Part II

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Dexemel 40g/litre Solvent for intraperitoneal use.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 1 litre contains:

Icodextrin	40.0	g
Sodium Chloride	5.4	g
S (+) Sodium Lactate (60%w/w solution)	4.5	g
Calcium Chloride	257.0	mg
Magnesium Chloride	51.0	mg

Theoretical osmolarity 278 (milliosmoles per litre).

Electrolyte solution content per 1000ml:

Sodium	133.0	mmol
Calcium	1.75	mmol
Magnesium	0.25	mmol
Chloride	96.0	mmol
Lactate	40.0	mmol

For excipients see section 6.1.

3 PHARMACEUTICAL FORM

Solvent for intraperitoneal use.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Dexemel is recommended as a vehicle for the administration via the peritoneum of medicinal products compatible with the vehicle and shown to have been used safely and effectively by the intraperitoneal route.

See section 6.2.

4.2 Posology and method of administration

The Posology and technique applied depend on the pharmaco-kinetic attributes of the therapeutic agent which has been dissolved in Dexemel and are individually decided by the responsible physician.

1 Litre (approximately 15 ml/kg) may be instilled into the peritoneal cavity thrice weekly via a subcutaneously implanted port/catheter device.

2 Litres (approximately 30 ml/kg) may be instilled daily into the peritoneal cavity via a Tenckhoff catheter if drained out immediately prior to a second instillation.

The dosage frequency of the therapeutic agent should be determined by its known pharmacokinetic attributes.

Peritoneal administration requires the use of a specific and adequate ambulatory drug delivery system, permitting the connection between the Dexemel bag and the patient.

To reduce discomfort on administration, the solution may be warmed in the oversealed bag to a temperature of 37°C prior to use. This should be done using a device specially designed for the purpose.

If fluid is to be drained out, drainage should be by gravity at a rate which the patient finds comfortable.

The drained fluid should be inspected for the presence of fibrin or cloudiness, which may indicate the presence of infection.

4.3 Contraindications

Dexemel is not recommended for use in patients with a known allergy to starch based polymers**,** or in patients with maltose or isomaltose intolerance or in patients with glycogen storage disease.

Dexemel is also contraindicated in patients with bowel obstruction. The presence of abdominal fistulae, open wounds, herniae, or other conditions which compromise the integrity of the peritoneal cavity may also contraindicate the use of Dexemel.

4.4 Special warnings and precautions for use

Dexemel is not recommended for use in children.

Aseptic technique should be employed throughout the procedure of intraperitoneal instillation of fluid and draining.

Blood glucose measurement must be done with a glucose specific method to prevent maltose interference. Glucose dehydrogenase pyrroloquinolinequinone (GDH PQQ) - based method should not be used. It is recommended that reference is made to the relevant section of the glucose test kit product leaflet to ascertain that interference while using Icodextrin-based dialysis therapy is not described.

The Dexemel solution which is to be administered via the peritoneum should be used with caution, after careful evaluation of its potential risks and benefits, in patients with conditions which preclude normal nutrition, with impaired respiratory function or with hypokalaemia or hypomagnesemia.

In patients with clinically significant cardiorespiratory disease, careful monitoring to avoid over or under hydration using fluid balance records and body weight should be undertaken.

Blood chemistry, haematology and plasma osmolality should be monitored at regular intervals.

Dexemel remains in the peritoneal cavity longer than saline or glucose solutions. The pharmacokinetic attributes of the therapeutic agent dissolved in Dexemel must be taken into account by the prescribing physician when assessing the risk benefit of any substance given by this route.

4.5 Interaction with other medicinal products and other forms of interaction

None known. However, blood concentrations of dialysable drugs may be reduced by peritoneal dialysis. Corrective therapy should be instituted if necessary. In patients using cardiac glycosides, plasma levels of potassium and calcium must be carefully checked. In the event of abnormal levels, appropriate actions should be taken.

4.6 Pregnancy and lactation

Animal studies on the effects of icodextrin are insufficient with respect to effects on embryonal/foetal development and lactation.

There are no adequate data from the use of Dexemel in pregnant women.

Dexemel should not be used during pregnancy or while breast feeding unless clearly necessary.

Women of childbearing potential should be treated with Dexemel only when adequate contraceptive precautions have been taken.

4.7 Effects on ability to drive and use machines

No effects on ability to drive and use machines have been observed.

4.8 Undesirable effects

Undesirable effects associated with Dexemel have included peritonitis related to the administration procedure and abdominal pain. In patients receiving icodextrin 7.5% solution as part of a peritoneal dialysis regimen and on multi therapy there have been common reports of skin reactions, including rash and pruritis which are generally mild or moderate in severity. Occasionally these rashes have been associated with exfoliation. In the event of this occurring and depending on the severity, Dexemel should be withdrawn at least temporarily.

4.9 Overdose

No data are available on the effects of overdosage.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

ATC code: V07A B.

Icodextrin is an α 1-4 linked glucose polymer which when administered intra peritoneally as a 4% solution is capable of maintaining a constant reservoir of fluid within the peritoneal cavity for a period of 24 to 48 hours.

The clinical experience with Dexemel is limited. To date 105 patients have been studied. In these studies 5-fluorouracil (at different doses) alone and in combination with folinic acid have been administered in Dexemel.

5.2 Pharmacokinetic properties

When given intraperitoneally the polymer is largely retained within the peritoneal cavity. Some absorption occurs from the peritoneum into the systemic circulation where it is metabolised by amylase to smaller oligosaccharides, ultimately maltose and by maltase to glucose. Steady state plasma levels of 1.98 mg/ml have been measured for oligomers of glucose units greater than 7 and maltose levels of 0.14 mg/ml.

5.3 Preclinical safety data

Pre-clinical data reveal no specific hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, and genotoxicity.

Carcinogenicity studies with the product are not feasible but carcinogenic effects are unlikely given the chemical nature of the molecule, its lack of pharmacological effect, lack of target organ toxicity, and negative results in mutagenicity studies.

A reproduction toxicity study in rats demonstrated no effect on fertility or embryofoetal development.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Water for Injections
Sodium hydroxide or Hydrochloric acid q.s. to required pH

6.2 Incompatibilities

None known.

A range of antibiotics including vancomycin, cephazolin, ampicillin/flucloxacillin, ceftazidime, gentamycin, amphotericin; insulin; and 5FU have shown no evidence of incompatibility with a 7.5% solution of icodextrin.

Some medicinal products that may be dissolved in Dexemel may interact with the PVC bag.

6.3 Shelf Life

2 years.

Following admixture of medicinal products with Dexemel the solution should be used immediately and any unused solution should be discarded.

6.4 Special precautions for storage

Do not store above 30°C. Do not refrigerate or freeze.

6.5 Nature and contents of container

1L, 1.5L and 2.0L flexible PVC bags.

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

Do not store above 30°C. Do not refrigerate or freeze.

7 MARKETING AUTHORISATION HOLDER

Innovata plc
1 Mere Way
Ruddington
Nottingham, NG11 6JS
United Kingdom

8 MARKETING AUTHORISATION NUMBER

PA 0675/002/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

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Date of last renewal: 6th January 2004

10 DATE OF REVISION OF THE TEXT

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