SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Para-Denk 125 Suppos

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Active substance: paracetamol

Each suppository contains;
Paracetamol .....125 mg

Excipient with known effect: Each suppository
contains soya lecithin.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Suppository
White to slightly yellow, torpedo-shaped, homogenous suppositories without breaks or cracks.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Para-Denk 125 Suppos is used in the symptomatic treatment of mild to moderate pain and/or fever.

4.2 Posology and method of administration

Posology
The dosage complies with the specifications in the following table. The dosage of paracetamol administered depends upon body weight and age. The usual dose is 10 to 15 mg per kg body weight as a single dose and up to a maximum of 60 mg/kg body weight as total daily dose.

The respective interval between doses depends on the symptoms and the maximum total daily dose and should be at least 6 hours.

A doctor should be consulted if symptoms persist for longer than 3 days.

Body weight (Age)	**Single dose in number of suppositories (equivalent dose**	**Maximum daily dose (24 hours) in number of suppositories (equivalent dose of paracetamol)**

	of paracetamol)	
7 to 8 kg (6 to 9 months)	1 (125 mg paracetamol)	3 (375 mg paracetamol)
9 to 12 kg (9 months to 2 years)	1 (125 mg paracetamol)	4 (500 mg paracetamol)

Special patient groups

Liver dysfunction and slight renal impairment

The dosage must be reduced and/or the dosage interval prolonged in patients suffering from impaired liver or kidney function or Gilbert's syndrome.

A daily dose of 2 g for adults must not be exceeded without medical advice.

Severe renal failure

In cases of severe renal insufficiency (creatinine clearance <10 ml/min), there must be a dosage interval of at least 8 hours.

Elderly patients

Experience has shown that no special dose adjustment is required. However, in debilitated, immobilised elderly patients with impaired hepatic/renal function, a dose reduction or prolongation of the dosing interval may be required.

Without medical advice, the maximum daily dose of 60 mg/kg body weight (up to a maximum of 2 g paracetamol per day for adults) should not be exceeded in the following cases:

- a body weight of less than 50 kg
- chronic alcoholism
- dehydration
- chronic malnutrition

Children and adolescents with low body weight

Use of Para-Denk 125 Suppos is not recommended in children under the age of 6 months and/or in those with a body weight of less than 7 kg, as the dosage strength is not suitable for this age group. However, there are suitable dosage strengths and/or pharmaceutical forms available for this age group.

Method of administration

For rectal application

Para-Denk 125 Suppos are inserted deep into the anus, if possible, after a bowel movement. The suppository may be warmed in your hand or briefly immersed in hot water to improve lubrication.

4.3 Contraindications

Hypersensitivity to the active substance, soya, peanuts or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

In order to avoid the risk of an overdose, one should make sure that concomitant medicines do not contain paracetamol.

Paracetamol should be administered with particular caution in the following cases:

- hepatocellular failure
- chronic alcohol abuse
- severe renal insufficiency (creatinine clearance <50 ml/min (see section 4.2))
- Gilbert's syndrome (Meulengracht disease)
- concomitant use of medicines that impair liver function
- glucose-6-phosphate dehydrogenase deficiency (favism)
- haemolytic anaemia
- glutathione deficiency
- dehydration
- chronic malnutrition
- a body weight of less than 50 kg
- elderly patients

Cases of high anion gap metabolic acidosis (HAGMA) due to pyroglutamic acidosis have been reported in patients with severe illness such as severe renal impairment and sepsis, or in patients with malnutrition or other sources of glutathione deficiency (e.g. chronic alcoholism) who were treated with paracetamol at therapeutic dose for a prolonged period or a combination of paracetamol and flucloxacillin. If HAGMA due to pyroglutamic acidosis is suspected, prompt discontinuation of paracetamol and close monitoring is recommended. The measurement of urinary 5-oxoproline may be useful to identify pyroglutamic acidosis as underlying cause of HAGMA in patients with multiple risk factors.

A doctor should be consulted in cases of high temperature, signs of secondary infection or symptoms persisting for more than three days.

In general, medication containing paracetamol should not be taken for longer than a few days or in higher doses without consulting your doctor or dentist.

Prolonged, incorrect use of high doses of painkillers may cause headache which must not be treated with increased doses.

In general, the habitual use of painkillers, particularly in combination with other painkillers, may lead to permanent kidney damage associated with the risk of renal failure (analgesic nephropathy).

If high doses of painkillers that have been incorrectly used for prolonged periods of time are discontinued abruptly, headache, fatigue, muscle pain, nervousness or vegetative symptoms may occur. These withdrawal symptoms abate within a few days. Until then, painkillers should not be used and should not be taken again without consulting a doctor beforehand.

Single administration of the total daily dose can lead to severe liver damage; in such cases, medical assistance should be sought immediately.

4.5 Interaction with other medicinal products and other forms of interaction

- The administration of probenecid inhibits binding of paracetamol to glucuronic acid, thereby causing a reduction in paracetamol clearance by an approx. factor of 2. The dosage of paracetamol should therefore be reduced when administered concomitantly with probenecid.
- Particular caution should be exercised when administering concomitantly with drugs that may cause enzyme induction or damage to the liver (see section 4.9).
- Concomitant use of paracetamol and zidovudine increases the risk of developing neutropenia. This medication should therefore only be taken concomitantly with zidovudine upon medical advice.
- Cholestyramine reduces the absorption of paracetamol.
- Caution should be taken when paracetamol is used concomitantly with flucloxacillin as concurrent intake has been associated with high anion gap metabolic acidosis due to pyroglutamic acidosis, especially in patients with risk factors (see section 4.4).
- Repeated use of paracetamol over a period longer than one week increases the effect of anticoagulants, especially warfarin. For this reason, long-term use of paracetamol in patients treated with anticoagulants should only be undertaken under medical supervision. The occasional use of paracetamol has no significant effect on one's tendency to bleed.

Effect on laboratory test results
The use of paracetamol can affect uric acid determination by means of phosphotungstic acid or blood sugar determination by means of glucose oxidase-peroxidase.

4.6 Fertility, pregnancy and lactation

Pregnancy
A large amount of data on pregnant women indicate neither malformative, nor foetal/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
After use, paracetamol passes in small amounts into breast milk. No undesirable effects or adverse drug reactions have been observed to date during breast-feeding. Paracetamol may be administered in therapeutic doses during the nursing period.

4.7 Effects on ability to drive and use machines

Paracetamol has no influence on the ability to drive and to use machines.

4.8 Undesirable effects

Side effects have been reported with the following frequencies:

Rare (may effect up to 1 in 1,000 people) Rise in liver transaminases

Very rare (may effect up to 1 in 10,000 people)
Changes in blood count as thrombocytopenia, agranulocytosis
In predisposed people bronchospasm (analgesic-induced asthma)
Allergic reactions that are manifested by a simple rash up to urticaria and anaphylactic shock. Severe skin reactions (Stevens-Johnson syndrome, toxic epidermal necrolysis, acute generalised pustular exanthema)

Not known (cannot be estimated from the available data) High anion gap metabolic acidosis

Description of selected adverse reactions

High anion gap metabolic acidosis

Cases of high anion gap metabolic acidosis due to pyroglutamic acidosis have been observed in patients with risk factors using paracetamol (see section 4.4). Pyroglutamic acidosis may occur as a consequence of low glutathione levels in these patients

Reporting of suspected adverse reactions: Healthcare professionals are asked to report any suspected adverse reactions via pharmacy and poisons board, Pharmacovigilance Electronic Reporting System (PvERS) https://pv.pharmacyboardkenya.org

4.9 Overdose

Symptoms
There is a risk of poisoning, particularly in the elderly, small children, people suffering from liver disease, in cases of chronic alcohol abuse, chronic malnutrition and concomitant use of medications that cause enzyme induction. In cases such as these, an overdose can be fatal.

As a rule, symptoms occur within 24 hours: nausea, vomiting, anorexia, pallor and lower abdominal pain. Afterwards, the patient may feel better. However, mild abdominal pain persists indicating liver damage.

An overdose of approx. 6 g or more of paracetamol in a single dose in adults or of 140 mg/kg body weight as a single dose in children causes hepatic necrosis, which may progress to a completely irreversible necrosis, and eventually to hepatocellular failure, metabolic acidosis and encephalopathy. These, in turn, may progress to a coma that can be fatal. In addition, elevated liver transaminase levels (AST, ALT), lactate dehydrogenase and bilirubin were observed in conjunction with elevated prothrombin time, which may occur 12 to 48 hours after use.

Clinical symptoms of liver damage become apparent after 2 days as a rule and reach their peak after 4 to 6 days.

Acute renal failure associated with acute tubular necrosis may develop even in the absence of severe liver damage. Myocardial anomalies and pancreatitis are other liver-unrelated symptoms that have been observed following an overdose with paracetamol.

Medical treatment in case of overdose
Even if an overdose with paracetamol is just suspected, sulfhydryl group donors, such as N-acetyl cysteine should be administered intravenously in the first 10 hours. However, N-acetyl cysteine may still offer a certain degree of protection even after 10 and up to 48 hours. In this case, it should be taken for a longer period. The plasma concentration of paracetamol can be reduced by means of dialysis. Measuring the plasma concentration of paracetamol is advisable.

Further treatment options to treat intoxication with paracetamol are directed at the extent, stage and clinical symptoms commensurate to the standard treatment measures in intensive care medicine.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Other analgesics and antipyretics, anilides; ATC

Code: N02BE01 Mechanism of action
The analgesic and antipyretic mechanism of action of paracetamol has not been clearly resolved. A central and peripheral effect is probable. Pronounced inhibition of cerebral prostaglandin synthesis has been proven, while the peripheral prostaglandin synthesis is only mildly inhibited. Furthermore, paracetamol inhibits the effect of endogenous pyrogens on the hypothalamic temperature regulation centre.

5.2 Pharmacokinetic properties

Absorption

Paracetamol is 68 to 88% absorbed after rectal use. Peak plasma concentrations are not reached until after 3 to 4 hours.

Distribution
Paracetamol spreads rapidly to all tissues. Blood, plasma and saliva concentrations are comparable. Plasma protein binding is low.

Biotransformation
Paracetamol is metabolised predominately in the liver, in two principal ways: conjugation with glucuronic acid and sulphuric acid. At doses in excess of the therapeutic dose, this latter way becomes quickly saturated. A small element of metabolism is effected by the catalyst, cytochrome P 450 (principally CYP2E1) and leads to the formation of the metabolite N-acetyl-p-benzoquinone-imine, which is normally detoxified rapidly by glutathione and bound by cysteine and mercapturic acid. In cases of massive intoxication, the amount of this toxic metabolite is raised.

Elimination
Excretion occurs predominately in urine. 90% of the absorbed amount is excreted within 24 hours, primarily as glucuronide (60 to 80%) and sulphate conjugates (20 to 30%) via the kidneys. Less than 5% is excreted in unchanged form.

The elimination half-life is approximately two hours. The elimination half-life is prolonged in cases of liver and renal impairment, following overdoses and in newborns. The maximum effect and the average duration of effect (4 to 6 hours) more or less correlate with the plasma concentration.

Renal insufficiency
In cases of severe renal insufficiency (creatinine clearance <10 ml/min), there is delayed excretion of paracetamol and its metabolites.

Elderly
The conjugation ability is unchanged.

5.3 Preclinical safety data

Gastrointestinal lesions, altered blood count, degenerative changes of the liver and renal parenchyma as well as necroses were observed in animal experiments relating to acute, subchronic and chronic toxicity of paracetamol in rats and mice. The reason for these changes may be sought in the mechanism of action on the one hand and in the metabolism of paracetamol on the other hand. Those metabolites that are likely to be the cause of the toxic effect and resulting changes in organs were also found in humans. In very rare cases, a reversible, chronic aggressive hepatitis was observed during long-term use (i.e. 1 year) at maximum therapeutic doses. At subtoxic doses, intoxication symptoms may occur after 3 weeks of use. Paracetamol should therefore not be taken over longer periods or in higher doses.

Comprehensive studies revealed no evidence of a relevant genotoxic risk associated with paracetamol in the therapeutic, i.e. non-toxic, dosage range.

Long-term studies on rats and mice revealed no evidence of relevant tumorigenic effects in non-hepatotoxic doses of paracetamol.

Paracetamol crosses the placenta.
Animal studies and previous experience in humans have not shown any evidence of foetal damage.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Lecithin
(soybean) Hard
fat

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years

6.4 Special precautions for storage

Store below 30°C.

6.5 Nature and contents of container

PVC/PE blister
Pack size: 10 suppositories

6.6 Special precautions for disposal

No special requirements.

7. MARKETING AUTHORISATION HOLDER

DENK PHARMA GmbH & Co. KG
Prinzregentenstr. 79
81675 München
Germany

8. MARKETING AUTHORISATION NUMBER IN GERMANY

H2008/14882/R1

9. DATE OF FIRST AUTHORISATION IN GERMANY

21.08.2012

10. DATE OF REVISION OF THE TEXT

07/2025, 18th August 2026