Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Conray 280 mg/ml Solution for Injection

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

The solution for injection contains meglumine iotalamate 60% w/v (formed *in situ* by reaction of iotalamic acid and meglumine) equivalent to organically bound iodine: 280 mg per ml.

Concentration of iotalamic acid: 0.74 millimole/ml.

Each 50ml bottle contains the equivalent of 14g organically bound iodine.

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Solution for injection
Colourless to pale yellow aqueous solution.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

This medicinal product is for diagnostic use only.
X-ray contrast medium used for the opacification of vascular and renal systems and female genital tract.

4.2 Posology and method of administration

Route of administration: By intravenous, intra-uterine or intra-arterial injection or injection directly into the chamber of the heart, depending on the procedure.

Recommended Dosage:

Intravenous Urography

Adults: 40 to 80 ml.
In the absence of preliminary dehydration 40 to 100ml may be used.

Infants and children:
Under 12kg: 2ml/kg body weight.
Over 12kg: 1.5ml/kg. Minimum of 24 ml.

Over 10 years of age: Lower range of adult dosage.

Angiocardiography
May be used as a test dose in positioning catheter tip. Volumes of up to 20 ml have been used for this purpose prior to the diagnostic dose of a more concentrated medium.

Splenography
Adults: 20 - 40 ml.

Femoral Venography
Inferior Vena Cavography:
Adults: 20 to 60 ml.

Hysterosalpingography:
Adults**:** About 10ml is usually required, administered by slow injection into the uterine cervical canal via a syringe or suitable cannula.

4.3 Contraindications

1. Use in patients with severe hepatic or renal dysfunction.
2. Use in patients with manifest hyperthyroidism.
3. Use in proven or suspected hypersensitivity to iodine containing media.
4 This product must not be used for myelography.
5. Hypersensitivity to the active substance or to any of the excipients.

4.4 Special warnings and precautions for use

1. The use of these contrast media should be carried out under the supervision of trained personnel whose experience qualifies them in the safe conduct of such examinations as may be required.

2. If radiological examinations are required in women of childbearing capacity, they should be so arranged as to be carried out in the 10 days immediately following the onset of bleeding in the menstrual cycle.

3. Since those agents for intravenous administration are usually salts of moderately strong organic acids, soluble in water with a comparatively low viscosity in solution, they are readily excreted by the kidney and have a diuretic effect. Caution is required in patients with pre-existing renal disease as the injection of Conray may lead to a transient decrease in renal function in such patients. Acute renal failure has been reported in single cases.

Adequate hydration prior to injection is essential to minimise renal effects. High dose urography should not be used in the presence of dehydration.

4. The possibility of aggravation of dehydration or even the production of hypovolaemia should be borne in mind if these agents are to be used in patients suffering from debility or dehydration, or in infants and young children.

5. Adequate hydration may be of assistance in patients with multiple myeloma but use of these agents requires great caution in this condition particularly if associated with renal dysfunction or extensive proteinuria.

6. Contrast agents should be used with caution in patients in poor general health, with circulatory or cardiac insufficiency, bronchial asthma, or those with a history of allergy, atopy, epilepsy, alcoholism, thyrotoxicosis or who are receiving neuroleptics. They may be at higher risk from developing anaphylaxis or cardiovascular collapse. Consideration should be given to the use of non-ionic contrast media in such patients.

7. Increased attention is needed if patients with myasthenia gravis have to undergo a contrast enhanced X-ray examination. There are literature reports describing the worsening of symptoms after Conray administration.

8. Following the use of any contrast medium of this type, there is the remote possibility of severe sensitivity reactions, e.g. anaphylactoid reactions, occurring. When they do, they tend to occur in the first 15 minutes following injection and the patient should be kept under observation during this period. Equipment and medications appropriate for emergency treatment of reactions should always be immediately available.

9. The Patient should remain in the hospital environment (but not necessarily the radiology department) for one hour after time of injection. The patient should return to the radiology department if any symptoms develop.

4.5 Interaction with other medicinal products and other forms of interaction

1. Iodinated X-ray contrast media may reduce the capacity of the uptake of iodine by the thyroid gland. For this reason the results of PBI (protein bound iodine) and radioactive iodine uptake studies, which depend on iodine estimation, will not accurately reflect thyroid function for up to 16 days following administration of iodinated X-ray contrast media. However, thyroid function tests not depending on iodine estimations, e.g. T3 resin uptake and total or free thyroxine (T4) assays are not affected.

2. Acute renal failure has been associated with lactic acidosis in patients receiving Metformin at the time of an X-ray investigation involving parenteral administration of iodinated contrast media. Therefore, Metformin should be withheld for at least 48 hours prior and subsequent to the procedure.

4.6 Fertility, pregnancy and lactation

There is inadequate evidence as to the safety of Conray in human pregnancy. The pregnant female should not be submitted to X-rays unless the radiologist considers it essential.

It is not known whether iotalamic acic is excreted into human breast milk. However, many injectable contrast agents are excreted unchanged in breast milk in an amount of approximately 1%. Although it has not been established that adverse events due to Conray occur to nursed infants, caution should be exercised when intravascular X-ray contrast media are administered to nursing women because of potential adverse events, and consideration should be given to discontinuing nursing for one day.

4.7 Effects on ability to drive and use machines

There is no known effect on the ability to drive and operate machines. However, because of the risk of early reactions driving or operating machinery is not advisable for 1 hour following the time of injection.

4.8 Undesirable effects

Mild discomfort is commonly observed in a total of 10% to 50% of patients. It may consist of one or more of the following symptoms, e.g.:
Sensations of heat or cold, pain during the injection, or a transient taste perversion. Other side effects may occur in a total of approximately 12% of the patients. The most frequent symptoms are nausea (4-5%), urticaria (3-3.5%), pruritus (2.8-3.2%), vomiting (1.8-2.2%), and rhinitis (1.5-2%). All further symptoms are likely to occur in less than 1% of the patients. Adverse effects, which may occur in relation with the use of Conray, are generally independent of the dose administered. They are mild or moderate in the majority of cases, rarely serious or life-threatening. However, even mild adverse events may be the first indications of a serious, general reaction, which may occur in rare cases after the use of any iodinated X-ray contrast medium. Contrast medium-related hypersensitivity reactions can also occur with a delay of some hours up to several days. Common symptoms of delayed reactions are pruritus and urticaria.

In the subsequent compilation, all symptoms are listed which have been reported up to now in relation with the use of Conray, and which are probably or possibly related to Conray.

Blood and Lymphatic system disorders:
Rare (0.01%-0.1%): RES, stimulated.
Very rare (<0.01%): Thrombocytopenia.

Endocrine disorders:
Very rare (<0.01%): Sialoadenitis.

Psychiatric disorders:
Very rare (<0.01%): Anxiety, somnolence.

Nervous system disorders:
Very common (>10%): Hot flushes.
Occasional (0.1%-1%): Palpitation.
Rare (0.01%-0.1%: Dizziness; mouth dry; pallor; paraesthesia; sweating increased; taste perversion.
Very rare (<0.01%): Agitation; ataxia; confusion; convulsions; disorientation; dysphasia; incontinence; muscle cramps; paralysis; scotoma; speech disorder; stupor; tremor.

Eye disorders:
Rare (0.01%-0.1%): Conjunctivitis; lacrimation abnormal.
Very rare (<0.01%): Transient cortical blindness; visual disorder.

Ear and labyrinth disorders:
Very rare (<0.01%): Tinnitus.

Cardiac disorders:
Rare (0.01%-0.1%): Tachycardia, cardiac arrest.
Very rare (<0.01): Arrhythmias; bradycardia; circulatory failure; ECG abnormal; extrasystoles; myocardial ischemia; ventricular fibrillation.

Vascular disorders:
Occasional (0.1%-1%): Hypotension.
Rare (0.01%-0.1%): Syncope; vasodilation.
Very rare (<0.01%): Cerebrovascular disorder; cyanosis; hypertension; phlebitis; vasospasm.

Respiratory, thoracic and mediastinal disorders:
Common (1%-10%): Rhinitis.
Occasional (0.1%-1%): Coughing; dyspnoea; pharyngitis.
Rare (0.01%-0.1%): Larynx oedema; throat tightness.
Very rare (<0.01%): Apnoea; bronchospasm; hypoxia; pulmonary oedema; stridor.

Gastrointestinal disorders:
Common (1%-10%): Nausea; vomiting.
Rare (0.01%-0.1%): Dysphagia.
Very rare (<0.01%): Diarrhoea; hypersalivation; tongue oedema.

Skin and subcutaneous tissue disorders:
Common (1%-10%): Pruritus; urticaria.
Occasional (0.1%-1%): Erythema; rashes.
Rare (0.01%-0.1%): Angioedema.

Musculoskeletal, connective tissue and bone disorders:
Very rare (<0.01%): Back pain, rhabdomyolysis.

Renal and urinary disorders:
Very rare (<0.01%): Acute renal failure; BUN increase; decrease in renal function; decreased creatinine clearance oliguria and anuria.

General Disorders and administration site conditions:
Very common (>10%): Pain.
Common (1%-10%): Anaphylactoid reactions.
Occasional (0.1%-1%): Abdominal pain; face oedema.
Rare (0.01%-0.1%): Asthenia; chest pain; chills; general local reactions like e.g. pain, rash, or swelling, hay fever; periorbital oedema.
Very rare (<0.01%): Anaphylactic shock; cellulitis (injection site); fatigue; fever; headache; injection site necrosis; oedema.

Adverse symptoms may be classified as follows:
1. Pseudo-allergic intolerance reactions like e.g. nausea and vomiting, skin rashes, dyspnoea, hay fever, paraesthesia or hypotension. Serious anaphylactic reactions generally affect the cardiovascular and respiratory system. These may cause life-threatening conditions including anaphylactic shock, cardiac and respiratory arrest, or pulmonary oedema. Patients with a history of allergy are at increased risk of developing hypersensitivity reactions.

2. Local reactions at the injection site like e.g. rashes, swelling, vasospasm and inflammation.

3. Vasovagal reactions like e.g. dizziness or syncope, which may be caused either by the contrast medium administration, or by the procedure.

4. Cardiologic side effects during cardiac catheterisation like e.g. angina pectoris, ECG changes, cardiac arrhythmias, conductivity disorders and coronary spasm, which may be caused by the contrast medium administration, or by the catheterisation procedure.

5. Nephrotoxic reactions in patients with pre-existing renal damage or renal vasopathy like e.g. decrease in renal function with creatinine elevation. These adverse effects are transient in the majority of the cases. In single cases, acute renal failure has been observed.

6. Neurotoxic reactions after intra-arterial injection of the contrast medium like e.g. visual disorders, confusion, paralysis, convulsions, or fits. These symptoms are generally transient and abate spontaneously within several hours, or days. Patients with pre-existing damage of the blood-brain-barrier are at increased risk of developing neurotoxic reactions.

7. In the case of inadvertent extravasation, serious tissue reactions including ulceration may occur in rare cases the extent of which is dependent on the amount and strength of the contrast medium solution, which is distributed in the tissue.

4.9 Overdose

Overdose is unlikely in clinical practice, but in the event of inadvertent overdosage, it is important to keep the patient well hydrated, otherwise treatment should be symptomatic with particular reference to the cardiovascular system.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Water soluble, nephrotropic, high osmolar iodinated X-ray contrast media.
ATC code: V08AA04.

Conray is a high osmolar, ionic X-ray contrast medium. The organically bound iodine of the contrast agent permits radiographic visualisation of internal structures.

5.2 Pharmacokinetic properties

After intravascular injection, Conray will quickly be distributed within the extracellular space. Simultaneously, it will be eliminated by glomerular filtration with a mean half-life of about 80 minutes. There is a low level of binding to serum and plasma proteins. Renal elimination decreases with renal impairment, vicarious pathways become more important under these circumstances. These are the hepatobiliary pathway, the intestinal mucous membrane and the salivary glands. No significant metabolism, deiodination or biotransformation of Conray occurs.

5.3 Preclinical safety data

There were no findings in the preclinical testing of Conray which could be of relevance for the prescriber in recognising the safety of this product used for the authorised indications, and which is not already included in other sections of the SPC.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium calcium edetate dihydrate
Sodium dihydrogen phosphate monohydrate
Water for injections

6.2 Incompatibilities

This medicinal product must not be mixed with other medicinal products except those mentioned in Section 6.6.

6.3 Shelf life

5 years.

6.4 Special precautions for storage

Do not store above 25^{o}C. Do not freeze. Protect from X-rays.
Keep container in the outer carton in order to protect from light.

6.5 Nature and contents of container

Conray 280 is packaged in uncoloured bottles composed of type I glass (Ph. Eur.) fitted with a 32 mm latex-free bromobutyl rubber stopper and aluminium cap seals.

50 ml (boxes of 10).

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

The drug should not be used if there are particles in it or a discolouration can be observed. In case Conray is frozen or crystals are visible it has to be examined whether the container is damaged. If it is undamaged the crystals should be resolved by warming up to room temperature and vigorous shaking.

Conray is delivered in single-dose units. Remaining contrast medium should be discarded after the examination.

Apart from Water for Injections and Dextrose or Saline, Conray should not be mixed with any other substance.

7 MARKETING AUTHORISATION HOLDER

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Whiteley
Fareham
Hampshire PO15 7NY
United Kingdom

8 MARKETING AUTHORISATION NUMBER

PA 1850/1/1

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

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Date of last renewal: 07 May 2011

10 DATE OF REVISION OF THE TEXT

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