Summary of Product Characteristics

1. Name of the medicinal product

Acamoli Forte 50mg/ml Syrup Strawberry Flavour.

Acamoli Forte 50mg/ml Syrup Turri Frutti Flavour.

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2. Qualitative and quantitative composition

Active ingredients	**Per 5 ml**
Paracetamol	250 mg

Excipients:

Excipients with known effect:

Xylitol	1500 mg
Color Red FDC No. 40	0.10 mg
Propylene Glycol	625 mg

See section 4.4 for further information.

For a full list of excipients, see Section 6.1

3. Pharmaceutical form

Syrup for oral use.

Acamoli forte 50 mg/ml strawberry flacour: Red transparent solution with a strawberry odor.
Acamoli forte 50mh/ml tutti futti flavour: Pink red transparent solution with a fruit odor.

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4. Clinical particulars

4.1 Therapeutic indications

Analgesic, antipyretic.

4.2 Posology and method of administration

For oral use only.

Children:

This medicine is given from the age of 0 and a weight of at least 3 kg.
For babies weighing less than 3 kg, a doctor should be consulted.

Find the suitable dosage in the following tables.
If you know the child's weight - the dosage should be given as shown in the weight table indicating dosage according to weight. Only if the child's weight is not known- the dosage will be determined according to age, as shown in the age table indicating dosage according to the child's age.

Weight table for Acamoli Forte 50 mg/1 ml:

Child's weight	Dose in ml	Maximum number of doses per 24 hours
3 kg	0.9	Up to 5 times a day
4 kg	1.2	Up to 5 times a day
5 kg	1.5	Up to 5 times a day
6 kg	1.8	Up to 5 times a day

7 kg	2.1	Up to 5 times a day
8 kg	2.4	Up to 5 times a day
9 kg	2.7	Up to 5 times a day
10 kg	3.0	Up to 5 times a day
11 kg	3.3	Up to 5 times a day
12 kg	3.6	Up to 5 times a day
13 kg	3.9	Up to 5 times a day
14 kg	4.2	Up to 5 times a day
15 kg	4.5	Up to 5 times a day
16 kg	4.8	Up to 5 times a day
17 kg	5.1	Up to 5 times a day
18 kg	5.4	Up to 5 times a day
19 kg	5.7	Up to 5 times a day
20 kg	6	Up to 5 times a day
21 kg	6.3	Up to 5 times a day
22 kg	6.6	Up to 5 times a day
23 kg	6.9	Up to 5 times a day
24 kg	7.2	Up to 5 times a day
25 kg	7.5	Up to 5 times a day
26 kg	7.8	Up to 5 times a day
27 kg	8.1	Up to 5 times a day
28 kg	8.4	Up to 5 times a day
29 kg	8.7	Up to 5 times a day
30 kg	9	Up to 5 times a day

Age table for Acamoli forte 50mg/ml:
Children of identical ages can be of significantly different weights. Therefore,
an effort must be made to find out the child's weight and determine the dosage according to the weight table. Only if it is not possible to find out the child's weight can the dosage be determined according to this table.

Child's age	**Dose in ml**	**Maximum number of doses per 24 hours**
For babies weighing less than 3 kg, a doctor should be consulted		
0-3 months	0.8	Up to 5 times a day
4-11 months	1.6	Up to 5 times a day
12-23 months	2.4	Up to 5 times a day
2-3 years	3.2	Up to 5 times a day
4-5 years	4.8	Up to 5 times a day
6-8 years	6.4	Up to 5 times a day
9-10 years	8	Up to 5 times a day
11 years	9.6	Up to 5 times a day

Do not exceed the recommended dose or the maximum number of daily doses.
Take/administer the doses at intervals of at least 4 hours.

Children 12 years of age and above:
10 ml every 4-5 hours, as needed. Do not exceed the recommended dose.
Adults:
10 ml every 4-5 hours, as needed. Do not exceed 4 grams of paracetamol (found in 80ml syrup) within 24 hours.

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. Dosage may need to be reduced.

Refer to the doctor if the fever persists for more than 3 days or if the symptoms do not resolve within 5 days despite the use of the medicine.

4.3 Contraindications

Hypersensitivity to paracetamol or any of the other ingredients.

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.

Caution in patients with severely impaired liver or kidney function. The hazards of overdose are greater in those with noncirrhotic 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.

Paracetamol has been associated with a risk of rare but serious skin reactions. These skin reactions, known as Stevens-Johnson Syndrome (SJS), toxic epidermal necrolysis (TEN), and acute generalized exanthematous pustulosis (AGEP), can be fatal.

Reddening of the skin, rash, blisters, and detachment of the upper surface of the skin can occur with the use of drug products that contain paracetamol. These reactions can occur with first-time use of paracetamol or at any time while it is being taken.

Anyone who develops a skin rash or reaction while using paracetamol should **stop the drug** and seek medical attention right away. Anyone who has experienced a serious skin reaction with paracetamol should not take the drug again and should contact their health care professional to discuss alternative pain relievers/fever reducers.

Health care professionals should be aware of this rare risk and consider paracetamol along with other drugs already known to have such an association, when assessing patients with potentially drug induced skin reactions.

Paracetamol can cause accidental poisoning in toddlers and infants. Paracetamol-containing products should be kept well out of reach of children.

Potentially fatal hepatotoxicity can result from paracetamol overdosage. However, in rare cases, hepatotoxicity has occurred in patients receiving high or excessive doses within therapeutic doses. Certain patients may be more susceptible to paracetamol hepatotoxicity, e.g., chronic alcoholics, patients with liver disease, or those who are malnourished or taking other drugs that induce hepatic enzymes.

Because of the risk of hepatotoxicity, patients should be cautioned against the inadvertent administration of excessive doses of paracetamol by using multiple paracetamol-containing products at once, such as cough and cold remedies, analgesics or arthritic formulations, antipyretics or products for relief of menstrual symptoms or muscle spasm. Administration of paracetamol to children may be especially prone to error due to the many concentrations and strengths of products available. To avoid dosing errors, all product labels should be checked carefully to ensure calculation of the amount of paracetamol to be given**.**

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

Do not give this medicine with any other paracetamol-containing product.

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.

Caution is advised if paracetamol is administered concomitantly with flucloxacillin due to increased risk of high anion gap metabolic acidosis (HAGMA), particularly in patients with severe renal impairment, sepsis, malnutrition and other sources of glutathione deficiency (e.g. chronic alcoholism), as well as those using maximum daily doses of paracetamol. Close monitoring, including measurement urinary 5-oxoproline, is recommended.

Important information about some of the ingredients of this medicine

The medicine contains the sweetener xylitol in an amount of 1.5 grams in every 5 ml syrup.
There may be a mild laxative effect. The caloric value is 2.4 kcal per 1 gram xylitol.
• The medicine contains colour red FDC No. 40, which may cause an allergic reaction.
• The medicine contains sodium in an amount of 5.86 mg in every 5 ml syrup. The medicine contains less than 1 mmol (23 mg) sodium in every 5 ml syrup and is therefore considered sodium-free.
• This medicine contains 625 mg propylene glycol in every 5 ml syrup. Consult the doctor or pharmacist before starting treatment:
○ If your child is under 5 years of age, particularly if your child is being treated with other medicines containing propylene glycol or alcohol.
○ Do not take this medicine if you suffer from liver or kidney disease. The doctor may ask you to undergo additional tests while taking this medicine.

- Do not take the medicine if you are pregnant or breastfeeding, unless recommended by the doctor. The doctor may ask you to undergo additional tests while taking this medicine.

4.5 Interaction with other medicinal products and other forms of interaction

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.

Patients who have taken barbiturates, tricyclic antidepressants and alcohol may show diminished ability to metabolise large doses of paracetamol, the plasma half-life of which can be prolonged.

Alcohol can increase the hepatotoxicity of paracetamol overdosage and may have contributed to the acute pancreatitis reported in one patient who had taken an overdose of paracetamol.

Chronic ingestion of anticonvulsants or oral steroid contraceptives induce liver enzymes and may prevent attainment of therapeutic paracetamol levels by increasing first pass metabolism or clearance.

Care should be taken when paracetamol is used concomitantly with flucloxacillin as concurrent intake has been associated with high anion gap metabolic acidosis, especially in patients with risk factors (see section 4.4).

Probenecid causes an almost 2-fold reduction in clearance of Paracetamol by inhibiting its conjugation with glucuronic acid. A reduction of the Paracetamol dose should be considered for concomitant treatment with probenecid.

4.6 Fertility, pregnancy and lactation

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.

Breastfeeding

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

No adverse effects known.

4.8 Undesirable effects

Adverse drug reactions (ADRs) identified during clinical trials and postmarketing 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 and < 1/10
Uncommon	≥ 1/1,000 and <1/100
Rare	≥ 1/10,000 and <1/1,000
Very rare	<1/10,000
Not known	(cannot be estimated from the 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	Anaphylactic reaction
	Very rare	Hypersensitivity
Hepatobiliary disorders	Not known	Liver injury[2]
Skin and subcutaneous tissue disorders	Very rare	Rash
	Not known	Fixed eruption
	Not known	Rash pruritic
	Not known	Urticaria
Renal and urinary disorders	Uncommon	Nephropathy toxic
	Not known	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 their disease improved after paracetamol withdrawal.

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.

Any suspected adverse events should be reported to the Ministry of Health according to the National Regulation by using an online form https://sideeffects.health.gov.il

4.9 Overdose

Liver damage is possible in adults and adolescents (≥ 12 years of age) who have taken 7.5 g 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 lower doses equivalent to 5g or more of paracetamol may lead to liver damage if the patient has risk factors. These include if:

• They are undergoing long-term treatment with drugs that induce liver enzymes

• They regularly consume ethanol in excess of advised amounts

• They are likely to be glutathione deplete e.g. as in cystic fibrosis, eating disorders, HIV infection, starvation, cachexia

Symptoms:

Symptoms of paracetamol overdosage in the first 24 hours include pallor, nausea, hyperhidrosis, malaise, vomiting, anorexia and abdominal pain. Liver damage may become apparent 12 to 48 hours after ingestion as liver function tests become abnormal. 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 cases poisoning, hepaticliver failure may lead to encephalopathy, haemorrhage, hypoglycaemia, cerebral oedema coma and death. Acute renal failure with acute tubular necrosis, strongly suggested by loin pain, haematuria and proteinuria, may develop with or withouteven 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 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

ATC Code: N02BE01

Paracetamol is a peripherally acting analgesic with antipyretic activity.

5.2 Pharmacokinetic properties

Paracetamol is readily absorbed from the gastrointestinal tract with peak plasma concentrations occurring about 30 minutes to 2 hours after ingestion. Paracetamol is metabolised in the liver and excreted in the urine mainly as the glucuronide and sulphate conjugates, with about 10% as glutathione conjugates. Less than 5% is excreted as unchanged paracetamol.

Plasma protein binding is negligible at usual therapeutic concentrations, although this is dose dependent. The plasma elimination half life varies from about one to four 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

Acamoli forte 50mg/ml syrup strawberry flavour:
Water, xylitol, propylene glycol, glycerin, povidone, sodium citrate dihydrate, acesulfame potassium, citric acid monohydrate, flavour strawberry, ammonium glycyrrhizinate, flavour vanilla, colour red FDC No. 40

Acamoli forte 50mg/ml syrup tutti- frutti flavour:
Water, xylitol, propylene glycol, glycerin, povidone, sodium citrate dihydrate, acesulfame potassium, citric acid monohydrate, flavour tuttifrutti, ammonium glycyrrhizinate, flavour vanilla, colour red FDC No. 40, colour blue FDC No. 2

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

The expiry date of the product is indicated on the packaging materials.

6.4 Special precautions for storage

Store below 25°C. Do not store in the refrigerator.
After opening the bottle for the first time, the medicine can be used up to the expiry date.

6.5 Nature and contents of container

Each package contains a bottle of syrup and a syringe for dosage accuracy.
The package size is 50 ml or 100 ml.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

Medicines should not be disposed of via wastewater or household waste. Ask a pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

7. Manufacturer:

Vitamed Pharmaceuticals Industries Ltd. P.O. Box 114, Binyamina 3055002, Israel

8. Marketing authorisation holder:

Teva Israel Ltd., 124 Dvora HaNevi'a st., Tel Aviv 6944020.

9 Registration numbers:

Acamoli Forte 50 mg/1 ml Syr Strawberry Flavour: 140.18.31762
Acamoli Forte 50 mg/1 ml Syr Tutti-Frutti Flavour: 140.17.31761

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