NON-PROMOTIONAL ACTIVITIES CERTIFICATION (NPAC) FORM

Owner: Krupa Mehta

Item: PRESCRIBING INFORMATION Optiray™ (Ioversol) 300 mg I/ml, 320 mg I/ml and 350 mg I/ml

Job number: P-ORY-PI-UK-MAY2023

Electronic Certification Declaration

I have examined the electronic final form of this material and, in my belief, it is in accordance with the relevant Advertising Regulations, the ABPI Code of Practice, the ABHI Code of Ethical Business Practice, and the IPHA Code of Practice.

I certify the above is true.

Signatory	
Signature	Catherine Ludwig Digitally signed by Catherine Ludwig DN: cn=Catherine Ludwig, o=My Medical Department, ou=Medical, email=catherine@mymedicaldepartment.com, c=AU Reason: I am approving this document Location: Gold Coast, Australia Date: 2023.06.03 00:51:30 +10'00'
Name	Dr Catherine LUDWIG
Date	03 JUN 2023
Role	ABPI Medical Signatory

Final Form Certification and Release Declaration

I have examined the final printed / manufactured form of this material and it is identical to the electronically certified PDF with the same job number. In my belief, it is in accordance with the relevant Advertising Regulations, the ABPI Code of Practice, the ABHI Code of Ethical Business Practice, and the IPHA Code of Practice. It may be used or disseminated from the date below, according to the conditions specified in the job summary.

Signatory	
Signature	
Name	
Date	
Role	

NO CHANGES CAN BE MADE ONCE A NON-PROMOTIONAL ACTIVITY HAS BEEN CERTIFIED

PRESCRIBING INFORMATION

Optiray™ (Ioversol) 300 mg I/ml, Optiray™ (Ioversol) 320 mg I/ml and Optiray™ (Ioversol) 350 mg I/ml

See full Summary of Product Characteristics (SPC) before prescribing.

Presentation: solution for injection or infusion. **Indications:** This medicinal product is for diagnostic use only. Optiray™ is a non-ionic X-ray contrast medium for injection or infusion. *Common to all formulations:* In adults in peripheral and visceral angiography, venography, intravenous urography, and computed tomography of the head and body. *Optiray 300 mg I/ml only:* In children for cerebral, peripheral and visceral angiography and intravenous urography. License established within the paediatric population for Optiray™ 300mg/ml only. *Optiray 300 mg I/ml and Optiray 320 mg I/ml only:* cerebral angiography. *Optiray 300 mg I/ml and Optiray 350 mg I/ml only:* intraarterial and intravenous digital subtraction angiography (IA-DSA and IV-DSA). *Optiray 320 mg I/ml and Optiray 350 mg I/ml only:* coronary and renal angiography, aortography and left ventriculography. **Posology and Method of Administration:** The dosage of Optiray™ depends on several factors which include patient characteristics, the contrast medium concentration, the type of investigation and the radiological technique. *Common to all formulations:* In adults, the recommended dosage may vary from 1 or 2 ml to a maximum total dose of 250 ml. *Optiray 300 mg I/ml only:* In children the recommended dosage may vary from 1-3 ml/kg to a maximum total dose of 100 ml. *Please refer to the SPC for the recommended dosage schedule.* The lowest dose necessary to obtain adequate visualisation should be used. It is recommended that intravascularly administered iodinated contrast agents are warmed up to body temperature prior to injection. Appropriate resuscitation equipment should be available. **Contraindications:** Hypersensitivity to iodine-containing contrast media, the active substance, or to any of the excipients. Manifest hyperthyroidism. **Special Warnings and Precautions for Use (W&P):** *General comments/hypersensitivity:* Serious or fatal reactions have been associated with the administration of iodinated X-ray contrast media. It is of the utmost importance to be completely prepared to treat any contrast medium reaction. Diagnostic procedures should be performed 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 personnel competent in recognising and treating adverse reactions of all types should always be available during and for at least 30 to 60 minutes after administration. The patient should also be informed that allergic reactions may develop up to several days post administration; in such case, a physician should be consulted immediately. Pre-testing cannot be relied upon to predict severe reactions and may itself be hazardous. Consider pre-medication with antihistamines and corticosteroids. *Intolerance to ioversol:* Optiray™ may cause anaphylaxis or other manifestations of pseudo-allergic intolerance reactions, e.g. nausea, vomiting, dyspnoea, erythema, urticaria and hypotension. *Severe cutaneous adverse reactions (SCAR):* SCAR may develop from 1 hour to several weeks after administration. These reactions include Stevens-Johnson syndrome and toxic epidermal necrolysis (SJS/TEN); acute generalised 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; prophylactic medications may not prevent or mitigate SCAR. Avoid administering ioversol to patients with a history of SCAR to ioversol. *Coagulation disorders:* non-ionic contrast media have less anticoagulant effect than conventional ionic agents; meticulous angiographic techniques are recommended. *Thyroid:* evaluate risk prior to administration in patients with hyperthyroidism or autonomously functioning thyroid nodule (reports of thyroid storm). *Cardiovascular diseases and thromboembolic disorders:* In angiographic procedures, test injections are recommended to ensure proper catheter placement (risk of dislodging plaque or damaging vessel wall). Avoid angiography in patients with homocystinuria (risk of thrombosis and embolism). Special caution in patients with advanced atherosclerosis, serious hypertension, cardiac decompensation, senility, preceding cerebral thrombosis/embolism (cardiovascular reactions such as bradycardia and change in blood pressure may occur more often). 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. *Central nervous system:* Serious neurologic events have been observed following direct injection into cerebral arteries or vessels supplying the spinal cord, or in angiocardiography due to inadvertent filling of the carotids. Encephalopathy has been reported. Factors which increase blood-brain barrier permeability facilitate passage of contrast medium into cerebral tissue. If contrast encephalopathy is suspected, appropriate management should be initiated and administration of ioversol 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, 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. Patients should be well hydrated prior to and following the administration of Optiray. Preparatory dehydration is dangerous and may contribute to acute renal failure. *Phaeochromocytoma:* caution in known/suspected phaeochromocytoma; minimise dose; pre-medication with alpha- and beta-blockers is advisable (risk of hypertensive crisis). *Homozygous sickle cell disease:* hyperosmolar agents such as ioversol may affect sickling of erythrocytes. *General anaesthesia:* a higher incidence of adverse reactions has been reported. *Extravasation:* Optiray should be injected with caution to avoid perivascular application. 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. *Venography:* special caution in suspected phlebitis, serious ischaemia, local infection or complete vein occlusion. *Peripheral angiography:* there should be pulsation in the artery into which contrast medium is injected. Perform with special caution (if at all) in thrombangitis obliterans or ascending infections. *Paediatrics:* 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. Special attention in patients younger than 3 years as an underactive thyroid may harm neurological development. Evaluate thyroid function within 3 weeks following exposure, in all paediatric patients younger than 3 years. *Interference with lab tests:* Iodinated X-ray contrast media may reduce the capacity of the uptake of iodine by the thyroid gland. For this reason the results of 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**.** *For further information and indication specific warnings and precautions, please refer to the SPC.* **Interactions:** 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. Acute renal failure has been associated with lactic acidosis in patients receiving metformin after contrast medium injection. If the serum creatinine is normal, the examination should be performed and intake of metformin stopped from the time of 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. A higher rate of adverse reactions has been observed in patients who have received treatment with interleukin. 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. An arterial injection of an X-ray contrast medium should never be made following the administration of vasopressors, since they strongly potentiate neurologic effects. Renal toxicity has been reported in patients with liver dysfunction, who were given oral cholecystographic agents followed by intravascular contrast agents. Administration of any intravascular X-ray contrast agent should therefore be postponed in patients who have recently received a cholecystographic contrast agent. **Pregnancy and Lactation:** No clinical data in pregnant or lactating women are available. Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy. Caution should be exercised when prescribing to pregnant women. Many injectable contrast agents are excreted unchanged in breast milk to an amount of approximately 1 % of the given dose. Where contrast enhanced X-ray imaging is imperative, consideration should be given to discontinuing nursing for one day. Ioversol 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. **Effects on ability to drive and use machines:** It is not advisable to drive or operate machinery for one hour following the injection. **Undesirable Effects:** Adverse effects are usually mild to moderate, of short duration and resolve spontaneously without treatment. However, even mild adverse reactions may be the first indication of a serious reaction. Most adverse reactions occur within minutes of administration but some may occur with a delay of up to several days. *Very common:* feeling hot. *Common:* pain, nausea. *Serious:* cf. W&P; also: anaphylactoid reaction; anaphylactic shock; hypothyroidism; confusional state; agitation; anxiety; syncope; paralysis; speech disorders; somnolence; stupor; aphasia; dysphasia; seizure; amnesia; dyskinesia; transient blindness; tachycardia; heart block, arrhythmia, angina, ECG abnormal, bradycardia, atrial fibrillation, cardiac arrest; ventricular fibrillation; arteriospasm; coronary extrasystoles; palpitations; hyper- or hypotension; cerebrovascular disorder; shock; thrombosis; vasospasm; laryngeal spasm, oedema and obstruction; pulmonary oedema; hypoxia; respiratory arrest; asthma; bronchospasm; acute kidney injury; abnormal renal function; anuria.

Prescribers should consult the SPC in relation to other adverse reactions. **Legal Status**: Prescription only medicine. **Marketing Authorisation Holder:** Guerbet, BP 57400, 95943 Roissy CdG Cedex, France. **Product Licence Numbers:** OPTIRAY™ 300 PL 12308/0028; OPTIRAY™ 320 PL 12308/0029; OPTIRAY™ 350 PL 12308/0032**. List prices:** OPTIRAY™ 300 10x50ml vials: £128.23; OPTIRAY™ 320 10x100ml vials: £291.80; OPTIRAY™ 350 10x50ml vials: £148.75. **Date of Revision of Text:** May 2023. **P-ORY-PI-UK-MAY2023.**

Further information available from: Guerbet, BP 57400, 95943 Roissy CdG Cedex, France.

Adverse events should be reported. Reporting forms and information can be found at https://yellowcard.mhra.gov.uk/. Or Search for MHRA Yellow Card in the Google Play or Apple App Store. Adverse events should also be reported to Guerbet Laboratories Ltd., Avon House, 435 Stratford Road, Shirley, Solihull, B90 4AA. Tel: 0121 733 8542 Fax: 0121 733 3120 Email: uk.info@guerbet.com.