PROFESSIONAL INFORMATION

SCHEDULING STATUS

S4

1. NAME OF THE MEDICINE

Optiray 350 - 50 ml Solution for Injection

Optiray 350 - 75 ml Solution for Injection

Optiray 350 - 100 ml Solution for Injection

Optiray 350 - 125 ml Solution for Injection

Optiray 350 Solution for Injection

Optiray 320 - 50 ml Solution for Injection

Optiray 320 - 100 ml Solution for Injection

Optiray 300 - 30 ml Solution for Injection

Optiray 300 - 50 ml Solution for Injection

Optiray 300 - 100 ml Solution for Injection

Optiray 300 - 125 ml Solution for Injection

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Optiray 350: Each millilitre solution contains 741 mg of ioversol equivalent to 350 mg organically bound iodine.

Osmolality: 740 mOsm/kg

Viscosity: 8,3 mPa.s (at 37 °C)

Optiray 320: Each millilitre solution contains 678 mg of ioversol equivalent to 320 mg organically bound iodine.

Osmolality: 680 mOsm/kg

Viscosity: 6,1 mPa.s (at 37 °C)

Optiray 300: Each millilitre solution contains 636 mg of ioversol equivalent to 300 mg

organically bound iodine.

Osmolality: 643 mOsm/kg

Viscosity: 5,0 mPa.s (at 37 °C)

For the full list of excipients, see section 6.1

Sugar free.

3. PHARMACEUTICAL FORM

Solution for injection

Clear, colourless to pale yellow solution containing no solids.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Optiray is for diagnostic use only.

Optiray 350 is indicated in adults for angiography throughout the cardiovascular system. The uses include coronary, peripheral, visceral and renal angiography, aortography and left ventriculography. Optiray 350 is also indicated for contrast enhanced computed tomography of the head and body, intravenous urography, intravenous digital subtraction angiography and venography.

Optiray 320 is indicated in adults for angiography throughout the cardiovascular system. The uses include cerebral, coronary, peripheral, visceral and renal angiography, in aortography, left ventriculography and intravenous urography. Optiray 320 is also indicated for contrast enhanced computed tomography of the head and body

Optiray 320 is indicated in children for angiocardiography, contrast enhanced computed tomography of the head and body, and intravenous urography.

Optiray 300 is indicated in adults for cerebral, peripheral and visceral angiography, intravenous

urography, intravenous digital subtraction angiography and venography. Optiray 300 is also indicated for contrast enhanced computed tomography of the head and body

Optiray 300 is indicated in children for cerebral, peripheral and visceral angiography, and for intravenous urography.

4.2 Posology and method of administration

Please refer to table.

Adult dose:			
Procedure	**Product**	**Dosage and administration**	**Maximum total dose**
Cerebral angiography			
Carotid or vertebral artery	Optiray 320 or Optiray 300	2 - 12 ml	200 ml
Aortic arch	Optiray 320 or Optiray 300	20 - 50 ml	200 ml
Peripheral angiography Aortic-iliac runoff	Optiray 350 or Optiray 320 or Optiray 300	10 - 90 ml 60 ml (range 20 to 90 ml)	250 ml
Common iliac, femoral	Optiray 350 or Optiray 320 or Optiray 300	40 ml (range 10 to 50 ml)	
Subclavian, brachial	Optiray 350 or Optiray 320 or Optiray 300	20 ml (range 15 to 30 ml) These doses may be repeated as necessary.	

Adult dose:			
Procedure	**Product**	**Dosage and administration**	**Maximum total dose**
Venography	Optiray 350 or Optiray 300	50 – 100 ml per extremity. Following the procedure, the venous system should be flushed with Sodium Chloride Injection USP (United States Pharmacopeia) or 5 % Dextrose in water. Massage and elevation are also helpful for clearing the extremities.	250 ml
Left ventriculography	Optiray 350 or Optiray 320	30 – 50 ml Left ventricle: 40 ml. May be repeated as necessary. Several minutes should be permitted to elapse between each injection to allow for subsidence of possible haemodynamic disturbance.	250 ml

Adult dose:			
Procedure	**Product**	**Dosage and administration**	**Maximum total dose**
Coronary arteriography	Optiray 350 or Optiray 320	1 - 10 ml Left coronary artery: 8 ml (range 2 to 10 ml) Right coronary artery: 6 ml (range 1 to 10 ml) May be repeated as necessary. Several minutes should be permitted to elapse between each injection to allow for subsidence of possible haemodynamic disturbances.	250 ml
Visceral angiography	Optiray 350 or Optiray 320 or Optiray 300	12 - 60 ml Celiac: 45 ml (range 12 to 60 ml) Superior mesenteric: 45 ml (range 15 to 60 ml) These doses may be repeated as necessary.	250 ml
Aortography	Optiray 350 or Optiray 320	10 - 80 ml Aorta: 45 ml (range 10 to 80 ml) These doses may be repeated as necessary.	250 ml

Adult dose:			
Procedure	**Product**	**Dosage and administration**	**Maximum total dose**
Renal angiography	Optiray 350 or Optiray 320	6 - 15 ml Renal or inferior mesenteric: 9 ml (range 6 to 15 ml) These doses may be repeated as necessary.	250 ml
Urography	Optiray 350 or Optiray 320 or Optiray 300	50 - 75 ml 50 - 75 ml 50 - 75 ml	150 ml 150 ml 150 ml
Computed tomography			
Head imaging (Head CT)	Optiray 350 or Optiray 320 or Optiray 300	50 - 150 ml 50 - 150 ml 50 - 150 ml Scanning may be performed immediately after I.V. administration.	150 ml 150 ml 150 ml
Body imaging (Body CT)	Optiray 350 or Optiray 320 or Optiray 300	25 - 150 ml 25 - 150 ml 25 - 150 ml	150 ml 150 ml 150 ml

Adult dose:			
Procedure	**Product**	**Dosage and administration**	**Maximum total dose**
Digital subtraction angiography			
Intra-arterial (IA DSA)	Optiray 350 or Optiray 300	5 - 80 ml	250 ml
Intravenous (IV DSA)	Optiray 350 or Optiray 300	30 - 50 ml Injections may be repeated as necessary.	250 ml

Children (older than four weeks):		
Optiray 300 Recommended dosage schedule		
Procedure	**Dosage**	**Maximum total dose**
Cerebral angiography	1 – 3 ml/kg	100 ml
Peripheral angiogrpahy	1 – 3 ml/kg	100 ml
Visceral and renal angiography and aortography	1 – 3 ml/kg	100 ml
Intravenous urography	2 ml/kg (>1 year of age) 3 ml/kg (<1 year of age)	100 ml

Children (older than four weeks):		
Optiray 320 Recommended dosage schedule		
Procedure	**Dosage**	**Maximum total dose**
Computed tomography: Head imaging or Body	1 – 3 ml/kg	100 ml

Children (older than four weeks):		
Optiray 320 Recommended dosage schedule		
Procedure	**Dosage**	**Maximum total dose**
imaging		
Intravenous urography	0,5 – 3 ml/kg Paediatric: doses of 0,5 to 3 ml/kg have produced diagnostic opacification of the excretory tract. The usual dose is 1 to 1,5 ml/kg. Dosage for infants and children should be administered in proportion to age and body mass. The total administered dose should not exceed 3 ml/kg.	100 ml
Paediatric angiocardiography	1 to 1,5 ml/kg (usual single injection dose - 1,25 ml/kg body mass). When multiple injections are given, total administered dose should not exceed 5 ml/kg.	250 ml

Safety and effectiveness of Optiray 300 and Optiray 320 in children of four weeks or less, in any other indication than those listed above have not yet been established. Safety and effectiveness of Optiray 350 in children have not yet been established and should therefore not be used in children until further data becomes available.

Method of administration

Optiray formulations are sterile, non-pyrogenic, aqueous solutions intended for intravascular administration as diagnostic radio-opaque media.

The dosage depends on the type of investigation and the technique used. It is recommended that intravascularly administered iodinated contrast agents are warmed to body temperature prior to injection. The lowest dose necessary to obtain adequate visualisation should be used. If, during administration, a reaction occurs, the injection should be stopped until the reaction has subsided.

Patients should be well-hydrated prior to and following Optiray administration. No other medicines should be mixed with the solution due to the risk of chemical incompatibility. Sterile technique must be used in all vascular injections involving contrast media. All solutions should be inspected visually for particulate matter and discolouration prior to administration and should not be used if particles are observed or discolouration has occurred.

4.3 Contraindications

Hypersensitivity to ioversol or to any of the ingredients, including excipients.

Proven hypersensitivity to iodine-containing contrast media.

Manifest hyperthyroidism.

Pregnancy and lactation (see section 4.6 Fertility, Pregnancy and Lactation).

4.4 Special warnings and precautions for use

Diagnostic procedures which involve the use of iodinated intravascular contrast agents such as Optiray should be carried out under the direction of personnel skilled and experienced in the particular procedure to be performed.

A fully equipped emergency cart, or equivalent supplies and equipment, and healthcare

professional competent in recognising and treating adverse reactions of all types, should always be available.

Fatal reactions have been associated with the administration of water-soluble contrast media including Optiray. It is, therefore of the utmost importance that a course of action is carefully planned, in advance, for the treatment of serious reactions, and that appropriate and adequate facilities and personnel be readily available in case of a severe reaction. Patients should be observed for a possible severe reaction, during, and for at least 30 to 60 minutes after administration of Optiray. Patients with known or suspected hypersensitivity to iodinated contrast media should be closely observed.

The presence of renal damage in diabetic patients is one of the factors predisposing to renal impairment following Optiray administration. This may precipitate lactic acidosis in patients who are taking biguanides, such as metformin. As a precaution, biguanides should be stopped prior to the time of the Optiray examination for 48 hours and reinstated only after control of renal function has been regained.

Hypersensitivity

Patients should be informed that allergic reactions may develop up to several days post administration; in which case a medical practitioner should be consulted immediately.

Pre-testing cannot be relied on to confidently predict severe allergic reactions. The thorough assessment of the medical history of the specific patient may be more accurate in predicting potential adverse reactions. A positive history of allergies is not a contraindication but does require caution (see section 4.3 Contraindications). Pre-medication with antihistamines and corticosteroids to avoid or minimise allergic reactions should be considered. However, this pre-medication does not always prevent the occurrence, but may reduce both the incidence and severity of severe adverse events.

Intolerance to ioversol

Optiray may cause anaphylaxis or other manifestations of allergy, including nausea, vomiting, dyspnoea, erythema, urticaria and hypotension. An increased risk of such reactions is associated with patients who have a history of increased sensitivity to iodine, or known allergies, asthma or hypersensitivity. In such patients, the benefit should clearly outweigh the risk (see section 4.3 Contraindications).

Severe cutaneous adverse reactions (SCAR)

SCAR may develop from 1 hour to several weeks after intravascular contrast agent administration. These reactions include Stevens-Johnson syndrome and toxic epidermal necrolysis (SJS/TEN), acute generalized exanthematous pustulosis (AGEP), and drug reaction with eosinophilia and systemic symptoms (DRESS). Reaction severity may increase and time to onset may decrease with repeat administration of a contrast agent; prophylactic medications may not prevent or mitigate severe cutaneous adverse reactions. Avoid administering Optiray to patients with a history of a severe cutaneous adverse reaction to ioversol.

Coagulation disorders

The anticoagulant effect of non-ionic X-ray contrast media, such as **Optiray** has been shown, *in vitro,* to be less than that of conventional ionic agents at comparable concentrations. Similar results were found in some *in vivo* studies. Serious, rarely fatal, thromboembolic events causing myocardial infarction and stroke have been reported during angiographic procedures with both ionic and nonionic contrast media. Therefore, meticulous intravascular administration technique is necessary, particularly during angiographic procedures, to minimise thromboembolic events. For this reason, standard angiographic catheters should be flushed frequently and prolonged contact of blood with contrast agent in syringes and catheters should be avoided.

Thyroid disorders

Reports of thyroid storm following the intravascular use of iodinated radiopaque agents in patients with hyperthyroidism or with an autonomously functioning thyroid nodule, suggest that the additional risk be evaluated in such patients before use of Optiray (see section 4.3 Contraindications).

Cardiovascular diseases

In angiographic procedures, the possibility of dislodging plaques or damaging or perforating the vessel wall should be considered during catheter manipulations and **Optiray** injection. Test injections to ensure proper catheter placement are recommended.

Angiography should be avoided whenever possible in patients with homocystinuria because of the risk of inducing thrombosis and embolism.

Patients with congestive heart failure should be observed for several hours following the procedure to detect delayed haemodynamic disturbances, which may be associated with a transitory increase in the circulating osmotic load.

Thromboembolic disorders

In patients with advanced atherosclerosis, serious uncontrolled/severe hypertension, cardiac decompensation, senility, preceding cerebral thrombosis or embolism, special caution should be exercised. Cardiovascular reactions as bradycardia, rising or falling of blood pressure may occur more often.

Central nervous system disorders

Serious neurological events, including permanent paralysis, have been observed following direct injection into cerebral arteries or vessels supplying the spinal cord, or in angiocardiography. A cause-effect relationship to the contrast medium has not been established since the patients' pre-existing condition and procedural technique are causative factors in themselves.

Encephalopathy has been reported with the use of Optiray (see section 4.8). Contrast-induced encephalopathy may manifest with symptoms and signs of neurological dysfunction such as headache, visual disturbance, cortical blindness, confusion, seizures, loss of coordination, hemiparesis, aphasia, unconsciousness, coma, and cerebral oedema. Symptoms usually occur within minutes to hours after administration of ioversol and generally resolve within days. Factors which increase blood-brain barrier permeability facilitate the passage of the contrast medium into cerebral tissue, which can lead to central nervous system reactions, e.g. encephalopathy.

If contrast encephalopathy is suspected, appropriate medical management should be initiated, and administration of Optiray must not be repeated.

Renal insufficiency

Combinations with nephrotoxic medicines should be avoided. If this cannot be avoided, laboratory monitoring of renal function must be intensified.

Caution must be exercised in patients with severely impaired renal function, combined renal and hepatic disease, or anuria, diabetes mellitus, homozygous sickle cell disease, multiple myeloma or other paraproteinaemia, particularly when large doses are administered. Serious renal effects, including acute renal failure, may occur in these patients. Effective hydration prior to the administration of Optiray is essential and may decrease the risk of renal injury. Preparatory dehydration is dangerous and may contribute to acute renal failure especially in myelomatous patients since this may predispose the patient to precipitation of the myeloma protein.

Phaeochromocytoma

Administration of Optiray to patients known or suspected of having phaeochromocytoma should be performed with extreme caution. If, in the opinion of the, medical practitioner the possible benefits of such procedures outweigh the considered risks, the procedure may be performed; however, the amount of Optiray injected should be kept to an absolute minimum.

The blood pressure should be assessed throughout the procedure, and measures for treatment of a hypertensive crisis should be available. Due to risk of a hypertensive crisis, a premedication with α- and ß-blockers is advisable when Optiray is administered intravascularly.

Homozygous sickle cell disease

In patients with homozygous sickle cell disease, hyperosmolar agents such as X-ray contrast media, including Opitray, may affect sickling of the erythrocytes. Hence, there is a need for careful consideration before the intra-arterial administration of such agents to patients with homozygous sickle cell disease.

Extravasation

Optiray should be injected with caution to avoid perivascular application. This is especially important in patients with severe arterial or venous disease. However, significant extravasation of Optiray may occur, especially during the use of power injectors. Generally, it is tolerated without substantial tissue injury applying conservative treatment. However, serious tissue damage (e.g. ulceration) has been reported in isolated cases requiring surgical treatment.

Anaesthetised patient

General anaesthesia may be indicated in selected patients. However, a slightly higher incidence of adverse reactions has been reported in these patients, probably due to the hypotensive effect of the anaesthetic.

Venography

In patients with suspected phlebitis, serious ischaemia, local infections or complete occlusion of the venous system special caution should be exercised.

Peripheral angiography

There should be pulsation in the artery, into which the Optiray will be injected. In patients with thromboangiitis obliterans or ascending infections in combination with serious ischaemia the angiography should only be performed with special caution, if at all.

Coronary arteriography and left ventriculography

In these procedures cardiac decompensation, serious dysrhythmias, ischaemia and myocardial infarction may occur.

Paediatric angiocardiography

Paediatric patients at higher risk of experiencing adverse events during Optiray administration may include those having asthma, a sensitivity to medication and/or allergies, congestive heart failure, a serum creatinine greater than 132,6 µmol/L or those less than 12 months of age.

Paediatric population

Hypothyroidism or transient thyroid suppression may be observed after exposure to iodinated contrast media.

This adverse reaction should also be observed in newborns whose mothers have received an iodinated contrast medium during pregnancy (see section 4.6).

The incidence of hypothyroidism in patients younger than 3 years of age exposed to iodinated contrast media ranges between 1 % and 15 % depending on the age of the subjects and the dose of the iodinated contrast agent.

Younger age, very low birth weight, prematurity, and the presence of other conditions, such as, admission to neonatal or paediatric intensive care units, and cardiac conditions are associated with an increased risk.

Paediatric patients with cardiac conditions may be at the greatest risk given that they often require high doses of contrast during invasive cardiac procedures, such as catheterization, and computed tomography (CT).

Special attention should be paid to paediatric patients below 3 years of age because an

incident underactive thyroid during early life may be harmful for motor, hearing, and cognitive development and may require transient thyroxin (T4) replacement therapy.

Thyroid function should be evaluated in all paediatric patients younger than 3 years of age within 3 weeks following exposure to iodinated contrast media.

In neonates and particularly in premature neonates, it is recommended to control TSH level and T4, 7-10 days and 1 month after the administration of iodinated contrast media.

If hypothyroidism is detected, thyroid function should be monitored as appropriate even when replacement treatment is given.

Laboratory test interactions

Optiray may reduce the capacity of the uptake of iodine by the thyroid gland. 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 Optiray. However, thyroid function tests not dependent on iodine estimation, e.g. T3 resin uptake and total or free thyroxine (T4) assays are not affected.

4.5 Interaction with other medicines and other forms of interaction

The following interactions have been reported after the administration of other iodinated contrast media. They are generally accepted as being attributable to this class of contrast media.

No interaction studies have been performed.

Metformin

Acute renal failure has been associated with lactic acidosis in patients receiving metformin at the time of an X-ray examination involving parenteral administration of iodinated contrast media. Therefore, in diabetic patients taking metformin, the examination should be performed and intake of metformin stopped before the examination. The use of metformin should not be resumed for 48 hours, and should only be restarted if renal function/serum creatinine remains

within the normal range or has returned to baseline.

Interleukin

Patients treated with interleukin may develop a higher rate of adverse reactions. The reason has not yet been clarified. An increased or delayed occurrence of these reactions within a period of 2 weeks was observed after administration of interleukin.

Diuretics

In case of diuretic-induced dehydration, patients are at increased risk of acute renal failure when using iodinated contrast media. Close monitoring is required to ensure adequate hydration before administration of Optiray. The lowest necessary dose of Optiray consistent with a diagnostic result should be used.

Vasopressor

The arterial injection of Optiray should never be made following the administration of vasopressors, since they strongly potentiate neurological effects.

Oral cholecystographic agents

Renal toxicity has been reported in patients with liver dysfunction who were given oral cholecystographic medicines followed by intravascular contrast agents. Administration of **Optiray** should therefore be postponed in patients who have recently received a cholecystographic contrast agent.

4.6 Fertility, Pregnancy and Lactation

Not to be used during pregnancy or lactation (see section 4.3 Contraindications).

Safety in pregnancy and lactation has not been established.

Pregnancy

There has been limited human use of Optiray in pregnancy. However, since any X-ray investigation during pregnancy may involve a potential foetal risk, the risk/benefit ratio should be carefully weighed. If a better known and safer alternative is available, an X-ray investigation involving Optiray should be avoided.

Optiray contains iodine which may induce foetal dysthyroidism if the examination takes place after more than 14 weeks of amenorrhoea. Thyroid function of neonates should be closely monitored during the first week of life if iodinated contrast was administered to the mother during pregnancy. It is recommended that thyroid function be monitored again at 2 weeks of age.

Breastfeeding

It is not known whether Optiray is excreted in human breast milk. However, Optiray may be excreted unchanged in breast milk. Caution should be exercised when Optiray is administered to women breastfeeding their infants, because of potential adverse events, and mothers given Optiray should discontinue breastfeeding for one day.

4.7 Effects on ability to drive and use medicines

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

Frequencies for adverse drug reactions are defined as follows:

Very common (≥1/10)

Common (≥1/100 to <1/10)

Uncommon (≥1/1000 to <1/100)

Rare (≥1/10,000 to <1/1000)

Very rare (<1/10,000)

Not known (cannot be estimated from the available data)

a. Summary of the safety profile

Adverse reactions following the use of Optiray formulations are generally independent of the dose administered. Usually, they are mild to moderate, of short duration and resolve spontaneously (without treatment). However, even mild adverse reactions may be the first indication of a serious, generalized reaction that can occur rarely after iodinated contrast media. Such serious reactions may be life-threatening and fatal, and usually affect the cardiovascular system. Most adverse drug reactions to Optiray formulations occur within minutes after administration, however contrast related hypersensitivity reactions may occur with a delay of some hours up to several days.

b. Tabulated summary of adverse reactions

From clinical studies, mild discomfort, including sensation of heat or cold, pain during the injection, and/or transient taste perversion, was noted in 10 % to 50 % of patients. In a large post-marketing study, other side effects occurred in a total of 1,1 % of the patients; the most frequent were nausea (0,4 %), skin reactions such as urticaria or erythema (0,3 %), and vomiting (0,1 %). All other events occurred in less than 0,1 % of the patients.

The following adverse reactions have been collected after Optiray administration from clinical trials and post-market experience, including post-market surveys.

Infections and infestations

Rare: rhinitis

Immune system disorders

Very rare: anaphylactoid (hypersensitivity) reaction

Not known: anaphylactic shock

Endocrine disorders

Not known: hypothyroidism*

Psychiatric disorders

Very rare: confusional state; agitation; anxiety

Nervous system disorders

Uncommon: dizziness; dysgeusia; headache; paraesthesia

Rare: syncope; tremor

Very rare: loss of consciousness; paralysis; speech disorders; somnolence; stupor; aphasia; dysphasia; hypoaesthesia

Not known: seizure; contrast-induced encephalopathy; amnesia; dyskinesia

Eye disorders

Rare: vision blurred; eye swelling; periorbital oedema

Very rare: conjunctivitis allergic (including eye irritation, ocular hyperaemia, lacrimation increased, conjunctival oedema)

Not known: blindness transient

Ear and labyrinth disorders

Rare: vertigo

Very rare: tinnitus

Cardiac disorders

Rare: tachycardia

Very rare: heart block; arrhythmia; angina pectoris; bradycardia; atrial fibrillation; electrocardiogram abnormal

Not known: cardiac arrest; ventricular fibrillation; arteriospasm; coronary extrasystoles; palpitations

Vascular disorders

Uncommon: blood pressure increased

Rare: hypotension; flushing

Very rare: cerebrovascular disorder; phlebitis; hypertension; vasodilation

Not known: shock; thrombosis; vasospasm; cyanosis; pallor

Respiratory, thoracic and mediastinal disorders

Uncommon:	sneezing
Rare:	laryngeal oedema; laryngo spasm; dyspnoea; laryngeal obstruction (incl. throat tightness, stridor); nasal congestion; cough; throat irritation
Very rare:	pulmonary oedema; pharyngitis; hypoxia
Not known:	respiratory arrest; asthma; bronchospasm; dysphonia

Gastrointestinal disorders

Common:	nausea
Uncommon:	vomiting
Rare:	dry mouth
Very rare:	sialoadenitis; abdominal pain; tongue oedema; dysphagia; salivary hypersecretion
Not known:	diarrhoea

Skin and subcutaneous tissue disorders

Uncommon:	urticaria; erythema; pruritus
Rare:	rash
Very rare:	angioedema; hyperhidrosis (incl. cold sweat)
Not known:	Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS syndrome); Acute Generalized Exanthematous Pustulosis (AGEP); Erythema Multiforme (EM), Stevens Johnson Syndrome (SJS) / Toxic Epidermal Necrolysis (TEN)

Musculoskeletal, connective tissue and bone disorders

Very rare:	muscle spasms

Renal and urinary disorders

Rare:	micturition urgency
Very rare:	acute kidney injury; abnormal renal function; incontinence; haematuria; creatinine renal clearance decreased; blood urea increased
Not known:	anuria; dysuria

Congenital, familial and genetic disorders

Not known: congenital hypothyroidism

General disorders and administration site conditions

Very common: feeling hot

Common: pain

Rare: face oedema; pharyngeal oedema; feeling cold; tremor; chills

Very rare: chest pain; injection site reactions (incl. pain, erythema, and haemorrhage up to necrosis especially after extravasation); malaise; asthenia; fatigue; feeling abnormal, oedema, sluggishness

Not known: pyrexia

c. Description of selected adverse reactions

Adverse reactions may be classified as follows:

a. Hypersensitivity reactions:

   Serious anaphylactic reactions generally affect the cardiovascular and respiratory system. These may be life-threatening and include anaphylactic shock, cardiac and respiratory arrest, or pulmonary oedema. Patients with a history of allergic reactions are at increased risk of developing hypersensitivity reactions. Other type 1 (immediate) reactions such as nausea and vomiting, skin rashes, dyspnoea, rhinitis, paraesthesia or hypotension.

b. Vasovagal reactions:

   e.g. Dizziness or syncope which may be caused either by the contrast medium, or by the procedure.

c. Cardiologic side effects:

   During cardiac catheterisation e.g. angina pectoris, ECG changes, cardiac dysrhythmias, conductivity disorders and coronary spasm, which may be caused by the contrast medium or by the procedure.

d. Nephrotoxic reactions:

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

e. Neurotoxic reactions:

After intra-arterial injection of the contrast medium e.g. visual disorders, disorientation, 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.

f. Local reactions:

At the injection site e.g. rashes, swelling, vasospasm and inflammation.

g. Extravasation:

Can cause serious tissue reactions, the extent of which is dependent on the amount and strength of the contrast solution in the tissues.

d. Paediatric population

Frequency, type and severity of adverse reactions in children are expected to be the same as in adults.

*Thyroid dysfunction was observed in paediatric patients 0 to 3 years of age following the administration of iodinated radiopaque agents.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare providers are asked to report any suspected adverse reactions to SAHPRA via the “6.04 Adverse Drug Reactions Reporting Form” found online under SAHPRA publications:

SAHPRA: https://www.sahpra.org.za/Publications/Index/8.

Guerbet South Africa (Pty) Ltd: pharmacovigilance.za@guerbet.com

4.9 Overdose

In overdose, side effects will be exacerbated and exaggerated. Overdose of Optiray is potentially fatal and may affect the respiratory and cardiovascular system.

Treatment should be symptomatic & supportive. Dialysis can be used to remove Optiray from the blood.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

A 28 Contrast media

Pharmacotherapeutic group: Water soluble, nephrotropic, low osmolar X-ray contrast media

ATC code: V08AB07

Ioversol is a non-ionic X-ray contrast medium. Intravascular injection of ioversol opacifies those vessels in the path of the flow of the contrast medium, permitting radiographic visualisation of the internal structures until significant haemodilution occurs.

5.2 Pharmacokinetic properties

The pharmacokinetic profile of ioversol, together with its hydrophilic properties and a very low level of binding to serum and plasma proteins, indicate that ioversol, is distributed within the extracellular fluid space and eliminated through the kidneys by glomerular filtration. The mean ($\pm$ se*) half-lives after doses of 50 ml and 150 ml of ioversol, 320 were 113 $\pm$ 8,4 and 104 $\pm$ 15 minutes respectively. Elimination via the faeces is negligible. No significant metabolism, deiodination, or biotransformation of ioversol, has been observed.

More than 95 % of the administered dose is excreted within the first 24 hours, with the peak urine concentration occurring in the first 2 hours after administration.

*Standard error

5.3 Preclinical safety data

There were no findings in the preclinical testing of Optiray which could be of relevance for the

prescriber in recognising the safety of this product used for the authorised indications, and which are not already included in other sections of the leaflet.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Trometamol, trometamol hydrochloride, sodium hydroxide and/or hydrochloric acid (for pH: 6,0 to 7,4), sodium calcium edetate, water for injections.

6.2 Incompatibilities

No other medicine should be mixed with Optiray.

6.3 Shelf-life

3 years

The solution is supplied in single dose or multi-dose containers.

Any unused portion of single dose containers should be discarded.

Any unused portion of multi-dose containers (500 ml) should be discarded within 10 hours after first opening.

6.4 Special precautions for storage

Store at or below 25 ºC.

Keep the container in the outer carton in order to protect from light. Protect from X-rays.

Do not refrigerate.

Optiray may be stored for one month at 37 °C in a contrast media warmer with circulating air.

Discard the solution in case of discoloration or particulate matter.

6.5 Nature and contents of container

Optiray is packaged in type 1, colourless glass vials, fitted with 20 mm or 32 mm bromobutyl rubber closures and aluminium cap seals.

Optiray 300: 30 ml (box of 10)

50 ml (box of 10 and 25)

100 ml (box of 10 and 12)

Optiray 320: 50 ml (box of 10 and 25)

100 ml (box of 10 and 12)

Optiray 350: 50 ml (box of 10 and 25)

100 ml and 200 ml (box of 10 and 12)

500 ml (box of 5, 6 and 10)

Optiray is also supplied in prefilled hand-held syringes and power-injector syringes made of polypropylene. Blue syringe tip cap and piston are made of natural rubber.

Optiray 300, 320 and 350: 50 ml (box of 10) Prefilled hand-held syringes

75 ml, 100 ml (box of 10) Prefilled power-injector syringes

Optiray 300 and 350: 125 ml (box of 10) Prefilled power-injector syringes

Not all pack sizes and box sizes may be marketed.

6.6 Special precautions for disposal and other handling

The following precautions should be followed when using Optiray 350 500 ml vials: Optiray 350 500 ml vials must only be used with administration devices, e.g. infusion pumps or dual head injectors which are provided with reliable connecting tubes. Optiray 350 500 ml vials have a rubber stopper which can only be pierced once. The manufacturer's instructions for the device must be followed. Any Optiray 350 in 500 ml vials which is unused at the end of the day must be discarded.

7. HOLDER OF CERTIFICATE OF REGISTRATION

Guerbet South Africa (Pty) Ltd

Hertford Office Park, Building I

90 Bekker Road, Vorna Valley

Midrand, Gauteng, 1682

8. REGISTRATION NUMBERS

Optiray 350 – 50 ml: Z/28/420

Optiray 350 – 75 ml: A40/28/0246

Optiray 350 – 100 ml: Z/28/422

Optiray 350 – 125 ml: 30/28/0282

Optiray 350: 34/28/0101

Optiray 320 – 50 ml: Z/28/412

Optiray 320 – 100 ml: Z/28/421

Optiray 300 – 30 ml: Z/28/414

Optiray 300 – 50 ml: Z/28/418

Optiray 300 - 100 ml: Z/28/417

Optiray 300 – 125 ml: 30/28/0281

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

18 September 1992

10. DATE OF REVISION OF THE TEXT

31 October 2023

Botswana: Schedule 2

Optiray 300: BOT 0700947; Optiray 350: BOT 0700948

Namibia: Schedule 2

Optiray 300-30 ml 19/28/0001; Optiray 300-50 ml 19/28/0002; Optiray 300-100 ml

19/28/0004; Optiray 300-125 ml 19/28/0005; Optiray 350-50 ml 19/25/0007; Optiray 350-75

ml 19/28/0008; Optiray 350-100 ml 19/28/0009; Optiray 350-125 ml 19/28/0010; Optiray 350

19/28/0011