SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

NIOPAM 340, solution for injection

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

69.4% w/v Iopamidol equivalent to 340mg iodine/ml. Each ml contains 694 mg Iopamidol. For the full list of excipients, see 6.1.

3 PHARMACEUTICAL FORM

Solution for injection

Clear aqueous solution filled into colourless glass bottles

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

This medicinal product is for diagnostic use only.

X-ray contrast medium for injection, particularly in digital subtraction angiography.

4.2 Posology and method of administration

Intra-ventricular

Intra-arterial Intravenous Intra-articular

Posology

NIOPAM 340: DOSAGE SCHEDULE

Procedure	dosage
Peripheral arteriography and venography	Adults 10 - 50 ml Children: **
Angiocardiography and left ventriculography	Adults 30 - 80 ml Children **
Coronary arteriography	Adults: 4 - 8 ml * per artery
Aortography - retrograde	Adults: 30 - 80 ml *
Selective renal arteriography	Adults: 5 - 10ml Children: **
Selective visceral angiography Hepatic Coeliac Superior Mesenteric	Adults: 30 - 70 ml Adults: 40 - 70ml Adults: 25 - 70ml Adults: 5 - 30ml
Digital subtraction angiography (DSA) Intravenous injection Coronary arteriography - by intra-arterial DSA, Ventriculography	Adults 30 - 50 ml Children: ** Adults: 2-5ml Adults: 25ml* Children: 1.0- 1.5ml/kg
Computer tomography enhancement	Adults: 50 - 100ml
Intravenous urography	Adults: up to 1.5ml/kg Children: 1- 2.5ml/kg or **
Arthrography	Adults: 1 - 10ml according to the joint being examined

* repeat as necessary; ** according to body size and age;

Do not exceed 250 ml. Single injection volume depends on the vascular area to be examined.

The dosage must be adapted to the examination, the age, body weight, cardiac output, renal function, general condition of the patient and the technique used. Usually the same iodine concentration and volume are used with other iodinated x-ray contrast in current use.

Method of administration

As with all contrast media, the lowest dose necessary to obtain adequate visualisation should be used.

Non-ionic contrast media have less anti-coagulant activity in- vitro than ionic media. Meticulous attention should therefore be paid to angiographic technique. Non -ionic media should not be allowed to remain in contact with blood in the syringe and intravascular catheters should be flushed frequently, to minimise the risk of clotting, which rarely has led to serious thromboembolic complications after procedures. Factors such as length of procedure, catheter and syringe material, underlying disease state, and concomitant medications may contribute to the development of thromboembolic events. Therefore, meticulous angiographic techniques are recommended including close attention to guide wire and catheter manipulation, use of manifold systems and/or three-way stopcocks, frequent catheter flushing with heparinized saline solutions, and minimizing the length of the procedure.

As experience shows that warmed contrast media are better tolerated, the contrast medium should be warmed up to body temperature before administration.

No other drugs or contrast media should be mixed with the iopamidol solution for injection.

Peripheral arteriography and phlebography (enography)

Percutaneous injection into the appropriate blood vessel is used for visualisation of peripheral arteries and veins.

Angiocardiography, left ventriculography, selective coronary arteriography

Niopam may be administered by rapid injection through a catheter into a suitable peripheral artery or vein. It can also be introduced under pressure through a cardiac catheter into any of the heart chambers, or injected into large vessels for immediate visualisation. The contrast medium may also be administered during selective catheterisation of the coronary arteries.

Aortography

The contrast medium may be introduced directly by intra-arterial injection (retro-grade method) for visualisation of the aorta and its main branches.

Arthrography

Visualisation of joint cavities and articular surfaces can be achieved by either single or double contrast examination.

Selective visceral angiography

Visualisation can be achieved by selective catheterisation and injection into the hepatic, coeliac or mesenteric arteries.

Digital subtraction angiography

For cardiac imaging the contrast medium may be administered intra-arterially by selective catheterisation to provide subtracted images. Niopam 340 and 370 injected intravenously either centrally or peripherally is also recommended for use in this modality.

Urography

The contrast medium is injected intravenously and rapidly eliminated through the kidneys. In patients with severe renal failure, high dose urography should be used.

Computer tomography enhancement

Contrast enhancement for brain scans can be achieved between one and three minutes after i.v. injection. Niopam 200 and 300 are also used for total body scanning examinations after i.v. administration as a bolus, as a drip infusion or by a combination of the two methods.

4.3 Contraindications

Hypersensitivity to the active ingredient iopamidol or to any of the excipients.

4.4 Special warnings and precautions for use

Diagnostic procedures which involve the use of any radiopaque medium should be carried out under the direction of personnel with the prerequisite training and with a thorough knowledge of the particular procedure to be performed.

Appropriate facilities should be available for coping with any complication of the procedure, as well as for emergency treatment of severe reaction to the contrast medium itself.

During the examination an intravenous route for emergency treatment in the event of a reaction is required.
After the administration of the contrast medium, competent personnel, drugs and equipment for emergency resuscitation must be available for at least 30 minutes.

Caution during injection of contrast media is necessary to avoid extravasation.

Local tissue irritation can occur as an event of perivascular infiltration of the contrast media.

In patients who are known epileptics or have a history of epilepsy, anticonvulsant therapy should be maintained before and following myelographic procedures. In some instances, anticonvulsant therapy may be increased for 48 hours before the examination. If during the procedure a convulsive crisis occurs, it is recommended to administer intravenously diazepam or phenolbarbital.

Iopamidol injection should be used with caution in patients with hypercalcaemia and cerebral vascular disease.

The risk associated with a particular investigation may be increased by conditions such as advanced arteriosclerosis and hypertension.

The administration of iodinated contrast media may aggravate the symptoms of myasthenia gravis.

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

As with all other contrast media this product may provoke anaphylaxis or other manifestations of allergy with nausea, vomiting, dyspnoea, erythema, urticaria and hypotension. Occasional severe reactions with fatal outcome have been reported.
A positive history of allergy, asthma or untoward reaction during previous similar investigations indicates a need for extra caution; the benefit should clearly outweigh the risk in such patients.
Pre-treatment with antihistamines or corticosteroids to prevent or minimise possible allergic reactions in such patients may be considered.
The risk of bronchospasm-inducing reactions in asthmatic patients is higher after contrast media administration, especially in patients taking beta-blockers.

In patients with suspected or known hypersensitivity to contrast media, sensitivity testing is not recommended, as severe or fatal reactions to contrast media are not predictable from sensitivity tests.
The patient should also be informed that allergic reactions may develop up to several days after the procedure; in such case, a physician should be consulted immediately.

Particular care should be exercised in patients with moderate to severe impairment of renal function (as reflected by a raised blood urea). Substantial deterioration in renal function is minimized if the patient is well hydrated. Renal function parameters, especially urinary output should be monitored after the examination in these patients. Pre-existing renal impairment may predispose to acute renal dysfunction following contrast media administration.
In patients with impairment of renal function, the administration of potentially nephrotoxic drugs should be avoided until the contrast medium is completely excreted. In such patients, renal function parameters should be monitored after the procedure. Further administration of contrast media should be postponed until renal function has returned to its previous level.
Patients on dialysis may receive contrast media such as iopamidol, which can be removed without difficulty by dialysis.
Patients with severe hepatic, renal or combined hepato-renal insufficiency should not be examined unless absolutely indicated. Re- examination should be delayed for 5-7 days.

Care should be taken in renal impairment and diabetes. In these patients it is important to maintain hydration in order to minimise deterioration in renal function.
The presence of renal damage in diabetic patients is one of the factors predisposing to renal impairment following contrast media administration. This may precipitate lactic acidosis in patients who are taking metformin (see section 4.5 - Interaction with medicaments and other forms of interaction).

Patients must be sufficiently hydrated before and after radiographic procedures. Patients with severe functional impairment of the liver or myocardium, myelomatosis, diabetes, polyuria or oliguria, hyperuricemia, infants, elderly patients and patients with severe systemic disease should not be exposed to dehydration.
Fluid intake should not be limited and any abnormalities of fluid or electrolyte balance should be corrected prior to use of this hypertonic solution.

Patients with paraproteinaemia of Waldenström, with multiple myeloma or severely compromised hepatic and renal impairment are also more at risk: in these cases adequate hydration is recommended after contrast medium administration.

Contrast media may promote sickling in individuals who are homozygous for sickle cell disease when injected intravenously and intra-arterially. To prevent crises in patients with sickle cell disease adequate hydration should be assured and a minimal volume of low concentration should be used.

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..

In patients undergoing angiocardiographic procedures special attention should be paid to the status of the right heart and pulmonary circulation. Right heart insufficiency and pulmonary hypertension may precipitate bradycardia and systemic hypotension, when the organic iodine solution is injected. Right heart angiography should be carried out only when absolutely indicated.
During intracardiac and/or coronary arteriography, ventricular arrhythmias may infrequently occur.

Caution should be exercised in performing iodinated contrast-enhanced examinations in patients with, or with suspicion of, hyperthyroidism or autonomously functioning thyroid nodule(s), as thyroid storms have been reported following administration of iodinated contrast media.

Niopam should be used with caution in patients with hyperthyroidism. It is possible that hyperthyroidism may recur in patients previously treated for Graves' disease.

In patients scheduled for thyroid examination with a radioactive iodine tracer, one must take into consideration that iodine uptake in the thyroid gland will be reduced for several days (up to two weeks) after dosing with an iodinized contrast medium that is eliminated through the kidneys.

Patients with phaeochromocytoma may develop severe hypertensive crisis following intravascular Iopamidol. Pre-medication with α-receptor blockers is recommended.

Contrast-induced encephalopathy has been reported during cerebral angiography and angiocardiography. This can manifest with transient symptoms and signs of neurological dysfunction such as headache, visual disturbance, confusion, seizures, loss of coordination, hemiparesis, aphasia, unconsciousness, coma, brain oedema.

In the event of symptoms of encephalopathy, appropriate measures should be taken immediately.

In angiographic procedures, the possibility of dislodging plaque or damaging or perforating the vessel wall should be considered during catheter manipulation and contrast medium injection. Test injections to ensure proper catheter placements are recommended.
In examinations of the aortic arch the tip of the catheter should be positioned carefully to avoid hypotension, bradycardia and CNS injury due to excess pressure transmitted from the injector pump to the brachiocephalic branches of the aorta.
Angiography should be avoided whenever possible in patients with homocystinuria due to an increased risk of thrombosis and embolism.

In patients undergoing peripheral angiography, there should be pulsation in the artery into which the X-ray contrast medium will be injected. In patients with thromboangiitis obliterans or ascending infections in combination with serious ischemia the angiography should be performed, if at all, with special caution.

In patients undergoing venography, special caution should be exercised in patients with suspected phlebitis, serious ischaemia, local infections, or a complete venous occlusion.

Serious neurological events have been observed following direct injection of contrast media into cerebral arteries or vessels supplying the spinal cord or in angiocardiography due to inadvertent filling of the carotids.

Niopam should be administered with caution in elderly patients, in patients with symptomatic cerebrovascular diseases, recent stroke, or frequent TIA, altered permeability of the blood-brain barrier, increased intracranial pressure, suspicion of intracranial tumour, abscess or hematoma/hemorrhage, history of convulsive disorder, chronic alcoholism or multiple sclerosis. Patients with these conditions have an increased risk of neurological complications. Vasospasm and subsequent cerebral ischemic phenomena may be caused by intra-arterial injections of contrast media.

Severe cutaneous adverse reactions

Severe cutaneous adverse reactions (SCARs), such Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (Lyell's syndrome or TEN) and acute generalised exanthematous pustulosis (AGEP), which can be life threatening, have been reported in patients administered Niopam (see section 4.8, undesirable effects). At the time of initiation, patients should be advised of the signs and symptoms and monitored closely for severe skin reactions. If signs and symptoms suggestive of these reactions appear, further use of Niopam should be withheld. If the patient has developed a severe cutaneous adverse reaction with the use of Niopam, Niopam must not be re-administered in this patient at any time.

Intrathecal administration
An accurate evaluation of the risk/benefit ratio is needed if from clinical history there is a previous history of epilepsy or in the presence of blood in the cerebrospinal fluid or presence of local or systemic infection where bacteremia is likely.
The contrast medium should be removed as much as possible in case of spinal fluid blockage.
Use in Special Populations
Newborns, children
Infants (age<1year), and especially newborns are particularly susceptible to electrolyte imbalances and haemodynamic alterations. Care should be taken regarding the dosage to be used, the details of the procedure, and the patient's status.
When examining small children or babies, do not limit fluid intake before administering a hypertonic contrast solution. Also, correct any existing water and electrolyte imbalance.
In paediatric roentgenology, one should proceed with great caution when injecting the contrast medium into the right heart chambers of cyanotic neonates with pulmonary hypertension and impaired cardiac function.

Transient hypothyroidism may occur in neonates when the mother or the neonate has received an
iodinated contrast agent. Thyroid function tests (usually TSH and T4) are recommended in neonates
7-10 days and 1 month after exposure to Niopam especially in preterm neonates.

Elderly
The elderly are at special risk of reactions due to reduced physiological functions, especially when high dosage of contrast medium is used. Myocardial ischemia, major arrhythmias and

premature ventricular complexes are more likely to occur in these patients. The probability of acute renal insufficiency is higher in these patients.

Women of child-bearing potential

X-ray examination of women should if possible be conducted during the pre-ovulation phase of the menstrual cycle and should be avoided during pregnancy. Appropriate investigations and measures should be taken when exposing women of child-bearing potential to any X-ray examination, whether with or without contrast medium.

4.5 Interaction with other medicinal products and other forms of interaction

Following administration of iopamidol, the capacity of the thyroid tissue to take up iodine is reduced for 2-6 weeks.

Thyroid function tests: use of iodinated contrast media may interfere with tests for thyroid function which depend on iodine estimations, such as Protein Binding Iodine and radioactive iodine up take. As a consequence they will not accurately reflect thyroid function for up to 16 days following administration of iodinated contrast media. Thyroid function tests not depending on iodine estimations, e.g. T3 resin uptake and total or free thyroxine (T4) assays are not affected.

To prevent onset of lactic acidosis in diabetic patients under treatment with oral anti-diabetic agents of the biguanide class and with moderate renal impairment undergoing elective procedures, biguanides should be stopped 48 hours prior to the administration of the contrast medium and re-instated only after 48 hours if serum creatinine is unchanged. (See section 4.4 Special warnings and precautions).

In emergency patients in whom renal function is either impaired or unknown, the physician shall weigh out risk and benefit of an examination with a contrast medium. Metformin should be stopped from the time of contrast medium administration. After the procedure, the patient should be monitored for signs of lactic acidosis. Metformin should be restarted 48 hours after contrast medium if serum creatinine/eGFR is unchanged from the pre-imaging level.

Patients with normal renal function can continue to take Metformin normally.

Arterial thrombosis has been reported when Iopamidol was given following papaverine.

Cardiac and/or hypertensive patients under treatment with diuretics, ACE-inhibitors, and/or beta-blocking agents are at higher risk of adverse reactions when administered iodinated contrast media.

In patients reciving beta-blockers there is an elevated risk of more severe anaphylactoid reactions.

Beta-blockers may impair the response to treatment of bronchospasm induced by contrast medium.

The administration of vasopressors strongly potentiates the neurological effect of the intra-arterial contrast media.

Renal toxicity has been reported in patients with liver dysfunction who were given oral cholecystographic agents followed by intravascular contrast agents. Therefore, administration of intravascular contrast agents should be postponed in patients who have recently been given a cholecystographic contrast agent.

Contrast media may interfere with laboratory tests for bilirubin, proteins or inorganic substances (e.g. iron, copper, calcium, phosphate). These substances should not be assayed during the same day following the administration of contrast media.

Following administration of iopamidol atypical adverse reactions e.g. erythema, fever and flu symptoms have been reported in patients treated with interleukin-2.

Intrathecal administration

Neuroleptics must be absolutely avoided because they lower the seizure threshold. The same applies to analgesics, anti-emetics, antihistamines and sedatives of the phenothiazine group. Whenever possible, treatment with such drugs should be discontinued at least 48 hours before administration of the contrast medium and treatment can be resumed not earlier than 24 hours afterwards.

4.6 Fertility, Pregnancy and lactation

X-ray examination of women should if possible be conducted during the pre-ovulation phase of the menstrual cycle and should be avoided during pregnancy; also, since it has not been demonstrated that Niopam is safe for use in pregnant women, it should be administered only if the procedure is considered essential by the physician. Apart from radiation exposure of the foetus, benefit-risk consideration for iodine-containing contrast agents should also take into account the sensitivity of the foetal thyroid towards iodine.

Iodine-containing X-ray contrast agents are excreted into the breast milk in low amounts. From animal experience, Niopam is non toxic in animals after oral administration. From experience gained so far, harm to the nursing infant is unlikely to occur. Stopping breastfeeding is unnecessary

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 one hour following the last injection.

4.8 Undesirable effects

The use of iodinated contrast media may cause untoward side effects. They are usually mild to moderate and transient in nature. However, severe and life threatening reactions sometimes leading to death have been reported.

Anaphylaxis (anaphylactoid reactions/hypersensitivity) may manifest with: mild localized or more diffuse angioneurotic oedema, tongue oedema, laryngospasm or laryngeal oedema, dysphagia, pharyngitis and throat tightness, pharyngolaryngeal pain, cough, conjunctivitis, rhinitis, sneezing, feeling hot, sweating increased, asthenia, dizziness, pallor, dyspnoea, wheezing, bronchospasm, and moderate hypotension. Skin reactions may occur in the form of various types of rash, diffuse erythema, diffuse blisters, urticaria, and pruritus. These reactions, which occur

irrespective of the dose administered and the route of administration, may represent the first signs of incipient state of shock. Administration of the contrast medium must be discontinued immediately and – if necessary – specific treatment initiated via a venous access.

Following intravascular administration, in most cases reactions occur within minutes of dosage. However, delayed reactions, usually involving skin, may occur, mostly within 2-3 days, more rarely within 7 days, after the administration of the contrast medium.

More severe reactions involving the cardiovascular system such as vasodilatation with pronounced hypotension, tachycardia, dyspnoea, agitation, cyanosis and loss of consciousness progressing to respiratory and/or cardiac arrest may result in death. These events can occur rapidly and require full and aggressive cardio-pulmonary resuscitation.

Primary circulatory collapse can occur as the only and/or initial presentation without respiratory symptoms or without other signs or symptoms outlined above.

Severe cutaneous adverse reactions (SCARs), including Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN) and acute generalized exanthematous pustulosis (AGEP) have been reported in association with Niopam administration (see section 4.4).

Intravascular administration –Adults

The adverse reactions are classified by System Organ Class and frequency, using the following convention: 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)

System Organ Class	**Adverse Reactions**			
	Clinical Trials			**Post-marketing Surveillance**
	Common (≥1/100 to <1/10)	**Uncommon (≥1/1,000 to <1/100)**	**Rare (≥1/10,000 to <1/1,000)**	**Frequency unknown**
Blood and lymphatic system disorders				Thrombocytopenia
Immune system disorders				Anaphylaxis, Anaphylactoid reaction
Psychiatric disorders			Confusional state	
Nervous system disorders	Headache	Dizziness, Taste alteration	Paraesthesia	Coma, Transient ischaemic attack, Syncope, Depressed level of consciousness or loss of consciousness, Convulsion, Hemiplegia

Eye disorders				Transient blindness, Visual disturbance, Conjunctivitis, Photophobia
Cardiac disorders		Cardiac dysrhythmias such as extrasystoles, atrial fibrillation, ventricular tachycardia and ventricular fibrillation*	Bradycardia	Myocardial ischaemia or infarction, Cardiac failure, Cardio-respiratory arrest, Tachycardia, Kounis syndrome
Vascular disorders		Hypotension, Hypertension, Flushing		Circulatory collapse or shock
Respiratory, thoracic and mediastinal disorders			Pulmonary oedema, Asthma, Bronchospasm	Respiratory arrest, Respiratory failure, Acute respiratory distress syndrome, Respiratory distress, Apnoe Laryngeal oedema, Dyspnoea
Gastrointestinal disorders	Nausea	Vomiting, Diarrhea, Abdominal pain, Dry mouth		Salivary hypersecretion, Salivary gland enlargement
Skin and subcutaneous tissue disorders		Rash, Urticaria, Pruritus, Erythema, Sweating increased		Face oedema, muco-cutaneous syndromes*, Acute generalised exanthematous pustulosis (AGEP**)**
Musculoskeletal and connective tissue disorders		Back pain	Muscle spasms	Musculoskeletal pain, Muscular weakness
Renal and urinary disorders		Acute renal failure		
General disorders and administration site conditions	Feeling hot	Chest pain, Injection site pain***, Pyrexia, Feeling cold		Rigors, Pain, Malaise
Investigations		Blood creatinine increased		Electrocardiogram change including ST segment depression

* Cardiac reactions may occur as consequences of the coronary catheterization procedural hazard: these complications include coronary artery thrombosis and coronary artery embolism.

** As with other iodinated contrast media, very rare cases of muco-cutaneous syndromes, including Stevens-Johnson syndrome, toxic epidermal necrolysis (Lyell syndrome) and erythema multiforme, have been reported following the administration of Iopamidol

*** Injection site pain and swelling may occur. In the majority of cases it is due to extravasation of contrast medium. These reactions are usually transient and result in recovery without sequelae. However, inflammation and even skin necrosis have been seen on very rare occasions. In isolated reports extravasation led to the development of compartment syndrome

Intravascular administration – Pediatric Population
Frequency type and severity of adverse reactions in children are similar to those in adults.

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. Healthcare professionals are asked to report any suspected adverse reactions via the Yellow Card Scheme
Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store

4.9 Overdose

Dosages exceeding the specific package insert dose are not recommended, as they might lead to life-threatening adverse effects.

If needed, haemodialysis can be used to eliminate Iopamidol from the body.

Treatment of overdosage is directed toward the support of all vital functions and prompt institution of symptomatic therapy.

Intravascular

In the event of accidental intravascular overdose in humans, the water and electrolyte losses must be compensated by infusion. Renal function should be monitored for at least three days.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Iopamidol is contrast medium belonging to the new generation of non-ionic compound whose solubility is due to the presence of hydrophilic substitutes in the molecule. This results in a solution of low osmolality when compared with ionic media.

Iopamidol has been shown to be effective as an X-ray contrast medium in neuroradiology, angiography, venography, arthrography, urography, cerebral angiography and left ventriculography and coronary arteriography. Its toxicity particularly cardiac and CNS toxicity are less than those of ionic contrast media.

5.2 Pharmacokinetic properties

The pharmacokinetics of Iopamidol conform to an open two compartment pharmacokinetic model with first order elimination.

Distribution volume is equivalent to extracellular fluid.

Elimination is almost completely through the kidneys. Less that 1 % of the administered dose has been recovered in the faeces up to 72 hours after dosing. Elimination is rapid; up to half the administered dose may be recovered in the urine in the first two hours of dosing.

There is no evidence of biotransformation.

Serum protein binding is negligible.

5.3 Preclinical safety data

No adverse effects can be predicted from animal toxicology studies other than those documented from human use of Iopamidol.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Excipients are trometamol, hydrochloric acid and edetate calcium disodium.

6.2 Incompatibilities

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products

6.3 Shelf life

5 years.

6.4 Special precautions for storage

Protect from light.

No Data Held

6.5 Nature and contents of container

200 ml clear, colourless Type I or Type II glass bottles with rubber closures and aluminium caps

6.6 Special precautions for disposal

Discard if the solution is not clear of particulate matter.

Exceptionally, the event of crystallisation of Niopam could occur. It has been shown that such a phenomenon is caused by a damaged or defective container and therefore the product should not be used in this case.

The bottle, once opened, must be used immediately.

Any unused medicinal product or waste material should be disposed off in accordance with local requirements.

Niopam, as other iodinated contrast media, can react with metallic surfaces containing copper (e.g. brass), therefore the use of equipment, in which the product comes into direct contact with such surfaces, should be avoided.

7. **MARKETING AUTHORISATION HOLDER**

Bracco UK, Ltd
Magdalen Centre, The Oxford Science Park,Oxford, OX4 4GA,United Kingdom

8 MARKETING AUTHORISATION NUMBER(S)

PL18920/0034

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

13.01.1989 / 13.0l.1994

10 DATE OF REVISION OF THE TEXT

18/01/2022