The maximum daily dose must not exceed 3000 mg (see section 4.4). (See section 5.2). Impairment (creatinine clearance ≤ 30 ml/min), to reduce the dose and it is recommended, when giving paracetamol to patients with severe renal insufficiency:

- Severe renal insufficiency:
  - No more than 4 doses to be given in 24 hours.

* Preterm newborn infants:
  - Dosing based on patient weight (please see the dosing table here below).

**Pharmacokinetic data**

- Paracetamol solution is administered as a 15-minute intravenous infusion.
- Intravenous use.
- The volume to be administered should be withdrawn from the container and diluted in a sodium chloride 9 mg/ml (0.9%) solution or 50 mg/ml (5%) glucose solution or a combination of both.
- The user should be referred to the product information for dosing guidelines.
- The patient’s intravenous catheter should be flushed accurately.
- It is important to be careful to ensure the proper dose is communicated and dispensed. When writing prescriptions, include both the total dose in mg and the total volume in millilitre (ml), which could result in accidental overdose and death. Take care to ensure that other medicines administered over 15 minutes. See also section 6.6 administration.

**Packaging and storage**

- Packaged for 10 ml.
- This medicinal product contains 12.2 mg (0.53 mmol) sodium in 10 ml, 61.5 mg (2.6 mmol) in 50 ml, and 245 mg (10.5 mmol) in 150 ml.
- This medicinal product contains 12.2 mg (0.53 mmol) of sodium in 10 ml.
- Paracetamol solution is administered as a 15-minute intravenous infusion.
- Intravenous use.
- The volume to be administered should be withdrawn from the container and diluted in a sodium chloride 9 mg/ml (0.9%) solution or 50 mg/ml (5%) glucose solution or a combination of both.
- The user should be referred to the product information for dosing guidelines.
- The patient’s intravenous catheter should be flushed accurately.
- It is important to be careful to ensure the proper dose is communicated and dispensed. When writing prescriptions, include both the total dose in mg and the total volume in millilitre (ml), which could result in accidental overdose and death. Take care to ensure that other medicines administered over 15 minutes. See also section 6.6 administration.

**Packaging and storage**

- Packaged for 10 ml.
- This medicinal product contains 12.2 mg (0.53 mmol) sodium in 10 ml, 61.5 mg (2.6 mmol) in 50 ml, and 245 mg (10.5 mmol) in 150 ml.
- This medicinal product contains 12.2 mg (0.53 mmol) of sodium in 10 ml.

**Compatibility**

- Paracetamol solution is administered as a 15-minute intravenous infusion.
- Intravenous use.
- The volume to be administered should be withdrawn from the container and diluted in a sodium chloride 9 mg/ml (0.9%) solution or 50 mg/ml (5%) glucose solution or a combination of both.
- The user should be referred to the product information for dosing guidelines.
- The patient’s intravenous catheter should be flushed accurately.
- It is important to be careful to ensure the proper dose is communicated and dispensed. When writing prescriptions, include both the total dose in mg and the total volume in millilitre (ml), which could result in accidental overdose and death. Take care to ensure that other medicines administered over 15 minutes. See also section 6.6 administration.

**Packaging and storage**

- Packaged for 10 ml.
- This medicinal product contains 12.2 mg (0.53 mmol) sodium in 10 ml, 61.5 mg (2.6 mmol) in 50 ml, and 245 mg (10.5 mmol) in 150 ml.
- This medicinal product contains 12.2 mg (0.53 mmol) of sodium in 10 ml.

**Compatibility**

- Paracetamol solution is administered as a 15-minute intravenous infusion.
- Intravenous use.
- The volume to be administered should be withdrawn from the container and diluted in a sodium chloride 9 mg/ml (0.9%) solution or 50 mg/ml (5%) glucose solution or a combination of both.
- The user should be referred to the product information for dosing guidelines.
- The patient’s intravenous catheter should be flushed accurately.
- It is important to be careful to ensure the proper dose is communicated and dispensed. When writing prescriptions, include both the total dose in mg and the total volume in millilitre (ml), which could result in accidental overdose and death. Take care to ensure that other medicines administered over 15 minutes. See also section 6.6 administration.

**Packaging and storage**

- Packaged for 10 ml.
- This medicinal product contains 12.2 mg (0.53 mmol) sodium in 10 ml, 61.5 mg (2.6 mmol) in 50 ml, and 245 mg (10.5 mmol) in 150 ml.
- This medicinal product contains 12.2 mg (0.53 mmol) of sodium in 10 ml.
Paracetamol is metabolised mainly in the liver following two major hepatic pathways: glucuronidation and N-acetylation. The inactive glucuronide and acetylated metabolites are conjugated with cysteine, glutathione and eliminated in the urine after conjugation with cysteine. The latter route is rapidly saturable at doses that exceed the therapeutic doses. A small fraction (less than 4 %) is metabolised by cytochrome P450 to a reactive intermediate (N-acetyl benzoquinone imine) which is responsible for the toxic effects of paracetamol.

Overdose, 7.5 g or more of paracetamol in a single administration in adults or 140 mg/kg of body weight in a single administration in children causes hepatic necrosis. The formation of reactive intermediates is inversely proportional to the amount of glutathione present. The amount of glutathione in the liver is critical to the formation of the toxic metabolite, and the drug clearance in the liver is variably dependent on the amount of glutathione which may be limited by low doses of paracetamol.

The metabolic rate of paracetamol is reduced in patients with chronic malnutrition. The pharmacokinetics and the metabolism of paracetamol are not modified in elderly subjects. No dose adjustment is required in this population.

5. Pharmacological Properties

5.1 Pharmacodynamics

Acetaminophen as a central analgesic is used as an anti-inflammatory and anti-pyretic agent. Anticodal: N02BE01

Pharmacodynamic effects

Paracetamol is a non-opioid analgesic well absorbed following oral or rectal administration. The active metabolite (N-acetyl-p-benzoquinone imine) is formed in the liver and is responsible for the toxic effect.

5.2 Pharmacokinetics

Absorption: Paracetamol is well absorbed after oral administration.

Distribution: The volume of distribution of paracetamol is approximately 1.5 liters/kg.

Metabolism: The clearance of paracetamol is decreased in patients with impairment of liver function, renal disease, and elderly patients.

Elimination: The elimination half-life of paracetamol is prolonged in patients with impaired liver function.

5.3 Preclinical safety data

The safety and efficacy of paracetamol in guinea pigs.

5.4 Special precautions for storage

The infusion should commence immediately after connecting the container to the intravenous injection set.

6. Incompatibilities

No interactions have been found between paracetamol and other medicinal products, provided that they have been administered separately.

7. Date of revision of the text

03-2014

8. Contact for further details

B. Braun Melsungen AG

9. Germany