the central nervous system (CNS) and, to a lesser extent, through a peripheral action by blocking pain impulse generation. The peripheral action may also be due to inhibition of prostaglandin synthesis or to inhibition of the synthesis or actions of other substances that sensitise pain receptors to mechanical or chemical stimulation.

Paracetamol probably produces antipyresis by acting centrally on the hypothalamic heat regulating centre to produce peripheral vaso-dilation resulting in increased blood flow through the skin, sweating and heat loss. The central action probably involves inhibition of prostaglandin synthesis in the hypothalamus.

5.2 Pharmacokinetic properties

Oral absorption is rapid and almost complete, it may be decreased if Paracetamol is taken following a high carbohydrate meal.

There is no significant protein binding with doses producing plasma concentrations of below 60mcg (µg)/ml, but may reach moderate levels with high or toxic doses.

Approximately 90 - 95% of a dose is metabolised in the liver, primarily by conjugation with glucuronic acid, sulphuric acid and cysteine. An intermediate metabolite, which may accumulate in overdosage after primary metabolic pathways become saturated, is hepatotoxic and possibly nephrotoxic.

Half life is 1 to 4 hours; does not change with renal failure but may be prolonged in acute overdosage, in some forms of hepatic disease, in the elderly, and in the neonate; may be somewhat shortened in children.

Time to peak concentration, 0.5 - 2 hours; peak plasma concentrations, 5 - 20mcg (µg)/ml (with doses up to 650mg); time to peak effect, 1- 3 hours; duration of action, 3- 4 hours.

Elimination is by the renal route, as metabolites, primarily conjugates, 3% of a dose may be excreted unchanged.

Peak concentration of 10 - 15mcg(µg)/ml have been measured in breast milk, 1 - 2 hours following maternal ingestion of a single 650mg dose. Half life in breast milk is 1.35 - 3.5 hours.

5.3 Preclinical safety data

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

Sodium Benzoate, Sucrose, Glycerine, Ethanol, Amaranth, Citric acid, Citric acid, CMC, Banana flavour

6.2 Incompatibilities

None stated

6.3 Shelf life

36 months

6.4 Special precautions for storage

Store below 25°C. Protect from light. Store in the original package.

6.5 Nature and contents of container

Bottles:	Amber pet bottle
Closure:	HDPE, child resistant, tamper evident, ROPP Alu closure
Pack sizes:	60 ml
Dosing device:	2.5/5ml/10ml dispensing cup.

6.6 Special precautions for disposal and other handling

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. Marketing authorisation holder

First Vadis Pharmaceutical Industries Limited
Plot IN/2 Phase 2 Extension,
Emene Industrial Layout Enugu State

8. Marketing authorisation number(s)

NAFDAC REG. NO.: 04 – 0920

9. Date of first authorisation/renewal of the authorisation

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10. Date of revision of the text
