Drugfield PHARMACEUTICALS LIMITED

SUMMARY OF PRODUCT CHARACTERISTICS

(SmPC)

Drugamol® Intravenous Injection

(Paractamol 150mg)

1. NAME OF THE MEDICINAL PRODUCT

Drugamol® Intravenous Injection (Paracetamol 150mg)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml of injection contains Paracetamol BP 150mg

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution

4. Clinical particulars

4.1 Therapeutic indications

- Pyrexia of unknown origin
- Symptomatic relief of fever and pain associated with common childhood disorders, tonsillitis, upper respiratory tract infection and post immunization reactions after tonsillectomy.
- Conditions where patient is unable to take oral medications but Paracetamol injection can be administered with advantage.
- For prevention of febrile convulsion.

4.2 Posology and method of administration

For intramuscular/intravenous use:
Adults and children(10 years and above) : 2-3ml
Children up to 10 years: 1-2ml
Infants : $^{1}/_{2}$ml

4.3 Contraindications

Drugamol® Intravenous injection is contraindicated in:

- Patients with hypersensitivity to paracetamol
- Cases of severe hepatocellular insufficiency.
- Hypersensitivity to Sodium chloride, hypertonic uterus, hypernatremia and fluid retention.

4.4 Special warnings and precautions for use

- Not recommended for children under the age of 10 years.
- Care is advised in the administration of paracetamol to patients with severe renal or severe hepatic impairment. The hazard of overdose is greater in those with non-cirrhotic alcoholic liver disease.
- Do not exceed the recommended dose.
- Do not take for more than 3 days without consulting a doctor.
- Do not take with any other paracetamol-containing products.
- If symptoms persist consult your doctor.
- Keep out of the reach of children.
- 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 of urinary 5-oxoproline, is recommended.

- Immediate medical advice should be sought in the event of an overdose, even if you feel well, because of the risk of delayed, serious liver damage.
- Necessary precautions should be taken in cases of hepatic and renal impairment.
- Paracetamol should be used with extreme caution in both cases.

4.5 Interaction with other medicinal products and other forms of interaction

- Probenecid causes an almost two-fold reduction in clearance of paracetamol by inhibiting its conjugation with glucuronic acid.
- A reduction in the paracetamol dose should be considered if it is to be used concomitantly with probenecid.
- The risk of developing hepatotoxicity from paracetamol appears to be increased in patients who regularly consume ethanol. In these patients, hepatotoxicity is possible even at normal therapeutic dosages of paracetamol. Chronic ethanol use increases paracetamol – induced hepatotoxicity by inducing cytochrome P450 (CYP)ZE leading to increased formation of the hepatotoxic metabolite and by depleting liver glutathione stores. Administration of paracetamol should be limited or avoided altogether in alcoholics or patients who consume ethanol regularly.

4.6 Pregnancy and Lactation

Pregnancy

Epidemiological studies in human pregnancy have shown no ill effects due to paracetamol used in the recommended dosage, but patients should follow the advice of their doctor regarding its use. 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 if clinically needed however it should be used at the lowest effective dose for the shortest possible time and at the lowest possible frequency

4.7 Effects on ability to drive and use machines

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

4.8 Undesirable effects

The information below lists reported adverse reactions, ranked using the following frequency classification:

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 the available data).

Immune system disorders

Hypersensitivity including skin rash may occur.

Not known: anaphylactic shock; angioedema

Blood and lymphatic system disorders

Not known: blood dyscrasias including thrombocytopenia and agranulocytosis

Skin and subcutaneous disorders

Very rare cases of serious skin reactions have been reported.

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.

4.9 Overdose

Liver damage may occur following prolonged use of paracetamol.

5.0 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: analgesic and antipyretic agent
ATC code: N02B E01

Acetaminophen (paracetamol), also commonly known as *Tylenol*, is the most commonly taken analgesic worldwide and is recommended as first-line therapy in pain conditions by the World Health Organization (WHO).[10] It is also used for its antipyretic effects, helping to reduce fever.

Mechanism of action

According to its FDA labeling, acetaminophen's exact mechanism of action has not been fully established Label - despite this, it is often categorized alongside NSAIDs (nonsteroidal anti-inflammatory drugs) due to its ability to inhibit the cyclooxygenase (COX) pathways. It is thought to exert central actions which ultimately lead to the alleviation of pain symptoms.

One theory is that acetaminophen increases the pain threshold by inhibiting two isoforms of cyclooxygenase, COX-1 and COX-2, which are involved in prostaglandin (PG) synthesis. Prostaglandins are responsible for eliciting pain sensations. Acetaminophen does not inhibit cyclooxygenase in peripheral tissues and, therefore, has no peripheral anti-inflammatory effects. Though acetylsalicylic acid (aspirin) is an irreversible inhibitor of COX and directly blocks the active site of this enzyme, studies have shown that acetaminophen (paracetamol) blocks COX indirectly. Studies also suggest that acetaminophen selectively blocks a variant type of the COX enzyme that is unique from the known variants COX-1 and COX-2. This enzyme has been referred to as COX-3. The antipyretic actions of acetaminophen are likely attributed to direct action on heat-regulating centers in the brain, resulting in peripheral vasodilation, sweating, and loss of body heat. The exact mechanism of action of this drug is not fully understood at this time, but future research may contribute to deeper knowledge.

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. It is metabolised in the liver (90-95%) and excreted in the urine mainly as the glucuronide and sulphate conjugates. Less than 5% is excreted as unchanged paracetamol. The elimination half-life varies from about 1 to 4 hours. Plasma protein binding is negligible at usual therapeutic concentrations but increases with increasing concentrations.

A minor hydroxylated metabolite (N-acetyl-p-benzoquinoneimine) which is usually produced in very small amounts by mixed-function oxidases in the liver and which is usually detoxified by conjugation with liver glutathione may accumulate following paracetamol overdosage and cause liver damage. The time to peak plasma concentration of paracetamol is 0.5 to 2 hours, the time to peak effect 1 to 3 hours and the duration of action 3 to 4 hours.

5.3 Preclinical safety data

There are no preclinical data of relevance to the prescriber which are additional to that already included in other sections of the SPC.

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

6.0 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium Meatabisulphate
Benzyl Alcohol
Propylene Glycol
Polyethylene Glycol
Water for Injection

6.2 Incompatibilities

N/A

6.3 Shelf life

36months

6.4 Special precautions for storage

Store below 30°c
Protect from light and moisture.

6.5 Nature and contents of container and special equipment for use, administration or implantation

Drugamol injection is a clear colorless liquid filled in 15ml amber colored vial and grey stopper with silver seal.

6.6 Special precautions for disposal and other handling

Not applicable.

7.0 APPLICANT/MANUFACTURER

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