Guidance for the Administration of Medicinal Products by non-medical personnel as part of clinical nuclear medicine procedures

Report May 2016

British Nuclear Medicine Society Professional Standards Committee

Contents

Introduction

A number of nuclear medicine procedures require the administration of non-radioactive medicinal products in order to optimise the biodistribution of the radiopharmaceutical. The preparation and administration of these medicines is often undertaken by non-medical personnel including nurses, radiographers and nuclear medicine clinical practitioners.

This document provides guidance on the preparation and administration of these non-radioactive medicines and should be read in conjunction with 'Certificate for the administration of intravenous radiopharmaceuticals by healthcare professionals working in nuclear medicine' (BNMS Nurses and clinical practitioners Groups) [1] (Appendix and 'Safety in Doses: Improving the use of medicines in the UK' (NPSA) [2]

Non-medical clinical staff who administer medicines should have received appropriate specific training and demonstrated competence in the appropriate procedures. Guidance is given here but individuals should ensure that they also comply with all local requirements. This document is intended to be used to aid Trusts in preparing local Standard Operating Procedures, training programmes and assessment of competency for the administration of non-radioactive medicines by non-medical personnel for the purposes of undertaking clinical nuclear medicine procedures.

It is expected that non-medical nuclear medicine personnel administering non-radioactive medicines will have received training, and demonstrated competency, in administration of intravenous injections [1] (Appendix 6) and Intermediate Life Support satisfying all local requirements in this respect and will be working to locally agreed Standard Operating Procedures. Administration of medicines to children requires additional specialised training in drug administration and life support.

This guidance is intended to complement, and be used in conjunction with, the following documents:-

'Certificate for the administration of intravenous radiopharmaceuticals by healthcare professionals working in nuclear medicine' (BNMS Nurses and Clinical Practitioners Groups) [1]

'Safety in Doses: Improving the use of medicines in the UK (NPSA) [2]

'The Responsibilities of Chief Pharmacists for the Purchase and Supply of Radiopharmaceuticals' prepared by the UK Radiopharmacy group[3]

'Clinical competence in myocardial perfusion scintigraphic stress testing: General training guidelines and assessment'[4]

More detailed information on each licensed drug is available in the manufacturers Summary of Product Characteristics (SPC) and the British National Formulary (BNF)

This guidance is <u>not</u> intended to cover medicines used for clinical treatment of adverse events occurring during nuclear medicine procedures (eg. Reaction to any pharmaceutical administered including the relevant radiopharmaceutical, worsening of a pre-existing condition such as asthma) or non-pharmaceutical adjuncts used in nuclear medicine (eg. Lemon juice, fatty meals).

The document will be subject to annual review by the British Nuclear Medicine Society's Professional Standards Committee and any changes in the use of medicines in Nuclear Medicine will be reported to the Commission for Human Medicines via the ARSAC Secretariat.

BNMS Members are asked to inform the Society if they are aware of medicines being used in clinical Nuclear Medicine, as part of the procedure, that are not listed here so that this guidance can be maintained as a comprehensive list.

Local Protocols

Locally agreed written protocols must be available covering the following:

1. Procurement and storage of medicines in the nuclear medicine department.
2. Preparation of medicines
3. Administration of medicines. These should cross reference the relevant protocols for the nuclear medicine procedure
4. Training and competency requirements for non-medical staff who administer medicines.
5. Assessment and audit of risks of preparing medicines in clinical areas.

Preparation of Medicines

Training should be based on the NPSA Work competence statement – 'Preparation of injectable medicines' NPSA March 2007 (Injectable medicines competence 2)

Before authorization to prepare medicines the trainee should demonstrate knowledge and competency in the following areas:-

- Procurement and storage of the relevant medicines.
- Formulation and presentation.
- Dose calculation
- Facilities and equipment required for preparation
- Risks associated with preparation of the medicines
- Preparation procedures
    - Oral doses (tablets and liquid formulations)
    - Intravenous injections and infusions that require only withdrawal from primary container
    - Intravenous injections and infusions that require dilution before administration

    - Intravenous injections and infusions that require reconstitution before administration

- Storage and shelf-life of the prepared dose
- Relevant documentation

Administration of Medicines

Training should be based on the NPSA Workforce competence statement 'Administration of injectable medicines' March 2007 (Injectable medicines competence 3)

Before authorization to administer medicines the trainee should demonstrate knowledge and competency relevant to each individual medicine in the following areas:-

- Application to nuclear medicine procedure
- Formulation and presentation
- Route of administration
- Normal dose for nuclear medicine application
- Calculation of dose/volume
- Timing of administration in relation to the nuclear medicine procedure and administration of the radiopharmaceutical
- Main pharmacological actions
- Contraindications to administering the medicine including an understanding of the relevance of published contraindications to the dosage schedule used in nuclear medicine (normally single dose or short-term administration).
- Drug interactions including an understanding of the clinical significance of published interactions to the dosage schedule used in nuclear medicine (normally single dose or short-term administration).
- Adverse drug reactions including an understanding of the clinical significance of published adverse reactions to the dosage schedule used in nuclear medicine (normally single dose or short-term administration).
- Recognition of, and appropriate action to take, in the case of suspected adverse reaction
- Communication with patients;
    - eliciting relevant information on potential contraindications, allergies and concurrent drug therapy
    - obtaining consent to administer the medicine

- advice to patient about potential delayed affects and actions required

- Intravenous injection and infusion
- Intermediate Life Support
- Relevant documentation

Medicines used in Nuclear Medicine as part of the clinical procedure (2016)

[* Medicines for which this draft contains sample templates]

Acetazolamide	HMPAO Brain perfusion imaging
Adenosine *	Myocardial perfusion imaging
Atropine *	Myocardial perfusion imaging
Captopril	Renogram
Cimetidine *	Meckels Diverticulum
Dipyridamole *	Myocardial perfusion imaging
Diazepam	F-18 FDG PET imaging
Dobutamine *	Myocardial perfusion imaging
Furosemide *	Renogram
Glyceryl Trinitrate	Cardiac imaging
Laxative + dexamethasone	Adrenal
Laxatives	Octreoscan
Laxatives	Gallium imaging
Lugols iodine	Iodine-labelled RPx
Lysine/Arginine	Peptide Receptor Radionuclide Therapy
Methylphenidate	F-18 Fallypride
Morphine *	Hepato-cholescintigraphy
Omeprazole *	Meckels Diverticulum
Potassium iodide	Iodine-labelled RPx
Potassium iodate	Iodine-labelled RPx
Ranitidine *	Meckels Diverticulum
Regadenason*	Myocardial perfusion imaging
Sincalide*	Hepato-cholescintigraphy
Sodium Perchlorate	Iodine-labelled RPx
Thyrotropin Alpha	Thyroid imaging and therapy
Iohexol (Omnipaque) *	X-ray contrast media (CT)
Iodixanol (Visipaque) *	X-ray contrast media (CT)
Loversol (Optiray)*	X-ray contrast media (CT)
Iomeprol (Iomeron)*	X-ray contrast media (CT)
Lopamidol (Niopam) *	X-ray contrast media (CT)
Lobitridol (Xenetix) *	X-ray contrast media (CT)

Where adverse reactions are classified by frequency these are defined as: very common (>1/10), common (>1/100, <1/10), uncommon (>1/1000, <1/100), rare (>1/10000, <1/1000), very rare (<1/10000)

References

1. ‘Certificate for the administration of intravenous radiopharmaceuticals by healthcare professionals working in nuclear medicine’ (BNMS Nurses and Clinical Practitioners Groups) (*BNMS website)*

2. ‘Safety in Doses: Improving the use of medicines in the UK (National Patient Safety Agency). NPSA March 2007.

3. ‘The Responsibilities of Chief Pharmacists for the Purchase and Supply of Radiopharmaceuticals’ prepared by the UK Radiopharmacy group *(BNMS website)*

4. ‘Clinical competence in myocardial perfusion scintigraphic stress testing: General training guidelines and assessment’, Jones et al, Nuclear Medicine Communications, 2007 28(7): 575-80

Drug name:		**Adenosine**
Nuclear Medicine Procedure		Myocardial Perfusion Imaging
Usual clinical use	**Therapeutic Indications** **Diagnostic Indications**	Rapid conversion to a normal sinus rhythm of paroxysmal supraventricular tachycardias, including those associated with accessory by-pass tracts (Wolff-Parkinson-White Syndrome). Aid to diagnosis of broad or narrow complex supraventricular tachycardias. Although Adenosine will not convert atrial flutter, atrial fibrillation or ventricular tachycardia to sinus rhythm, the slowing of AV conduction helps diagnosis of atrial activity. Sensitisation of intra-cavitary electrophysiological investigations.
Relevant Pharmacological action		Antiarrhythmic
Drug Interactions		Dipyridamole is a known inhibitor of adenosine uptake so may potentiate the action of Adenosine; in one study dipyridamole was shown to produce a 4 fold increase in adenosine actions. Asystole has been reported following concomitant administration. It is therefore suggested that Adenosine should not be administered to patients receiving dipyridamole; if use of Adenosine is essential, its dosage should be reduced. Theophylline and other xanthines such as caffeine are known strong inhibitors of adenosine. Adenosine may interact with drugs tending to impair cardiac conduction.
Contraindications		Second or third degree AV block (except in patients with a functioning artificial pacemaker). Sick sinus syndrome (except in patients with a functional artificial pacemaker). Asthma Hypersensitivity to adenosine.
Adverse Reactions	**Nervous system disorders**	Side effects are generally mild, of short duration (usually less than 1 minute) and well tolerated by the patient. However severe reactions can occur. Headache, dizziness / lightheadedness - Commonly Transient, and spontaneously and rapidly reversible worsening of intracranial hypertension - Very rarely

	Psychiatric disorders **Special senses disorders**	Apprehension - Commonly Blurred vision, metallic taste - Uncommonly
	Gastro-intestinal system disorders	Nausea - Commonly:
	Cardiovascular disorders:	Very commonly: - facial flush - bradycardia - asystole - sinus pause - atrioventricular block - atrial extrasystoles - skipped beats -ventricular excitability disorders such as ventricular extrasystoles, non-sustained ventricular tachycardia Uncommonly: - sinus tachycardia - palpitations Very rarely: - severe bradycardia which is not corrected by atropine and may require temporary pacing - atrial fibrillation - torsade de pointes - ventricular fibrillation Adenosine induced bradycardia predisposes to ventricular excitability disorders, including ventricular fibrillation and torsade de pointes. The above mentioned cardiac arrhythmias occur at the time of conversion to normal sinus rhythm
	Respiratory system disorders	Very commonly: dyspnoea Uncommonly: hyperventilation Very rarely: bronchospasm, apnoea (usually in patients with evidence of pre-existing asthma/COPD)

	General disorders **Application site**	Commonly: Feeling of thoracic constriction / chest pain / chest pressure, burning sensation Uncommonly: head pressure, heaviness in arms, neck and back pain, sweating Very rarely: feeling of discomfort Very rarely: injection site reactions
Typical dose range used in nuclear medicine procedure		0.14mg/Kg/min over 6 mins to a max total dose of 0.84mg/kg
Preparation		Clear, colourless sterile solution for injection requiring appropriate dose to be drawn-up into a syringe for administration by intravenous infusion. See Appendix 2.
Administration		Patients stressed with adenosine must abstain from caffeine-containing foods, beverages and medications for a minimum of 12 hours prior to the test and preferably for 24hours.Aminophylline and theophylline must be stopped 24 hours before the test. Patients on dipyridamole should discontinue the drug for a minimum of 24 hours prior to vasodilator stress. 1.Adenosine should be administered undiluted as a continuous peripheral intravenous infusion at a dose of 140 µg/kg/min for six minutes using an infusion pump. Separate venous sites for Adenosine and radionuclide administration are recommended to avoid an adenosine bolus effect. 2. After three minutes of Adenosine infusion, the radionuclide is injected to ensure sufficient time for peak coronary blood flow to occur. The optimal vasodilator protocol is achieved with six minutes of Adenosine infusion. 3. To avoid an adenosine bolus effect, blood pressure should be measured in the arm opposite to the Adenosine infusion. See Appendix 3
Drug name:		Atropine Injection
Nuclear Medicine Procedure		Myocardial Perfusion Imaging
Usual clinical use		Acute myocardial infarction with AV conduction block due to excess vagal tone (Wenkebach Type I, second-degree AV block) and sinus bradycardia, with associated hypotension and increased ventricular irritability.

		Atropine can also be used in cardiopulmonary resuscitation for the treatment of sinus bradycardia accompanied by hypotension, hypoperfusion or ectopic arrhythmias. Parenteral atropine is indicated as an antisialogogue in anaesthetic premedication to prevent or reduce secretions of the respiratory tract. During anaesthesia, atropine may be used to prevent reflex bradycardia and restore cardiac rate and arterial pressure resulting from increased vagal activity associated with laryngoscopy, tracheal intubation and intra-abdominal manipulation. It may also be administered to block muscarinic effects when neostigmine is used to counteract muscle relaxants such as tubocurarine. Parenteral atropine is an antidote for cardiovascular collapse following overdose of anticholinesterases; in the treatment of poisoning from organophosphorous insecticides or from chemical warfare 'nerve' gases and in the treatment of mushroom poisoning.
Relevant Pharmacological action		Atropine is an antimuscarinic agent which competitively antagonizes acetylcholine at postganglionic nerve endings, thus affecting receptors if the exocrine glands, smooth muscle, cardiac muscle and the central nervous system. Peripheral effects include decreased production of saliva, sweat, nasal, lachrymal and gastric secretions, decreased intestinal motility and inhibition of micturition. Atropine increases sinus rate and sinoatrial and AV conduction. Usually heart rate is increased, but there may be an initial bradycardia. Atropine inhibits secretions throughout the respiratory tract and relaxes bronchial smooth muscle producing bronchodilation.
Drug Interactions		The effects of atropine may be enhanced by the concomitant administration of other drugs with anticholinergic activity eg. tricyclic antidepressants, antispasmodics, anti-parkinsonian drugs, some antihistamines, phenothiazines, disopyramide and quinidine. By delaying gastric emptying, atropine may alter the absorption of other drugs.

Contraindications		Contra-indications are not applicable to the use of atropine in life-threatening emergencies (eg. asystole). Atropine is contraindicated in patients with known hypersensitivity to the drug, obstruction of the bladder neck eg due to prostatic hypertrophy, reflux oesophagitis, closed angle glaucoma, myasthenia gravis (unless used to treat the adverse effects of an anticholinesterase agent), paralytic ileus, severe ulcerative colitis and obstructive disease of the gastrointestinal tract.
Adverse Reactions		Adverse effects are dose-related and usually reversible when therapy is discontinued. In relatively small doses, atropine reduces salivary, bronchial and sweat secretions; dry mouth and anhidrosis may develop, these effects being intensified as the dosage is increased. Reduced bronchial secretion may cause dehydration of residual secretion and consequent formation of thick bronchial plugs that are difficult to eject from the respiratory tract. Larger doses dilate the pupil and inhibit accommodation of the eye, and block vagal impulses with consequent increase in heart rate with possible atrial arrhythmias, A-V dissociation and multiple ventricular ectopics; parasympathetic control of the urinary bladder and gastrointestinal tract is inhibited, causing urinary retention and constipation. Further increase in dosage inhibits gastric secretion. Anaphylaxis, urticaria and rash occasionally progressing to exfoliation may develop in some patients. Other effects include hallucinations, increased ocular tension, loss of taste, headache, nervousness, drowsiness, weakness, dizziness, flushing, insomnia, nausea, vomiting and bloated feeling. Mental confusion and/or excitement may occur especially in the elderly.
Typical dose range used in nuclear medicine procedure		1mg max if required
Preparation		Clear colourless sterile solution for injection requiring withdrawal of appropriate dose from glass ampoule. See Appendix 2.
Administration		Intravenous injection. See Appendix 3.
Drug name:		Cimetidine

Nuclear Medicine Procedure		Meckels Diverticulum Imaging
Usual clinical use		Cimetidine is a histamine H2-receptor antagonist which rapidly inhibits both basal and stimulated gastric secretion of acid and reduces pepsin output. Cimetidine is indicated in the treatment of duodenal and benign gastric ulceration, including that associated with non-steroidal anti-inflammatory agents, recurrent and stomal ulceration, oesophageal reflux disease and other conditions where reduction of gastric acid by Cimetidine has been shown to be beneficial: persistent dyspeptic symptoms with or without ulceration, particularly meal-related upper abdominal pain, including such symptoms associated with non-steroidal anti-inflammatory agents; the prophylaxis of gastrointestinal haemorrhage from stress ulceration in seriously ill patients; before general anaesthesia in patients thought to be at risk of acid aspiration (Mendelson's) syndrome, particularly obstetric patients during labour; to reduce malabsorption and fluid loss in the short bowel syndrome; and in pancreatic insufficiency to reduce degradation of enzyme supplements. Cimetidine is also recommended in the management of the Zollinger-Ellison syndrome.
Relevant Pharmacological action		
Drug Interactions		Cimetidine can prolong the elimination of drugs metabolised by oxidation in the liver. Although pharmacological interactions with a number of drugs (e.g. diazepam, propranolol) have been demonstrated, only those with oral anticoagulants, phenytoin, theophylline and intravenous lidocaine appear, to date, to be of clinical significance. Close monitoring of patients on Cimetidine receiving oral anticoagulants or phenytoin is recommended and a reduction in the dosage of these drugs may be necessary. In patients on drug treatment or with illnesses that could cause falls in blood cell count, the possibility that H2-receptor antagonism could potentiate this effect should be borne in mind. Cimetidine has the potential to affect the absorption, metabolism or renal excretion of other drugs which is particularly important when drugs with a narrow therapeutic index are administered concurrently. The altered pharmacokinetics may necessitate dosage adjustment of the affected drug or discontinuation of treatment. Interactions may occur by several mechanisms including:

		1) Inhibition of certain cytochrome P450 enzymes (including CYP1A2, CYP2C9, CYP2D6 and CYP3A3/A4, and CYP2C18); Inhibition of these enzymes may result in increased plasma levels of certain drugs including warfarin-type coumarin anticoagulants (e.g. warfarin), tricyclic antidepressants (e.g. amitriptyline), class I antiarrhythmics (e.g. lidocaine, quinidine), calcium channel blockers (e.g. nifedipine, diltiazem), oral sulfonylureas (e.g. glipizide), phenytoin, theophylline and metoprolol. 2) Competition for renal tubular secretion; This may result in increased plasma levels of certain drugs including procainamide, quinidine, metformin, ciclosporin and tacrolimus. 3)Alteration of gastric pH; The bioavailability of certain drugs may be affected. This can result in either an increase in absorption (e.g. atazanavir) or a decrease in absorption (e.g. some azole antifungals such as ketoconazole, itraconazole or posaconazole). 4) Unknown mechanisms; Cimetidine may potentiate the myelosuppressive effects (e.g. neutropenia, agranulocytosis) of chemotherapeutic agents such as carmustine, fluorouracil, epirubicin, or therapies such as radiation. Isolated cases of clinically relevant interactions have been documented with narcotic analgesics (e.g. morphine).
Contraindications		Hypersensitivity to cimetidine.
Adverse Reactions	**Blood and lymphatic system disorders** **Immune system disorders** **Psychiatric disorders** **Nervous system disorders**	Uncommon: Leukopenia Rare: Thrombocytopenia, aplastic anaemia Very rare: Pancytopenia, agranulocytosis Very rare: Anaphylaxis Anaphylaxis is usually cleared on withdrawal of the drug. Uncommon: Depression, confusional states, hallucinations Confusional states, reversible within a few days of withdrawing cimetidine, have been reported, usually in elderly or ill patients. Common: Headache, dizziness

	Cardiac disorders	Uncommon: Tachycardia Rare: Sinus bradycardia Very rare: Heart block
	Gastrointestinal disorders	Common: Diarrhoea Very rare: Pancreatitis Pancreatitis cleared on withdrawal of the drug.
	Hepatobiliary disorders	Uncommon: Hepatitis Rare: Increases in serum transaminase levels Hepatitis and increases in serum tranaminase levels cleared on withdrawal of the drug.
	Skin and subcutaneous tissue disorders	Common: Skin rashes Very rare: Reversible alopecia and hypersensitivity vasculitis Hypersensitivity vasculitis usually cleared on withdrawal of the drug.
	Musculoskeletal and connective tissue disorders	Common: Myalgia Very rare: Arthralgia
	Renal and urinary disorders	Uncommon: Increases in plasma creatinine Rare: Interstitial nephritis Interstitial nephritis cleared on withdrawal of the drug. Small increases in plasma creatinine have been reported, unassociated with changes in glomerular filtration rate. The increases do not progress with continued therapy and disappear at the end of therapy.
	Reproductive system and breast disorders	Uncommon: Gynaecomastia and reversible impotence Gynaecomastia is usually reversible upon discontinuation of cimetidine therapy. Reversible impotence has been reported particularly in patients receiving high doses (e.g. in Zollinger-Ellison Syndrome). However, at regular dosage, the incidence is similar to that in the general population. Very rare: Galactorrhoea

	General disorders and administration site conditions	Common: Tiredness Very rare: Fever Fever cleared on withdrawal of the drug.
Typical dose range used in nuclear medicine procedure		400mg twice daily for 3 days before scanning
Preparation		Oral tablets or suspension
Administration		Orally.
Drug name:		Diazepam
Nuclear Medicine Procedure		
Usual clinical use		Diazepam may be used in severe or disabling anxiety and agitation; for the control of status epilepticus, epileptic and febrile convulsions; to relieve muscle spasm; as a sedative in minor surgical and dental procedures; or other circumstances in which a rapid effect is required. It is used in the short-term treatment of anxiety and tension states, as a sedative and premedicant, in the control of muscle spasm and in the management of alcohol withdrawal symptoms.
Relevant Pharmacological action		Diazepam is a psychotropic substance from the class of 1,4-benzodiazepines with marked properties of suppression of tension, agitation and anxiety as well as sedative and hypnotic effects. In addition, diazepam demonstrates muscle relaxant and anticonvulsive properties
Drug Interactions	**Anaesthetics and narcotic analgesics:** **Antibacterials:**	Enhanced sedation or respiratory and cardiovascular depression. If such centrally acting depressant drugs are given parenterally in conjunction with intravenous diazepam, severe respiratory and cardiovascular depression may occur; careful monitoring is required. When intravenous diazepam is to be administered concurrently with a narcotic analgesic agent (e.g. fentanyl), it is recommended that diazepam be given after the analgesic and that the dose be carefully titrated to meet the patient's needs. Premedication with diazepam may decrease the dose of fentanyl derivatives required for induction of anaesthesia. Agents that interfere with metabolism by hepatic enzymes (e.g. erythromycin and isoniazid) may reduce the clearance of benzodiazepines and potentiate their action. Known inducers of hepatic enzymes, for example, rifampicin, may increase the clearance of benzodiazepines.

	Antidepressants	Enhanced sedation or respiratory and cardiovascular depression. Diazepam plasma levels increased by concomitant fluvoxamine.
	Antiepileptics:	Enhanced sedation or respiratory and cardiovascular depression. Known inducers of hepatic enzymes, for example, carbamazepine and phenytoin, may increase the clearance of benzodiazepines. Serum phenytoin levels may rise, fall or remain unaltered. In addition, phenytoin may cause diazepam serum levels to fall. Concomitant sodium valproate may increase serum levels of diazepam, with associated drowsiness.
	Antihistamines:	Enhanced sedation or respiratory and cardiovascular depression with sedative antihistamines.
	Antihypertensives	Enhanced hypotensive effect, enhanced sedative effect with alpha blockers and possibly moxonidine.
	Antipsychotics	Enhanced sedation or respiratory and cardiovascular depression. Increased plasma concentrations of zotepine. Severe hypotension, collapse, respiratory depression, potentially fatal respiratory arrest and unconsciousness have been reported in a few patients on benzodiazepines and clozapine. Caution is advised when initiating clozapine therapy in patients taking benzodiazepines.
	Antivirals:	Amprenavir and ritonavir have been shown to reduce the clearance of benzodiazepines and may potentiate their actions, with risk of extreme sedation and respiratory depression – avoid concomitant use.
	Anxiolytics:	Enhanced sedation or respiratory and cardiovascular depression with other anxiolytics.
	Other drug interations	Reduced clearance of digoxin. Disulfiram: has been shown to reduce clearance and may potentiate actions of benzodiazepines. Dopaminergic agents: diazepam may cause inhibition of levodopa. Hypnotics: Enhanced sedation or respiratory and cardiovascular depression. Lofexidine: Enhanced sedation or respiratory and cardiovascular depression. Muscle relaxants: Increased CNS depressant effects with baclofen and tizanidine. Nabilone: Enhanced sedation or respiratory and cardiovascular depression. Nicotine: Diazepam metabolism is accelerated by smoking. Oral contraceptives: Reduce the clearance of benzodiazepines and may potentiate their actions.

		Sedatives: Enhanced sedation or respiratory and cardiovascular depression. Theophylline: Diazepam metabolism is accelerated by theophylline. Ulcer-healing drugs: Cimetidine and omeprazole have been shown to reduce the clearance of benzodiazepines and may potentiate their actions.
Contraindications		Known sensitivity to benzodiazepines or any of the ingredients Severe or acute respiratory insufficiency/depression Sleep apnoea syndrome Severe hepatic insufficiency Avoid injection in neonates (contains benzyl alcohol) Diazepam injection should not be used in phobic or obsessional states nor be used alone in the treatment of depression or anxiety associated with depression due to the risk of suicide being precipitated in this patient group. Diazepam Injection should not be used for the primary treatment of psychotic illness. In common with other benzodiazepines the use of diazepam may be associated with amnesia and Diazepam Injection should not be used in cases of loss or bereavement as psychological adjustment may be inhibited.
Adverse Reactions		The side effects of diazepam are usually mild and infrequent.
	Cardiovascular	Hypotension, particularly with high dosage, bradycardia, chest pain. Diazepam injection may be associated with thrombophlebitis.
	CNS	Elderly or debilitated patients are particularly susceptible to the CNS effects of benzodiazepines. It is recommended that dosage be limited to the smallest effective dose and increased gradually, if necessary, to decrease the possibility of development of ataxia, dizziness, and oversedation, which may lead to falls and other accidents
	Disorders of the eye:	Visual disturbances.
	Gastrointestinal:	Dry mouth, gastrointestinal disturbances.
	General:	Fatigue and a hangover effect. Diazepam injection may be associated with pain.
	Haematological	Blood dyscrasias

	Hepatic:	Raised liver enzymes, jaundice
	Immunological:	Hypersensitivity reactions, including anaphylaxis, are rare.
	Musculoskeletal	Muscle weakness.
	Neurological:	Headaches, confusion, slurred speech, tremor, reduced alertness. Anterograde amnesia may occur using therapeutic doses, the risk increasing at higher doses. Amnestic effects may be associated with inappropriate behaviour.
	Psychiatric	Numbed emotions. In susceptible patients, an unnoticed depression may become evident. Paradoxical reactions (including aggressive behaviour, hostility, disinhibition, euphoria, excitation, irritability, increased anxiety and insomnia) are known to occur with benzodiazepines and may be quite severe with diazepam. They are more likely to occur in children and the elderly.
	Reproductive	Changes in libido, gynaecomastia.
	Respiratory	Rarely, respiratory depression and apnoea, particularly with high dosage.
	Skin	Skin reactions.
	Urinary:	Urinary retention, incontinence.
Typical dose range used in nuclear medicine procedure		2-10mg
Preparation		n/a
Administration		Oral tablet. Rarely needed with PET/CT
Drug name:		Dipyridamole
Nuclear Medicine Procedure		Myocardial perfusion Imaging

Usual clinical use	**Adults:** **Children:**	As an alternative to exercise stress in thallium-201 myocardial imaging, particularly in patients unable to exercise or in those for whom exercise may be contraindicated. As an alternative to exercise stress in myocardial perfusion imaging, particularly in children unable to exercise or in those for whom exercise may be contraindicated. More specifically, this may include children with Kawasaki disease complicated by coronary artery involvement, or those with congenitally abnormal coronary circulations
Relevant Pharmacological action		1. Coronary vasodilator. 2. Inhibitor of platelet aggregation and adhesion.
Drug Interactions		Xanthine derivatives (e.g. caffeine and theophylline) can potentially reduce the vasodilating effect of dipyridamole and should therefore be avoided 24 hours before myocardial imaging with DIPYRIDAMOLE. Dipyridamole increases plasma levels and cardiovascular effects of adenosine. Dipyridamole may increase the hypotensive effect of drugs which reduce blood pressure. Dipyridamole may counteract the anticholinesterase effect of cholinesterase inhibitors thereby potentially aggravating myasthenia gravis.
Contraindications		Hypersensitivity to any of the components of the product. Patients with dysrhythmias, second- or third degree atrioventricular block or with sick sinus syndrome should not receive intravenous DIPYRIDAMOLE (unless they have a functioning pacemaker). Patients with baseline hypotension (systolic blood pressure < 90 mmHg), recent unexplained syncope (within 4 weeks) or with recent transient ischaemic attacks are not suitable candidates for dipyridamole testing. Patients with severe coronary artery disease, including unstable angina and recent myocardial infarction (within 4 weeks), left ventricular outflow obstruction or haemodynamic instability (e.g. decompensated heart failure). Patients with bronchial asthma or a tendency to bronchospasm.

		Patients with myasthenia gravis. (See Interactions.) Pregnancy and lactation.
Cautions in use		The potential clinical information to be gained through use of intravenous DIPYRIDAMOLE as an adjunct in myocardial imaging must be weighed against the risk to the patient. Comparable reactions to exercise-induced stress may occur. Therefore dipyridamole nuclear cardiology scanning should be performed with continuous ECG monitoring of the patient. When myocardial imaging is performed with intravenous DIPYRIDAMOLE, parenteral aminophylline should be readily available for relieving adverse effects such as bronchospasm or chest pain. Vital signs should be monitored during and for 10 - 15 minutes following the intravenous infusion of DIPYRIDAMOLE and an electrocardiographic tracing should be obtained using at least one chest lead. Sedation may be necessary in young children. Use with caution in young infants with immature hepatic metabolism. Should severe chest pain or bronchospasm occur, parenteral aminophylline may be administered by slow intravenous injection; for adults, doses ranging from 75 mg to 100 mg aminophylline, repeated if necessary, are appropriate; for children, doses of 3-5 mg/kg aminophylline have been used. In the case of severe hypotension, the patient should be placed in a supine position with the head tilted down if necessary, before administration of parenteral aminophylline. If aminophylline does not relieve chest pain symptoms within a few minutes, sublingual nitroglycerin may be administered. If chest pain continues despite use of aminophylline and nitroglycerin, the possibility of myocardial infarction should be considered. If the clinical condition of a patient with an adverse effect permits a one minute delay in the administration of parenteral aminophylline, the radiopharmaceutical may be injected and allowed to circulate for one minute before the injection of aminophylline. This will allow initial thallium perfusion imaging to be performed before reversal of the pharmacologic effects of dipyridamole on the coronary circulation.

		Patients being treated with regular oral doses of dipyridamole should not receive additional intravenous dipyridamole. Clinical experience suggests that patients being treated with oral dipyridamole who also require pharmacological stress testing with intravenous dipyridamole should discontinue drugs containing oral dipyridamole for twenty-four hours prior to stress testing. Caution should be exercised in patients with known pre-existing first-degree heart block.
Adverse Reactions		Approximately 47% of patients given intravenous dipyridamole will experience an adverse event, of which 0.26% would be expected to be severe. When using dipyridamole as an adjunct to myocardial imaging, the following adverse events have been reported: cardiac death, cardiac arrest, myocardial infarction (rarely fatal), chest pain/angina pectoris, electrocardiographic changes (most commonly ST-T changes), arrhythmias (e.g.sinus node arrest, heart block, tachycardia, bradycardia, fibrillation), syncope and cerebrovascular events (e.g. stroke, TIA, seizures).dipyridamole may cause severe hypotension and hot flushes. Hypersensitivity reactions such as rash, urticaria, angio-oedema, laryngospasm, severe bronchospasm, and very rarely anaphylactoid reactions have been reported. Other adverse reactions reported include: abdominal pain, vomiting, diarrhoea, nausea, dizziness, headache, paraesthesia, myalgia, hypertension, blood pressure lability, fatigue and dyspepsia. A bitter taste has been experienced after i.v. injection.
Typical dose range used in nuclear medicine procedure		The dose of intravenous dipyridamole as an adjunct to nuclear myocardial perfusion imaging should be adjusted according to the weight of the patient. The recommended dose is 0.142 mg/kg/minute (0.567 mg/kg total) infused over 4 minutes.
Preparation		Clear colourless sterile solution for injection requiring withdrawal of appropriate dose from glass ampoule. See Appendix 2.
Administration		Patients stressed with the vasodilators dipyridamole must abstain from caffeine-containing foods, beverages and medications for a minimum of 12 hours prior to the test and preferably for 24 hours. Aminophylline and theophylline must be stopped 24 hours before the test. Patients on dipyridamole should discontinue the drug for a minimum of 24 hours prior to vasodilator stress. The appropriate dose of the radiopharmaceutical should be injected within 3-5 minutes following the 4-minute infusion of dipyridamole. See Appendix 3.
Drug name:		Dobutamine

Nuclear Medicine Procedure		Myocardial Perfusion Imaging
Usual clinical use		Dobutamine Concentrate is indicated in adults who require inotropic support in the treatment of low output cardiac failure associated with myocardial infarction, open heart surgery, cardiomyopathies, septic shock and cardiogenic shock. Dobutamine Concentrate can also increase or maintain cardiac output during positive end expiratory pressure (PEEP) ventilation. Dobutamine Concentrate may also be used for cardiac stress testing as an alternative to exercise in patients for whom routine exercise cannot be satisfactorily performed. This use of dobutamine should only be undertaken in units which already perform exercise stress testing and all normal care and precautions required for such testing are also required when using dobutamine for this purpose.
Relevant Pharmacological action		Dobutamine directly stimulates □ □adrenergic receptors and is generally considered a selective □1-adrenergic agonist, but the mechanisms of action of the drug are complex. It is believed that the□ □-adrenergic effects result from stimulation of adenyl cyclase activity. In therapeutic doses, dobutamine also has mild □2 - and □1 - adrenergic receptor agonist effects, which are relatively balanced and result in minimal net direct effect on systemic vasculature. Unlike dopamine, dobutamine does not cause release of endogenous norepinephrine. The main effect of therapeutic doses of dobutamine is cardiac stimulation. While the positive inotropic effect of the drug on the myocardium appears to be mediated principally via □1-adrenergic stimulation, experimental evidence suggests that □1-adrenergic stimulation may also be involved and that the □1- adrenergic activity results mainly from the (-) -stereoisomer of the drug. The □1-adrenergic effects of dobutamine exert a positive inotropic effect on the myocardium and result in an increase in cardiac output due to increased myocardial contractility and stroke volume in healthy individuals and in patients with congestive heart failure. Increased left ventricular filling pressure decreases in patients with congestive heart failure. In therapeutic doses, dobutamine causes a decrease in peripheral resistance; however, systolic blood pressure and pulse pressure may remain unchanged or be increased because of augmented cardiac output. With usual doses, heart rate is usually not substantially changed. Coronary blood flow and myocardial oxygen

		consumption are usually increased because of increased myocardial contractility. Electrophysiologic studies have shown that dobutamine facilitates atrio-ventricular conduction and shortens or causes no important change in intraventricular conduction. The tendency of dobutamine to induce cardiac arrhythmias may be slightly less than that of dopamine and is considerably less than that of isoproterenol or other catecholamines. Pulmonary vascular resistance may decrease if it is elevated initially and mean pulmonary artery pressure may decrease or remain unchanged. Unlike dopamine, dobutamine does not seem to affect dopaminergic receptors and causes no renal or mesenteric vasodilatation; however, urine flow may increase because of increased cardiac output.
Drug Interactions	**Halogenated anaesthetics:** **Entacapone:** **Beta-blockers:**	Although it is less likely than adrenaline to cause ventricular arrhythmias, Dobutamine concentrate should be used with great caution during anaesthesia with cycloproprane, halothane and other halogenated anaesthetics. The effects of Dobutamine concentrate may be enhanced by entacapone. The inotropic effect of dobutamine stems from stimulation of cardiac beta1 receptors, this effect is reversed by concomitant administration of beta-blockers. Dobutamine has been shown to counteract the effect of beta-blocking drugs. In therapeutic doses, dobutamine has mild alpha1- and beta2-agonist properties. Concurrent administration of a non-selective beta-blocker such as propranolol can result in elevated blood pressure, due to alpha-mediated vasoconstriction, and reflex bradycardia. Beta-blockers that also have alpha-blocking effects, such as carvedilol, may cause hypotension during concomitant use of dobutamine due to vasodilation caused by beta2 predominance.
Contraindications		Hypersensitivity to dobutamine, sodium metabisulphite or any of the other ingredients. Phaeochromocytoma.
Adverse Reactions	 **Immune system disorders:**	Infusions for up to 72 hours have revealed no adverse effects other than those seen with shorter infusions. There is evidence that partial tolerance develops with continuous infusions of dobutamine concentrate for 72 hours or more; therefore, higher doses may be required to maintain the same effects. Hypersensitivity reactions including rash, fever, eosinophilia and bronchospasm have been reported. Anaphylactic reactions and severe life-threatening asthmatic episodes may be due to sulphite sensitivity

	Metabolism and nutrition disorders:	As with other catecholamines, decreases in serum potassium concentrations have occurred. Consideration should be given to monitoring serum potassium.
	Cardiac disorders:	Increased heart rate, palpitations, angina pectoris, chest pain, ectopic heart beats, arrhythmia, atrial fibrillation, ventricular fibrillation, ventricular tachycardia, myocardial ischaemia, coronary artery spasm, electrocardiogram ST segment elevation, myocardial infarction. Left ventricular outflow tract obstruction has been reported during dobutamine stress echocardiography. There have been very rare reports of fatal cardiac rupture during dobutamine stress testing. Eosinophilic myocarditis has been noted in explanted hearts of patients who had undergone treatment with multiple medications including dobutamine or other inotropic agents prior to transplantation.
	Vascular disorders:	Hypertension. Marked increase in systolic blood pressure indicates overdose. Hypotension.
	Nervous system disorders:	Myoclonus has been reported in patients with severe renal failure receiving dobutamine.
	Respiratory, thoracic and mediastinal disorders:	Shortness of breath, bronchospasm, asthma (see Immune system disorders)
	General/Other disorders:	Non-specific chest pain, headache, nausea. Reactions at the site of intravenous infusion: Phlebitis has occasionally been reported and local inflammatory changes have been described following inadvertent infiltration. Very rare cases of cutaneous necrosis have been reported.
Typical dose range used in nuclear medicine procedure		5 - 10microgm/Kg/min at 3 min steps until target heart rate, max 40mcg/kg/min

Preparation		Dobutamine Concentrate must be diluted to at least 50 ml prior to administration in an IV container with one of the intravenous solutions listed below: Sodium Chloride Intravenous Infusion BP 5% Dextrose Intravenous Infusion BP 5% Dextrose + 0.9% Sodium Chloride Intravenous Infusion BP 5% Dextrose + 0.45% Sodium Chloride Intravenous Infusion BP Sodium Lactate Intravenous Infusion BP See Appendix 2
Administration		Patients should stop beta-adrenoceptor antagonists for five half-lives or at least 24 hours before the test unless contraindicated. Because of its short half-life, Dobutamine Concentrate is administered as a continuous intravenous infusion. After dilution, it should be administered through an intravenous needle or catheter using an IV drip chamber or other suitable metering device to control the rate of flow. See Appendix 3.
Drug name:		Furosemide
Nuclear Medicine Procedure		Renogram
Usual clinical use		Furosemide is a potent diuretic with a rapid action used to treat oedema and hypertensive crises; acute or chronic renal failure
Relevant Pharmacological action		Furosemide is a short-acting sulphonamide diuretic, chemically similar to the thiazides. With parenteral administration, the diuretic effect is immediate and lasts approximately two hours. Furosemide primarily inhibits the reabsorption of sodium in the proximal and distal tubules as well as in the Loop of Henle, thus increasing the urinary excretion of sodium, chloride and water. Urinary excretion of potassium, calcium and magnesium are also increased, together with bicarbonate; urinary pH rises.
Drug Interactions		The ototoxic and nephrotoxic effects of other medications may be increased by concomitant administration of furosemide.

		Some electrolyte disturbances (e.g. hypokalaemia, hypomagnesaemia) may increase the toxicity of certain drugs (e.g. drugs inducing QT interval prolongation syndrome such as amisulpride, atomoxetine, pimozide, sotalol, sertindole). There is increased risk of hypokalaemia when furosemide is used in combination with beta-2 sympathomimetics in large doses, theophylline, corticosteroids, liquorice, carbenoxolone, prolonged use of laxatives, reboxetine, or amphotericin. Furosemide may sometimes attentuate the effect of other drugs e.g. the effect of anti-diabetics and of pressor amines. Probenecid, methotrexate and other drugs which, like furosemide, undergo significant renal tubular secretion may reduce the effect of furosemide. Conversely, furosemide may decrease renal elimination of these drugs. In case of high-dose treatment (in particular, of both furosemide and the other drugs), this may lead to increased serum levels and an increased risk of adverse effects due to furosemide or the concomitant medication.
	Cardiac glycosides	The potassium loss caused by potassium depleting diuretics such as furosemide increases the toxic effects of digoxin and other digitalis glycosides.
	Anti-arrhythmic drugs:	Hypokalaemia caused by loop diuretics may increase the cardiac toxicity of anti-arrhythmic drugs such as amiodarone, disopyramide, flecainide, quinidine and sotalol, and may antagonise the effects of lidocaine and mexiletine.
	Antihypertensive drugs:	The dosage of concurrently administered diuretics, antihypertensive agents or other drugs with blood pressure lowering potential may require adjustment as a more pronounced fall in blood pressure must be anticipated if given with furosemide. A marked fall in blood pressure and deterioration in renal function may be seen when angiotensin-converting enzyme (ACE) inhibitors or angiotensin II receptor antagonists are added to furosemide therapy, or when the dosage is increased. The dose of furosemide should be reduced for at least three days, or the drug stopped before initiation of ACE-inhibitor or angiotensin II receptor antagonist therapy, or before their dose is increased.

	Lithium:	In common with other diuretics, serum lithium levels may be increased when furosemide is given to patients stabilised on this therapy, resulting in increased lithium toxicity (cardiotoxicity, neurotoxicity). It is recommended that lithium levels are carefully monitored and where necessary the lithium dosage adjusted during concurrent use.
	Non-steroidal anti-inflammatory drugs:	Certain NSAIDs (including indometacin, ketorolac, acetylsalicylic acid) may decrease the effectiveness of furosemide and may cause acute renal failure in cases of pre-existing hypovolaemia or dehydration. Salicylate toxicity may be increased by furosemide.
	Antibiotics:	Furosemide may potentiate the nephrotoxicity and ototoxicity of aminoglycosides and other ototoxic drugs. Since this may lead to irreversible damage, these drugs must only be used with furosemide when there are compelling medical reasons. There is an increased risk of ototoxicity when loop diuretics are given with vancomycin or polymyxins (colistin). Impairment of renal function may develop in patients receiving concurrent treatment with furosemide and high doses of certain cephalosporins (e.g. cephaloridine).
	Cytotoxic agents:	There is a risk of ototoxicity if cisplatin and furosemide are given concurrently. Low doses of furosemide (e.g. 40 mg in patients with normal renal function) should be used and a positive fluid balance maintained when furosemide is used to achieve forced diuresis during cisplatin treatment to reduce the risk of additional nephrotoxicity. Methotrexate and other drugs which, like furosemide, undergo significant renal tubular secretion may reduce the effect of furosemide. Conversely, furosemide may decrease renal elimination of methotrexate. This may lead to increased serum levels and increased risk of adverse events, especially with high dose therapy of methotrexate or furosemide.
	Ciclosporin:	Concomitant use of ciclosporin and furosemide is associated with an increased risk of gouty arthritis.
	Anti-convulsants:	Phenytoin may decrease the effectiveness of furosemide. Concomitant administration of carbamazepine may increase the risk of hyponatraemia.
	Corticosteroids:	Concurrent use of corticosteroids may cause sodium retention and increased risk of developing hypokalaemia.

	Chloral hydrate/Triclofos: **Neuromuscular blocking agents:**	Bolus doses of intravenous furosemide may induce flushing, sweating, tachycardia and variations in blood pressure in patients receiving chloral hydrate or triclofos. Furosemide may affect the response to neuromuscular blocking agents (increased or decreased effect).
Contraindications		Hypersensitivity to furosemide or any of the excipients. Patients allergic to sulphonamides may show cross-sensitivity to furosemide. • Hypovolaemia, dehydration, anuria. • Renal failure with anuria not responding to furosemide. • Severe hypokalaemia or hyponatraemia. • Comatose or pre-comatose states associated with hepatic encephalopathy. • Renal failure due to poisoning by nephrotoxic or hepatotoxic drugs. • Renal failure associated with hepatic coma. • Breastfeeding.
Adverse Reactions	**Blood and lymphatic system disorders:** **Immune system disorders:** **Metabolism and nutrition disorders:**	The most common undesirable effect is fluid and electrolyte imbalance. Other undesirable effects are relatively uncommon. Eosinophilia is rare. Occasionally, thrombocytopenia may occur. In rare cases, leucopenia and, in isolated cases, agranulocytosis, aplastic anaemia or haemolytic anaemia may develop. Bone marrow depression has been reported as a rare complication and necessitates withdrawal of treatment. Severe anaphylactic or anaphylactoid reactions (e.g. with shock) occur rarely. The incidence of allergic reactions, such as skin rashes, photosensitivity, vasculitis, fever, interstitial nephritis or shock is very low, but when these occur treatment should be withdrawn. Electrolyte and water balance may be disturbed as a result of diuresis. Furosemide causes increased excretion of sodium and chloride and consequently water, and hyponatraemia may occur. The diuretic action of furosemide may lead to or contribute towards hypovolaemia and

		dehydration, especially in elderly patients. Severe fluid depletion may lead to haemoconcentration with a tendency for thromboses to develop.
	Psychiatric/Nervous system disorders: **Eye disorders:** **Ear and labyrinth disorders:** **Cardiac disorders:** **Vascular disorders:** **Gastrointestinal disorders:** **Hepatobiliary disorders:** **Skin and subcutaneous tissue disorders:** **Musculoskeletal disorders:** **Renal and urinary disorders:**	Excretion of other electrolytes is increased, and hypokalaemia, serum calcium depletion and hypomagnesaemia may occur. Symptomatic electrolyte disturbances and metabolic alkalosis may develop following gradual electrolyte depletion or acute severe electrolyte losses during higher dose therapy. Warning signs of electrolyte disturbances include increased thirst, headache, hypotension, confusion, muscle cramps, tetany, muscle weakness, disorders of cardiac rhythm and gastrointestinal symptoms. Pre-existing metabolic alkalosis (e.g. in decompensated cirrhosis of the liver) may be aggravated by furosemide treatment. Serum cholesterol and triglyceride levels may rise during furosemide treatment. During long-term therapy they will usually return to normal within six months. Furosemide may provoke hyperglycaemia and glycosuria but less so than thiazide diuretics. Glucose tolerance may decrease with furosemide. In patients with diabetes mellitus, this may lead to a deterioration of control; latent diabetes mellitus may become manifest. Furosemide can increase serum uric acid levels and may precipitate attacks of gout in some patients. Rarely paraesthesia may occur. Symptoms of hypotension may include dizziness, light-headedness, sensation of pressure in the head, headache, drowsiness, concentration impairment and slowed reactions. Headache, lethargy or confusion may be warning signs of electrolyte disturbances. Visual disturbances, blurred vision. Hearing disorders, including deafness and tinnitus, may occur in rare cases, particularly in patients with renal failure, hypoproteinaemia (e.g. nephrotic syndrome) and/ or when intravenous furosemide has been given too rapidly. Although symptoms are usually transient, permanent deafness may occur, especially in patients treated with other ototoxic medications Cardiac rhythm disturbances may occur as a consequence of electrolyte imbalance. If furosemide is administered to premature infants during the first weeks of life, it may increase the risk of persistence of patent ductus arteriosus. Hypotension and orthostatic hypotension may occur, especially in patients taking other medications which lower blood pressure.

	General disorders:	Allergic vasculitis has been reported very rarely. Nausea, vomiting, diarrhoea and dry mouth may occur but are not usually severe enough to necessitate withdrawal of treatment. Hepatic encephalopathy in patients with hepatocellular insufficiency may occur (see Section 4.3). In isolated cases, intrahepatic cholestatsis, an increase in liver transaminases or acute pancreatitis may develop. Skin and mucous membrane reactions may occasionally occur eg pruritis, urticaria, other rashes or bullous lesions, erythema multiforme, exfoliative dermatitis and purpura. Serum calcium levels may be reduced, muscle spasms or muscle weakness may indicate electrolyte disturbances. In very rare cases tetany has been observed. Treatment with furosemide may lead to transient increases in blood creatinine and urea levels. Renal failure may occur as a consequence of fluid and electrolyte depletion, especially during concurrent treatment with NSAIDs or nephrotoxic medications. Increased production of urine may provoke or aggravate complaints in patients with an obstruction of urinary outflow. Acute retention of urine with possible secondary complications may occur, for example, in patients with bladder emptying disorders, prostatic hyperplasia or narrowing of the urethra (see section 4.4 Special warnings and precautions for use). Nephrocalcinosis/nephrolithiasis has been reported in premature infants, and in adults, generally after long-term therapy. There have been very rare reports of interstitial nephritis. Asthenia, malaise, fever. Following intramuscular injection, local reactions such as pain may occur.

Typical dose range used in nuclear medicine procedure	**Adults** **Children**	20-40mg (max 40mg) 0.5-1mg/kg <6 mo 5mg 6-12 mo 10mg >12 mo 20mg, to a max of 30mg
Preparation		Clear colourless sterile solution for injection requiring withdrawal of appropriate dose from glass ampoule. See Appendix 2.
Administration		A maximum diuretic response is obtained by the administration of furosemide 0.5mg/kg (or 40 mg for an adult) intravenously 15 minutes before the start of the study ("F-15"). If venous access is difficult, there is some evidence to suggest that furosemide given immediately before the tracer through the same cannula ("F+0") is almost as effective. See Appendix 3.
Drug name:		Morphine
Nuclear Medicine Procedure		Hepato-cholescintigraphy
Usual clinical use		Opiate analgesic
Relevant Pharmacological action		Morphine is obtained from opium, which acts mainly on the CNS and smooth muscle. Morphine is a potent analgesic with competitive agonist actions at the μ-receptor, which is thought to mediate many of its other actions of respiratory depression, euphoria, inhibition of gut motility and physical dependence. It is possible that analgesia, euphoria and dependence may be due to the effects of morphine on a μ-1 receptor subtype, while respiratory depression and inhibition of gut motility may be due to actions on a μ-2 receptor subtype. Morphine is also a competitive agonist at the κ-receptor that mediates spinal analgesia, miosis and sedation. Morphine has no significant actions at the other two major opioid receptors, the δ- and the σ-receptors. Morphine directly suppresses cough by an effect on the cough centre in the medulla. Morphine also produces nausea and vomiting by directly stimulating the chemoreceptor trigger zone in the area postrema of the medulla. Morphine provokes the release of histamine.
Drug Interactions	**Alcohol:**	enhanced sedative and hypotensive effects.

	Anti-arrhythmics:	There may be delayed absorption of mexiletine.
	Antibacterials:	The opioid analgesic papaveretum has been shown to reduce plasma ciprofloxacin concentration. The manufacturer of ciprofloxacin advises that premedication with opioid analgesics be avoided.
	Antidepressants, anxiolytics, hypnotics:	Severe CNS excitation or depression (hypertension or hypotension) has been reported with the concurrent use of pethidine and monoamine oxidase inhibitors (MAOIs) including selegiline, moclobemide and linezolid. As it is possible that a similar interaction may occur with other opioid analgesics, morphine should be used with caution and consideration given to a reduction in dosage in patients receiving MAOIs. The sedative effects of morphine (opioid analgesics) are enhanced when used with depressants of the central nervous system such as hypnotics, anxiolytics, tricyclic antidepressants and sedating antihistamines.
	Antipsychotics:	possible enhanced sedative and hypotensive effect.
	Antidiarrhoeal / antiperistaltic agents	(such as loperamide and kaolin): concurrent use may increase the risk of severe constipation.
	Antimuscarinics:	agents such as atropine antagonise morphine-induced respiratory depression and can partially reverse biliary spasm but are additive to the gastrointestinal and urinary tract effects. Consequently, severe constipation and urinary retention may occur during intensive antimuscarinic-analgesic therapy.
	Metoclopramide and domperidone:	There may be antagonism of the gastrointestinal effects of metoclopramide and domperidone.
Contraindications		Acute respiratory depression, known morphine sensitivity, biliary colic, acute alcoholism. Conditions in which intracranial pressure is raised, comatose patients, head injuries, as there is an increased risk of respiratory depression that may lead to elevation of CSF pressure. The sedation and pupillary changes produced may interfere with accurate monitoring of the patient. Morphine is also contraindicated where there is a risk of paralytic ileus, or in acute diarrhoeal

		conditions associated with antibiotic-induced pseudomembranous colitis or diarrhoea caused by poisoning (until the toxic material has been eliminated). Phaeochromocytoma (due to the risk of pressor response to histamine release).
Adverse Reactions		The most serious hazard of therapy is respiratory depression. The commonest side-effects of morphine are nausea, vomiting, constipation, drowsiness and dizziness. Tolerance generally develops with long term use, but not to constipation. Other side effects include the following:
	Anaphylaxis:	Anaphylactic reactions following intravenous injection have been reported rarely.
	Cardiovascular	facial flushing bradycardia, palpitations, tachycardia, orthostatic hypotension.
	Central Nervous System:	mental clouding, confusion (with large doses), hallucinations, headache, vertigo, mood changes including dysphoria and euphoria.
	Gastrointestinal	dry mouth, biliary spasm.
	Disorders of the eye:	blurred or double vision or other changes in vision, miosis.
	Skin:	pruritus, urticaria, rash, sweating. Contact dermatitis has been reported and pain and irritation may occur on injection.
	Urinary:	difficulty with micturition, ureteric spasm, urinary retention, antidiuretic effect. Tolerance develops to the effects of opioids on the bladder.
Typical dose range used in nuclear medicine procedure		0.04mg/kg body weight
Preparation		Clear colourless sterile solution for injection requiring withdrawal of appropriate dose from glass ampoule. See Appendix 2.
Administration		Intravenous injection – See Appendix 3. Note: Morphine is a Controlled Drug and therefore subject to additional storage and prescribing rules.
Drug name:		Omeprazole

Nuclear Medicine Procedure		Meckels Diverticulum imaging
Usual clinical use		Prophylaxis of acid aspiration.
Relevant Pharmacological action		Omeprazole reduces gastric acid secretion through a unique mechanism of action. It is a specific inhibitor of the gastric proton pump in the parietal cell. It is rapidly acting and produces reversible control of gastric acid secretion with once daily dosing.
Drug Interactions		Due to the decreased intragastric acidity, the absorption of ketoconazole or itraconazole may be reduced during omeprazole therapy as it is during treatment with other acid secretion inhibitors. As omeprazole is metabolised in the liver through cytochrome P450 it can prolong the elimination of diazepam, phenytoin, warfarin and other vitamin K antagonists, which are in part substrates for this enzyme. Monitoring of patients receiving phenytoin is recommended and a reduction of the phenytoin dose may be necessary when Omeprazole is added to treatment. However, concomitant treatment with Omeprazole 20 mg orally daily, did not change the blood concentration of phenytoin in patients on continuous treatment with phenytoin. In patients receiving warfarin or other vitamin K antagonists, monitoring of INR is recommended and a reduction of the warfarin (or other vitamin K antagonist) dose may be necessary. Concomitant treatment with Omeprazole 20 mg orally daily, did not change coagulation time in patients on continuous treatment with warfarin. Plasma concentrations of omeprazole and clarithromycin are increased during concomitant oral administration. There is no interaction with metronidazole or amoxicillin. These antimicrobials are used together with omeprazole for eradication of Helicobacter pylori . There is no evidence of an interaction with phenacetin, theophylline, caffeine, propranolol, metoprolol, ciclosporin, lidocaine, quinidine, estradiol, or antacids when Omeprazole is given orally. The absorption of Omeprazole given orally is not affected by alcohol or food. There is no evidence of an interaction with piroxicam, diclofenac or naproxen, this is considered useful when patients are required to continue these treatments.

		Simultaneous treatment with omeprazole and digoxin in healthy subjects led to a 10% increase in the bioavailability of digoxin as a consequence of the increased intragastric pH. Interaction with other drugs also metabolised via the cytochrome P450 system cannot be excluded. Co-administration of omeprazole (40mg once daily) with atazanavir 300 mg/ritonavir 100mg to healthy volunteers resulted in a substantial reduction in atazanavir exposure (approximately 75% decrease in AUC, Cmax, and Cmin). Increasing the atazanavir dose to 400mg did not compensate for the impact of omeprazole on atazanavir exposure. PPIs including omeprazole should not be co-administered with atazanavir. Concomitant administration of omeprazole and tacrolimus may increase the serum levels of tacrolimus. Concomitant administration of omeprazole and a CYP2C19 and CYP3A4 inhibitor, voriconazole, resulted in more than doubling of the omeprazole exposure. Omeprazole (40 mg once daily) increased voriconazole (a CYP2C19 substrate) Cmax and AUCτ by 15% and 41%, respectively. A dose adjustment of omeprazole is not regularly required in either of these situations. However, dose adjustment should be considered in patients with severe hepatic impairment and if long-term treatment is indicated.
Contraindications		Known hypersensitivity to any of the constituents of the formulation. Omeprazole like other PPIs should not be administered with atazanavir .
Adverse Reactions	**Central and peripheral nervous system** **Endocrine** **Gastrointestinal** **Haematological** **Hepatic**	Headache - common Dizziness, paraesthesia, somnolence, insomnia and vertigo - uncommon Reversible mental confusion, agitation, aggression, depression and hallucinations, predominantly in severely ill patients – rare Gynaecomastia - rare Diarrhoea, constipation, abdominal pain, nausea/vomiting and flatulence – common Dry mouth, stomatitis and gastrointestinal candidiasis – rare Leukopenia, thrombocytopenia, agranulocytosis and pancytopenia – rare Increased liver enzymes – uncommon

		Encephalopathy in patients with pre existing severe liver disease; hepatitis with or without jaundice, hepatic failure, increased liver enzymes - rare
	Musculoskeletal	Arthritic and myalgic symptoms and muscular weakness – rare
	Reproductive system and breast disorders	Impotence - rare
	Skin	Rash, dermatitis and/or pruritus, urticaria - uncommon Photosensitivity, bullous eruption erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis (TEN), alopecia - rare
	Other	Malaise – uncommon Hypersensitivity reactions e.g. angioedema, fever, broncho-spasm, interstitial nephritis and anaphylactic shock. Increased sweating, peripheral oedema, blurred vision, taste disturbance and hyponatraemia - rare Isolated cases of irreversible visual impairment have been reported in critically ill patients who have received Omeprazole Intravenous Injection, particularly at high doses, however no causal relationship has been established.
Typical dose range used in nuclear medicine procedure		40mg morning before and of scan
Preparation		n/a
Administration		Orally
Drug name:		Ranitidine
Nuclear Medicine Procedure		Meckels Diverticulum imaging
Usual clinical use	**Adults:**	Rantitidine Injection is indicated for the treatment of duodenal ulcer, benign gastric ulcer, post - operative ulcer, reflux oesophagitis, Zollinger - Ellison Syndrome and the following conditions where reduction of gastric secretion and acid output is desirable: the prophylaxis of gastrointestinal haemorrhage from stress ulceration in seriously ill patients, the prophylaxis of recurrent haemorrhage in patients with bleeding peptic ulcers and before

	Children (6 months to 18 years):	general anaesthesia in patients considered to be at risk of acid aspiration (Mendelson's Syndrome), particularly obstetric patients during labour. Rantitidine Injection is indicated for the short term treatment of peptic ulcer and the treatment of gastro-oesophageal reflux, including reflux oesophagitis and symptomatic relief of gastro-oesophageal reflux disease.
Relevant Pharmacological action		Ranitidine is a specific, rapidly acting H2-antagonist. It inhibits basal and stimulated secretion of gastric acid, reducing both the volume of the acid and pepsin content of the secretion. Ranitidine has a relatively long duration of action and a single 150mg dose effectively suppresses gastric acid secretion for twelve hours.
Drug Interactions		Ranitidine has the potential to affect the absorption, metabolism or renal excretion of other drugs. The altered pharmacokinetics may necessitate dosage adjustment of the affected drug or discontinuation of treatment Interactions occur by several mechanisms including: 1) Inhibition of cytochrome P450-linked mixed function oxygenase system: Ranitidine at usual therapeutic doses does not potentiate the actions of drugs which are inactivated by this enzyme system such as diazepam, lidocaine, phenytoin, propanolol and theophylline. There have been reports of altered prothrombin time with coumarin anticoagulants (e.g. warfarin). Due to the narrow therapeutic index, close monitoring of increased or decreased prothrombin time is recommended during concurrent treatment with ranitidine. 2) Competition for renal tubular secretion: Since ranitidine is partially eliminated by the cationic system, it may affect the clearance of other drugs eliminated by this route. High doses of ranitidine (e.g. such as those used in the treatment of Zollinger-Ellison syndrome) may reduce the excretion of procainamide and N-acetylprocainamide resulting in increased plasma level of these drugs. 3) Alteration of gastric pH: The bioavailability of certain drugs may be affected. This can result in either an increase in absorption (e.g. triazolam, midazolam, glipizide) or a decrease in absorption (e.g. ketoconazole, atazanavir, delaviridine, gefitnib)..
Contraindications		Ranitidine is contraindicated for patients known to have hypersensitivity to any component of the preparation.

Adverse Reactions	**Blood & Lymphatic System Disorders**	Very Rare: Blood count changes (leucopenia, thrombocytopenia). These are usually reversible. Agranulocytosis or pancytopenia, sometimes with marrow hypoplasia or marrow aplasia.
	Immune System Disorders	Rare: Hypersensitivity reactions (urticaria, angioneurotic oedema, fever, bronchospasm, hypotension and chest pain). Very Rare: Anaphylactic shock These events have been reported after a single dose.
	Psychiatric Disorders	Very Rare: Reversible mental confusion, depression and hallucinations. These have been reported predominantly in severely ill and elderly patients.
	Nervous System Disorders	Very Rare: Headache (sometimes severe), dizziness and reversible involuntary movement disorders.
	Eye Disorders	Very Rare: Reversible blurred vision. There have been reports of blurred vision, which is suggestive of a change in accommodation.
	Cardiac Disorders	Very Rare: As with other H2 receptor antagonists bradycardia and A-V Block.
	Vascular Disorders	Very Rare: Vasculitis.
	Gastrointestinal Disorders	Very Rare: Acute pancreatitis. Diarrhoea.
	Hepatobiliary Disorders	Rare: Transient and reversible changes in liver function tests. Very Rare Hepatitis (hepatocellular, hepatocanalicular or mixed) with or without jaundice, these were usually reversible.
	Skin and Subcutaneous Tissue Disorders	Rare: Skin Rash. Very Rare: Erythema multiforme, alopecia.
	Musculoskeletal and Connective Tissue Disorders	Very Rare: Musculoskeletal symptoms such as arthralgia and myalgia.
	Renal and Urinary Disorders	
	Reproductive System and Breast Disorders	

		Very rare: Acute interstitial nephritis. Very Rare: Reversible impotence. Breast symptoms in men. The safety of ranitidine has been assessed in children aged 0 to 16 years with acid-related disease and was generally well tolerated with an adverse event profile resembling that in adults.
Typical dose range used in nuclear medicine procedure	**Adult** **Children**	150mg x 2 Ranitidine syrup 2mg/kg
Preparation		n/a
Administration		Orally
Drug name:		Regadenoson
Nuclear Medicine Procedure		Myocardial Perfusion Imaging
Usual clinical use	**Adults:** **Children (6 months to 18 years):**	Rapiscan is a selective coronary vasodilator for use as a pharmacological stress agent for radionuclide myocardial perfusion imaging (MPI) in adult patients unable to undergo adequate exercise stress It is for diagnostic use only The safety and efficacy of Rapiscan in children below the age of 18 years have not yet been established. No data are available
Relevant Pharmacological action		Coronary blood flow Regadenoson causes a rapid increase in CBF which is sustained for a short duration. In patients undergoing coronary catheterisation, pulsed-wave Doppler ultrasonography was used to measure the average peak velocity (APV) of CBF before and up to 30 minutes after administration of Rapiscan (400 micrograms, intravenously). Mean APV increased to greater than twice baseline by 30 seconds and decreased to less than half of the maximal effect within 10 minutes (see section 5.2).

		Myocardial uptake of the radiopharmaceutical is proportional to CBF. Because regadenoson increases blood flow in normal coronary arteries with little or no increase in stenotic arteries, regadenoson causes relatively less uptake of the radiopharmaceutical in vascular territories supplied by stenotic arteries. Myocardial radiopharmaceutical uptake after Rapiscan administration is therefore greater in areas perfused by normal relative to stenosed arteries.
Drug Interactions		No studies of interaction with other medicinal products have been performed. Methylxanthines Methylxanthines (e.g., caffeine and theophylline) are non-specific adenosine receptor antagonists and may interfere with the vasodilation activity of regadenoson (see section 5.1). Patients should avoid consumption of any products containing methylxanthines as well as any medicinal products containing theophylline for at least 12 hours before Rapiscan administration Aminophylline (100 mg, administered by slow intravenous injection over 60 seconds) injected 1 minute after 400 micrograms regadenoson in subjects undergoing cardiac catheterisation, was shown to shorten the duration of the coronary blood flow response to regadenoson as measured by pulsedwave Doppler ultrasonography. Aminophylline has been used to attenuate adverse reactions to Rapiscan Dipyridamole Dipyridamole increases blood adenosine levels and the response to regadenoson may be altered when blood adenosine levels are increased. When possible, dipyridamole should be withheld for at least two days prior to Rapiscan administration (see section 4.2). Cardioactive medicinal products In clinical studies, Rapiscan was administered to patients taking other cardioactive medicinal products (i.e., β-blockers, calcium channel blockers, ACE inhibitors, nitrates, cardiac glycosides, and angiotensin receptor blockers) without apparent effects on the safety or efficacy profile of Rapiscan. Other interactions Regadenoson does not inhibit the metabolism of substrates for CYP1A2, CYP2C8, CYP2C9, CYP2C19, CYP2D6, or CYP3A4 in human liver microsomes, indicating that it is unlikely to alter the pharmacokinetics of medicinal products metabolised by these cytochrome P450 enzymes.
Contraindications		• Hypersensitivity to the active substance or to any of the excipients • Second or third degree atrioventricular (AV) block or sinus node dysfunction, unless these patients have a functioning artificial pacemaker. • Unstable angina that has not been stabilised with medical therapy.

		• Severe hypotension. • Decompensated states of heart failure.
Adverse Reactions **Assessment of adverse reactions for regadenoson is based on safety data from clinical studies and post-marketing experience. All adverse reactions are presented in the table below and are listed by system organ class and frequency. Frequencies are defined as very common (≥ 1/10), common (≥ 1/100 to <1/10) and uncommon (≥ 1/1,000 to < 1/100). Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness.**	**General disorders and administration site conditions** **Psychiatric Disorders** **Nervous System Disorders** **Eye Disorders** **Ear and labyrinth Disorders** **Cardiac Disorders** **Vascular Disorders** **Gastrointestinal Disorders** **Skin and Subcutaneous Tissue Disorders** **Musculoskeletal and Connective Tissue Disorders** **Respiratory, thoracic and**	Very common - Chest pain Common - Malaise, asthenia Uncommon -Pain at injection site, general body pain Uncommon - Anxiety, insomnia Very common - Headache, dizziness Common - Paraesthesia, hypoaesthesia, dysgeusia Uncommon - Convulsions, syncope, transient ischaemic attack, unresponsiveness to stimuli, depressed level of consciousness, tremor, somnolence Uncommon - Vision blurred, eye pain Uncommon - Tinnitus Very common - Electrocardiogram ST segment changes Common - Angina pectoris, atrioventricular block, tachycardia, palpitations, other ECG abnormalities including electrocardiogram QT corrected interval prolonged Uncommon - Cardiac arrest, myocardial infarction, complete AV block, atrial fibrillation/flutter, bradycardia Very common - Flushing Common - Hypotension Uncommon - Hypertension, pallor, peripheral coldness Very common - Gastrointestinal discomfort Common - Vomiting, nausea, oral discomfort Uncommon - Abdominal distension, diarrhoea, faecal incontinence

	mediastinal disorders	Common - Hyperhidrosis Uncommon – Erythema Common - Back, neck or jaw pain, pain in extremity, musculoskeletal discomfort Uncommon – Arthralgia Very common - Dyspnoea Common - Throat tightness, throat irritation, cough Uncommon - Tachypnoea
Typical dose range used in nuclear medicine procedure	**Adult** **Children**	The recommended dose of Rapiscan is a single injection of 400 micrograms regadenoson (5 ml) into a peripheral vein, with no dose adjustment necessary for body weight The safety and efficacy of Rapiscan in children below the age of 18 years have not yet been established.
Preparation	**N/A**	Ready to use injection
Administration	**Intravenous injection**	• Rapiscan should be administered as a rapid, 10-second injection into a peripheral vein using a 22-gauge or larger catheter or needle. • 5 ml of sodium chloride 9 mg/ml (0.9%) solution for injection should be administered immediately after the injection of Rapiscan. • The radiopharmaceutical for the myocardial perfusion imaging agent should be administered 10-20 seconds after the sodium chloride 9 mg/ml (0.9%) solution for injection. The radiopharmaceutical may be injected directly into the same catheter as Rapiscan.

Drug name:		**Iohexol (Omnipaque) strength range 140, 240, 300, 350 mg I/ml**
Nuclear Medicine Procedure		X-ray contrast medium
Usual clinical use	**Adults and Children**	X-ray contrast medium for use in adults and children for urography, phlebography, i.v. DSA, CT, arteriography, cardioangiography and i.a. DSA. Myelography. For use in body cavities: Arthrography, ERP/ERCP, herniography, hysterosalpingography, sialography and use in the G-I tract.
Relevant Pharmacological action		Close to 100 per cent of the intravenously injected iohexol is excreted unchanged through the kidneys within 24 hours in patients with normal renal function. The maximum urinary concentration of iohexol appears within approximately 1 hour after injection. No metabolites have been detected. The protein binding of Omnipaque is very low (less than 2 %).
Drug Interactions		Use of iodinated contrast media may result in a transient impairment of renal function and this may precipitate lactic acidosis in diabetics who are taking metformin. Patients treated with interleukin-2 less than two weeks previously have been associated with an increased risk for delayed reactions (flu-like symptoms or skin reactions). All iodinated contrast media may interfere with tests on thyroid function, thus the iodine binding capacity of the thyroid may be reduced for up to several weeks. High concentrations of contrast media in serum and urine can interfere with laboratory tests for bilirubin, proteins or inorganic substances (e.g. iron, copper, calcium and phosphate). These substances should therefore not be assayed on the day of examination.
Contraindications		Manifest thyrotoxicosis. History of serious reaction to Omnipaque
Caution in Use		A positive history of allergy, asthma or untoward reactions to iodinated contrast media indicates a need for special caution. Premedication with corticosteroids or histamine H_1 and H_2 anatgonists might be considered in these cases. Adequate hydration should be assured before and after administration. This applies especially to patients with multiple myeloma, diabetes mellitus, renal dysfunction, as well to infants, small

		children and elderly patients. Young infants and especially neonates are susceptible to electrolyte disturbance and haemodynamic alterations. Care should also be taken in patients with serious cardiac disease and pulmonary hypertension as they may develop haemodynamic changes or arrhythmias. Patients with acute cerebral pathology or history of epilepsy are predisposed for seizures and merit particular care. Also alcoholics and drug addicts have an increased risk for seizures and neurological reactions. To prevent acute renal failure following contrast media administration, special care should be exercised in patients with pre-existing renal impairment and diabetes mellitus as they are at risk Patients with paraproteinemias are also at risk A potential risk of transient hepatic dysfunction exists. Particular care is required in patients with severe disturbance of both renal and hepatic function as they may have significantly delayed contrast medium clearance. Patients on haemodialysis may receive contrast media. Correlation of the time of contrast media injection with the haemodialysis session is unnecessary. The administration of iodinated media may aggravate the symptoms of myasthenia gravis. Special care should be exercised in patients with hyperthyroidism. Patients with multinodular goiter may be at risk of developing hyperthyroidism following injection of iodinated contrast media. Patients must be kept under observation for 15 minutes following injection as the majority of severe reactions occur at this time.
Adverse Reactions The frequencies of undesirable effects are defined as follows: Very common (≥1/10), common (≥1/100), uncommon (≥1/1000 to <1/100), rare (≥1/10,000 to <1/1000), very rare	**General**	Serious reactions as well as fatalities are only seen on very rare occasions. Undesirable effects associated with Omnipaque are usually mild to moderate and transient in nature Hypersensitivity reactions may occur irrespective of the dose and mode of administration and mild symptoms may represent the first signs of a serious anaphylactoid reaction/shock. Administration must be discontinued immediately and if necessary, specific therapy instituted via the vascular access. Patients using beta blockers may present with atypical symptoms of hypersensitivity, which may be misinterpreted as a vagal reaction.

(<1/10,000) and not known (cannot be estimated from the available data)	**Immune system disorders:**	Rare: hypersensitivity (including dyspnoea, rash, erythema, urticarial, pruritus, skin reaction, angioneurotic oedema, laryngeal oedema, laryngospasm, bronchospasm or non-cardiogenic pulmonary oedema). They may appear either immediately or after the injection or up to a few days later. Severe and even toxic skin reactions have been reported. Not known: anaphylactoid reaction/shock
	Nervous system disorders:	Rare: headache Very rare: dysguesia (transient metallic taste)
	Cardiac disorders:	Rare: bradycardia
	Vascular disorders:	Very rare: hypertension, hypotension
	Gastrointestinal disorders	Uncommon: nausea Rare: vomiting Very rare: diarrhoea, abdominal pain/discomfort
	General disorders:	Not known: salivary gland enlargement Common: feeling hot Rare: pyrexia Very rare: chills
	Injury, poisoning and procedural complications:	Not known: iodism
	Intravasular use (intraarterial and intravenous use)	

	Endocrine disorders:	Not known: thyrotoxicosis
	Psychiatric disorders:	Not known: confusional state
	Nervous system disorders:	Very rare: convulsion Not known: motor dysfunction, sensory disturbance
	Eye disorders:	Not known: transient blindness
	Cardiac disorders:	Rare: arrhythmia Not known: cardiac arrest, myocardial ischaemia
	Vascular disorders:	Very rare: flushing Not known: arterial spasm, ischaemia, thrombophlebitis and thrombosis
	Respiratory, thoracic and mediastinal disorders:	Rare: cough Very rare: dyspnoea, non-cardiogenic pulmonary oedema Not known: bronchospasm, laryngospasm
	Renal and urinary system disorders:	Rare: acute renal failure
	Musculoskeletal, connective tissue and bone disorders:	Not known: arthralgia
		Common: feeling hot

	General disorders:	Uncommon: pain Not known: injection site reaction
Typical dose range used in nuclear medicine procedure		Dependent upon type of procedure. Undertaken in accordance with local procedure
Preparation		Should be stored at or below 30ºC protected from light and secondary X-rays Product should be drawn into the syringe immediately before use
Administration	**Intravenous injection**	Adequate hydration should be assured before and after administration
Drug name:		Iodixanol (Visipaque) strength range 270 , 320 mg I / ml
Nuclear Medicine Procedure		X-ray contrast medium
Usual clinical use	**Adults and Children**	X-ray contrast medium for cardioangiography, cerebral angiography (conventional), peripheral arteriography (conventional), abdominal angiography (i.a.DSA), urography, venography, CT-enhancement. Lumbar, thoracic and cervical myelography. Arthrography, hysterosalpingography (HSG) and studies of the gastrointestinal tract. In children it is used for cardioangiography, urography, CT-enhancement and studies of the upper gastrointestinal tract.
Relevant Pharmacological action		Iodixanol is rapidly distributed in the body with a mean distribution half-life of approximately 21 minutes. The apparent volume of distribution is of the same magnitude as the extracellular fluid (0.26 l/kg b.w.), indicating that iodixanol is distributed in the extra-cellular volume only. No metabolites have been detected. The protein binding is less than 2%. The mean elimination half-life is approximately 2 hours in normal adults. In infants the elimination of iodixanol is prolonged (t½ approx. 4 hours in newborns). Iodixanol is excreted

		mainly through the kidneys by glomerular filtration. Approximately 80% of the administered dose is recovered unmetabolized in the urine within 4 hours and 97% within 24 hours after intravenous injection in healthy volunteers. Only about 1.2% of the injected dose is excreted in faeces within 72 hours. The maximum urinary concentration appears within approximately 1 hour after injection. No dose dependent kinetics has been observed in the recommended dose range.
Drug Interactions		All iodinated contrast media may interfere with tests on thyroid function, thus the iodine binding capacity of the thyroid may be reduced for up to several weeks. High concentrations of contrast medium in serum and urine can interfere with laboratory tests for bilirubin, proteins or inorganic substances (e.g. iron, copper, calcium and phosphate). These substances should therefore not be assayed on the day of examination. Use of iodinated contrast media may result in a transient impairment of renal function and this may precipitate lactic acidosis in diabetics who are taking metformin. Patients treated with interleukin-2 less than two weeks previous to an iodinated contrast medium injection have been associated with an increased risk for delayed reactions (flu-like symptoms or skin reactions).
Contraindications		Hypersensitivity to the active substance or to any of the excipients. Manifest thyrotoxicosis.
Caution in Use		A positive history of allergy, asthma, or untoward reactions to iodinated contrast media indicates a need for special caution. Premedication with corticosteroids or histamine H1 and H2 antagonists might be considered in these cases. The risk of serious reactions in connection with use of Visipaque is regarded as remote. However, iodinated contrast media may provoke anaphylactoid reactions or other manifestations of hypersensitivity. A course of action should therefore be planned in advance with necessary drugs and equipment available for immediate treatment, should a serious reaction occur. It is advisable always to use an indwelling cannula or catheter for quick intravenous access throughout the entire X-ray procedure.

		Non-ionic contrast media have less effect on the coagulation system in vitro, compared to ionic contrast media. When performing vascular catheterization procedures one should pay meticulous attention to the angiographic technique and flush the catheter frequently (e.g.: with heparinised saline) so as to minimise the risk of procedure-related thrombosis and embolism. Adequate hydration should be assured before and after contrast media administration. This applies especially to patients with multiple myeloma, diabetes mellitus, renal dysfunction, as well as to infants, small children and elderly patients. Young infants (age < 1 year) and especially neonates are susceptible to electrolyte disturbance and haemodynamic alterations. Care should also be taken in patients with serious cardiac disease and pulmonary hypertension as they may develop haemodynamic changes or arrhythmias. Patients with acute cerebral pathology, tumours or a history of epilepsy are predisposed to seizures and merit particular care. Also alcoholics and drug addicts have an increased risk of seizures and neurological reactions. To prevent acute renal failure following contrast media administration, special care should be exercised in patients with pre-existing renal impairment and diabetes mellitus as they are at risk. Patients with paraproteinemias (myelomatosis and Waldenström's macroglobulinemia) are also at risk. Preventive measures include: - Identification of high risk patients - Ensuring adequate hydration. If necessary by maintaining an i.v. infusion from before the procedure until the contrast medium has been cleared by the kidneys. - Avoiding additional strain on the kidneys in the form of nephrotoxic drugs, , arterial clamping, renal arterial angioplasty, or major surgery, until the contrast medium has been cleared. - Postponing a repeat contrast medium examination until renal function returns to pre-examination levels. Diabetic patients receiving metformin. There is a risk of the development of lactic acidosis when iodinated contrast agents are administered to diabetic patients treated with metformin, particularly in those with impaired renal

		function. To reduce the risk of lactic acidosis, the serum creatinine level should be measured in diabetic patients treated with metformin prior to intravascular administration of iodinated contrast media and the following precautions undertaken in the following circumstances. Normal serum creatinine (<130µmol/litre)/normal renal function: Administration of metformin should be stopped at the time of administration of contrast medium and not resumed for 48 hours unless renal function/serum creatinine remains in the normal range. Abnormal serum creatinine (>130µmol/litre)/impaired renal function: Metformin should be stopped and the contrast medium examination delayed for 48 hours. Metformin should only be restarted if renal function is not diminished (if serum creatinine is not increased) compared to pre-contrast values. Emergency cases: In emergency cases where renal function is impaired or unknown, the physician should evaluate the risk/benefit of the contrast medium examination, and the following precautions should be implemented: Metformin should be stopped. The patient should be fully hydrated prior to contrast medium administration and for 24 hours afterwards. Renal function (e.g. serum creatinine), serum lactic acid and blood pH should be monitored. A pH< 7.25 or a lactic acid level of >5 mmol/litre are indicative of lactic acidosis. The patient should be observed for symptoms of lactic acidosis. These include vomiting, somnolence, nausea, epigastric pain, anorexia, hyperpnoea, lethargy, diarrhoea and thirst. Particular care is required in patients with severe disturbance of both renal and hepatic function as they may have significantly delayed contrast medium clearance. Patients on haemodialysis may receive contrast media for radiological procedures. Correlation of the time of contrast media injection with the haemodialysis session is unnecessary. The administration of iodinated contrast media may aggravate the symptoms of myasthenia gravis. In patients with phaeochromocytoma undergoing interventional procedures, alpha blockers should be given as prophylaxis to avoid a hypertensive crisis. Special care should be exercised in patients with hyperthyroidism. Patients with multinodular goiter may be at risk of developing hyperthyroidism following injection of iodinated contrast media. One should also be aware of the possibility of inducing transient hypothyroidism in premature infants receiving contrast media. Extravasation of Visipaque has not been reported, but it is likely that Visipaque due to its isotonicity gives rise to less local pain and extravascular oedema than hyperosmolar contrast

		media. In case of extravasation, elevating and cooling the affected site is recommended as routine measures. Surgical decompression may be necessary in cases of compartment syndrome. Observation time Patients must be kept under close observation for 15 minutes following the last injection as the majority of severe reactions occur at this time. The patient should remain in the hospital environment (but not necessarily the radiology department) for one hour after the last injection, and should return to the radiology department if any symptoms develop.
Adverse Reactions **The frequencies of undesirable effects are defined as follows:** **Very common (≥1/10), common (≥1/100), uncommon (≥1/1000 to <1/100), rare (≥1/10,000 to <1/1000), very rare (<1/10,000) and not known (cannot be estimated from the available data)**	**Intravascular administration:** **Immune system disorders:** **Psychiatric disorders:** **Nervous system disorders:** **Eye disorders:** **Cardiac disorders:** **Vascular disorders:** **Respiratory, thoracic and**	Undesirable effects associated with Visipaque are usually mild to moderate and transient in nature. Serious reactions as well as fatalities are only seen on very rare occasions. Hypersensitivity reactions may present as respiratory or cutaneous symptoms like dyspnoea, rash, erythema, urticaria, pruritus, skin reactions including severe bullous or pustular reactions, angioneurotic oedema, hypotension, fever, laryngeal oedema, bronchospasm or pulmonary oedema. They may appear either immediately after the injection or up to a few days later. Hypersensitivity reactions may occur irrespectively of the dose and mode of administration and mild symptoms may represent the first signs of a serious anaphylactoid reaction/shock. Administration of the contrast medium must be discontinued immediately and, if necessary, specific therapy instituted via the vascular access. Patients using beta blockers may present with atypical symptoms of hypersensitivity which may be misinterpreted as a vagal reaction. A minor transient increase in serum creatinine is common after iodinated contrast media, but is usually of no clinical relevance. Uncommon: Hypersensitivity Not known: Anaphylactoid reaction, anaphylactoid shock; severe pustular or bullous skin reactions Not known: Confusional state Uncommon: Headache

	mediastinal disorders: **Gastrointestinal disorders:** **Musculoskeletal and connective tissue disorders:** **Renal and urinary disorders:** **General disorders and administration site conditions:** **Injury, poisoning and procedural complications:**	Rare: Dizziness Very rare: Sensory disturbance, amnesia Not known: Motor dysfunction, disturbance in consciousness, convulsion, transient contrast-induced encephalopathy including hallucination and other neurological symptoms. Very rare: Blindness transient Rare: Arrhythmia (including bradycardia, tachycardia), myocardial infarction Very rare: Cardiac arrest Not known: Ventricular hypokinesia, myocardial ischaemia, cardio-respiratory arrest Rare: Hypotension Very rare: Hypertension, ischaemia Not known: Arterial spasm, thrombosis, thrombophlebitis Rare: Cough Very rare: Dyspnoea Not known: Non-cardiogenic pulmonary oedema Uncommon: Nausea, vomiting Very rare: Abdominal pain/discomfort Not known: Arthralgia Very rare: Acute renal failure Uncommon: Feeling hot Rare: Pain, shivering (chills), pyrexia administration site reactions including extravasation Very rare: Feeling cold, asthenic conditions (e.g. malaise, fatigue)

		Not known: Iodism
Typical dose range used in nuclear medicine procedure		Dependent upon type of procedure. Undertaken in accordance with local procedure
Preparation		Product should be drawn into the syringe immediately before use
Administration	**Intravenous injection**	Adequate hydration should be assured before and after administration
Drug name:		Loversol (Optiray); strength range 240, 300, 320 , 350 mg I/ ml
Nuclear Medicine Procedure		X-ray contrast medium
Usual clinical use	**Adults and Children**	Optiray 350 is a non-ionic X-ray contrast medium that is indicated in adults for angiography throughout the cardiovascular system including coronary, peripheral, visceral and renal angiography, aortography and left ventriculography. Optiray 350 is also indicated in adults for use in computed tomography of the head and body, intravenous urography, venography and intravenous and intraarterial digital subtraction angiography (IADSA and IVDSA). Optiray 320 is a non-ionic X-ray contrast medium that is indicated in adults for use in cerebral, coronary, peripheral, visceral and renal angiography, in aortography, left ventriculography, venography, and in intravenous urography. Optiray 320 is also indicated in adults for use in computed tomography (CT) of the head and body. The safety and efficacy of Optiray 350, 320 and 240 in children have not been established. The medicinal product should therefore not be used in children aged up to 18 years, until further data becomes available. For cerebral, peripheral and visceral angiography and for intravenous urography Optiray 300 may be used in children.

		Optiray 300 is a non-ionic X-ray contrast medium that is indicated in adults for use in cerebral, peripheral and visceral angiography including intraarterial and intravenous digital subtraction angiography (IA DSA and IV DSA), venography, intravenous urography, and in computed tomography (CT) of the head and body. Optiray 300 may also be used in children for cerebral, peripheral and visceral angiography and for intravenous urography. Optiray 240 is a non-ionic X-ray contrast medium that is indicated in adults for use in cerebral angiography, venography, intravenous urography and intraarterial digital subtraction angiography (IA DSA). Optiray 240 is also indicated in adults for use in computed tomography (CT) of the head and body.
Relevant Pharmacological action		The pharmacokinetic profile of Optiray, together with its hydrophilic properties and a very low level of binding to serum and plasma proteins, indicate that Optiray is distributed within the extracellular fluid space and eliminated quickly through the kidneys by glomerular filtration. The mean (± se) half-lives after doses of 50 ml and 150 ml were 113 ± 8.4 and 104 ± 15 minutes respectively. Elimination via the faeces is negligible. No significant metabolism, deiodination, or biotransformation of Optiray has been observed.
Drug Interactions		Renal toxicity has been reported in single 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. The literature reports that patients who had been treated with Interleukin may develop a higher rate of adverse reactions. The reason has not yet been clarified. According to the literature an increased or delayed occurrence of these reactions within a period of 2 weeks was observed after administration of Interleukin. 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. 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. No interaction studies have been performed.
Contraindications		Hypersensitivity to iodine-containing contrast media, the active substance, or to any of the excipients. Manifest hyperthyroidism.
Caution in Use		Serious or fatal reactions have been associated with the administration of iodinated X-ray contrast media. It is of utmost importance to be completely prepared to treat any contrast medium reaction. 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. Since severe delayed reactions have been known to occur, the patient should be observed and emergency facilities and competent personnel should be available for at least 30 to 60 minutes after administration. As with all other X-ray contrast media, Optiray may cause anaphylaxis or other manifestations of pseudo-allergic intolerance reactions, e.g. nausea, vomiting, dyspnoea, erythema, urticaria and hypotension. A higher incidence of such reactions has been observed in patients with a history of previous intolerance reactions to other contrast media, or any history of asthma, allergy or hypersensitivity. A positive history of allergies does not arbitrarily contraindicate the use of a contrast agent when a diagnostic procedure is thought essential, but caution should be exercised. Appropriate resuscitation measures should be immediately available.

		Pre-medication with antihistamines and corticosteroids to avoid or minimise allergic reactions should be considered. Reports indicate that such pre-treatment does not prevent serious life-threatening reactions, but may reduce both their incidence and severity. General anaesthesia may be indicated in the performance of some procedures in selected patients; however, a higher incidence of adverse reactions has been reported in these patients, and may be attributable to the inability of the patient to identify untoward symptoms or to the hypotensive effect of anaesthesia. 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 placement are recommended. In patients with advanced atherosclerosis, serious 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. Angiography should be avoided whenever possible in patients with homocystinuria due to an increased risk of 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. 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. 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 any contrast medium. Caution must be exercised in patients with severely impaired renal function, combined renal and hepatic disease, diabetes mellitus, homozygous sickle cell disease, multiple myeloma or other paraproteinaemia, anuria, particularly when large doses are administered. Serious renal effects, including acute renal failure, may occur in these patients. Although neither the contrast agent nor dehydration has been proved separately to be the cause of renal failure, it has been speculated that

		the combination of both may be causative. The risk in patients with impaired renal function is not a contraindication to the procedure: however, special precautions, including maintenance of normal hydration and close monitoring, are required. An 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. Administration of radiopaque materials to patients known or suspected of having phaeochromocytoma should be performed with caution. However, the amount of radiopaque medium 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. In patients with homozygous sickle cell disease, hyperosmolar agents such as X-ray contrast media may effect sickling of erythrocytes. Hence, there is a need for careful consideration before the intra-arterial administration of such agents to patients with homozygous sickle cell disease. The anticoagulant effect of non-ionic X-ray contrast media 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. For this reason, meticulous angiographic techniques are recommended, e.g. frequent flushing of standard angiographic catheters and avoiding prolonged contact of blood with the contrast agent in syringes and catheters. 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. A cause-effect relationship to the contrast medium has not been established, since the patient's pre-existing condition and procedural techniques are causative factors in themselves. 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.

Adverse Reactions **The frequencies of undesirable effects are defined as follows:** **Very common (≥1/10), common (≥1/100), uncommon (≥1/1000 to <1/100), rare (≥1/10,000 to <1/1000), very rare (<1/10,000) and not known (cannot be estimated from the available data)**	**Immune system disorders:**	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. Very rare: anaphylactoid (hypersensitivity) reaction Not known: anaphylactic shock
	Endocrine disorders:	Not known: transient neonatal hypothyroidism
	Psychiatric disorders:	Very rare: confusional state; agitation; anxiety
	Nervous system disorders:	Rare: syncope; tremor; vertigo (including dizziness, light-headedness); headache; paraesthesia; Very rare: loss of consciousness; paralysis; speech disorders; somnolence; stupor; aphasia; dysphasia; hypoaesthesia
	Eye disorders:	Not known: convulsions; dyskinesia; amnesia
	Ear and labyrinth disorders:	Rare: vision blurred Very rare: conjunctivitis allergic (including eye irritation, ocular hyperaemia, watery eyes, swelling of conjunctiva, etc.) Not known: blindness transient
	Cardiac disorders:	Very rare:tinnitus
	Gastrointestinal disorders:	
	Skin and subcutaneous tissue disorders:	Rare: tachycardia Very rare: heart block; arrhythmia; angina; ECG abnormal; bradycardia; atrial fibrillation Not known: cardiac arrest; ventricular fibrillation; coronary artery spasm; cyanosis; extrasystole; palpitationsdysgeusia

	Musculoskeletal, connective tissue and bone disorders: **Renal and urinary disorders:** **General disorders and administration site conditions:** **Respiratory, thoracic and mediastinal disorders:**	Rare: hypotension; flushing Very rare: cerebrovascular disorder; phlebitis; hypertension; vasodilation Unknown: Shock; thrombosis; vasospasm Rare: laryngeal spasm, oedema and obstruction (incl. throat tightness, stridor, etc.); dyspnoea; rhinitis (incl. sneezing, nasal congestion); throat irritation; cough Very rare: pulmonary oedema; pharyngitis; hypoxia Not known: respiratory arrest; asthma; bronchospasm; dysphonia Uncommon :nausea Rare: vomiting; dry mouth Very rare: sialoadenitis; abdominal pain; tongue oedema; dysphagia; hypersalivation Not known: Diarrhoea Uncommon: urticaria Rare: erythema; pruritus; rash Very rare: angioedema; hyperhidrosis (incl. cold sweat) Not known: toxic epidermal necrolysis; acute generalized erythematous pustulosis; erythema multiforme; pallor Very rare: muscle cramps Rare: micturition urgency Very rare: acute renal failure; abnormal renal function; incontinence; haematuria; decreased creatinine clearance; BUN increased Not known: anuria; dysuria Very common: feeling hot

		Common: pain Rare: face oedema (incl. eye swelling, periorbital oedema, etc.); pharyngeal oedema; chills (incl. shaking chills, feeling cold) Very rare: oedema; injection site reactions (incl. pain, erythema, and haemorrhage up to necrosis especially after extravasation); chest pain; asthenic conditions (incl. malaise, tiredness, sluggishness, etc.); feeling abnormal Not known:Pyrexia Rare: laryngeal spasm, oedema and obstruction, dyspnoea, rhinitis, throat irritation, cough Very rare: pulmonary oedema, pharyngitis, hypoxia Not known: respiratory arrest, asthma, bronchospasm, dysphonia Adverse reactions may be classified as follows: a. Hypersensitivity or anaphylactoid reactions are mostly mild to moderate with symptoms like rash, pruritus, urticaria and rhinitis. However, serious reactions may occur. 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. Fatal cases were reported. Patients with a history of allergic reactions are at increased risk of developing a hypersensitivity reaction. Other type 1 (immediate) reactions include symptoms like 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 arrhythmias, conductivity disorders, as well as coronary spasm and thrombosis. Such reactions are very rare and 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 are 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 may occur in very rare cases and include rashes, swelling, inflammation and oedema. Such reactions occur probably in most cases due to extravasation of the contrast agent. Extended paravasation may necessitate surgical treatment. g. Extravasation can cause serious tissue reactions including blistering and skin exfoliation, the extent of which is dependent on the amount and strength of the contrast solution in the tissues. Frequency, type and severity of adverse reactions in children are expected to be the same as in adults. Transient hypothyroidism was observed in neonates following the administration of iodinated radiopaque agents.
Typical dose range used in nuclear medicine procedure		Dependent upon type of procedure. Undertaken in accordance with local procedure
Preparation		Store below 30OC. Protect from light. Protect from X-rays Product should be drawn into the syringe immediately before use
Administration	**Intravenous injection**	
Drug name:		Lomeprol (Iomeron) ; Strength range 400, 350 , 300, 250 mg I/ml
Nuclear Medicine Procedure		X-ray contrast medium
Usual clinical use	**Adults and Children**	Iomeron 400: X-ray contrast medium used for: peripheral arteriography; aortography; angiocardiography and left ventriculography; coronary arteriography; visceral arteriography; digital subtraction angiography; computed tomography enhancement; urography; dacryocystography; sialography; fistulography; galactography Iomeron 350 X-ray contrast medium used for:

		peripheral arteriography; venography; aortography; angiocardiography and left ventriculography; coronary arteriography; visceral arteriography; digital subtraction angiography; computed tomography enhancement; urography; dacryocystography; sialography; fistulography; galactography Iomeron 300 X-ray contrast medium used for: peripheral arteriography; venography; angiocardiography and left ventriculography; cerebral arteriography; visceral arteriography; digital subtraction angiography; computed tomography enhancement; urography; ERCP; dacryocystography; sialography; fistulography; galactography myelography Iomeron 250 X-ray contrast medium used for: Venography; cerebral arteriography; digital subtraction angiography; computed tomography enhancement; urography; cavernosography; myelography
Relevant Pharmacological action		The pharmacokinetics of intravascularly administered iomeprol are similar to those of other iodinated contrast media and conform to a two-compartment model with a rapid distribution and a slower elimination phase. In healthy subjects, the mean distribution and elimination half-lives of iomeprol were 0.5 hours and 1.9 hours respectively. Distribution volume is similar to that of extra cellular fluid. There is no significant serum protein binding and iomeprol is not metabolized. Elimination is almost exclusively through the kidneys (90% of the dose recovered in the urine within 96 hours of its administration) and is rapid (50% of an intravascularly administered dose within 2 hours).
Drug Interactions		Use of the product may interfere with tests for thyroid function. Vasopressor agents should not be administered prior to iomeprol. Treatment with drugs that lower the seizure threshold such as certain neuroleptics (MAO inhibitors, tricyclic antidepressants), analeptics, and anti-emetics and phenotiazine derivatives

		should be discontinued 48 hours before the examination. Treatment should not be resumed until 24 hours post-procedure. It has been reported that 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. Beta-blockers may impair the response to treatment of bronchospasm induced by contrast medium. Patients with normal renal function can continue to take metformin normally. In diabetic patients with diabetic nephropathy, under treatment with metformin and with moderate renal impairment, metformin should be stopped at the time of, or prior to the procedure and withheld for 48 hours subsequent to the procedure and reinstituted only after renal function has been re-evaluated and found to be normal. Metformin should be stopped from 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. Allergy-like reactions to contrast media are more frequent and may manifest as delayed reactions in patients treated with immuno-modulators, like Interleukin-2 (IL-2).
Contraindications		Hypersensitivity to the active substance or any of the excipients.
Caution in Use		In consideration of possible complications, the patient should be kept under observation for at least 30 minutes after the examination. Extreme caution during injection of contrast media is necessary to avoid extravasation. A normal diet should be maintained until the patient refrains from eating 2 hours before the procedure. Hydration Any severe disorders of water and electrolyte balance must be corrected prior to administration. Adequate hydration must be ensured particularly in patients with diabetes mellitus, polyuria,

		oliguria and hyperuricaemia; also in babies, small children and the elderly. Rehydration prior to use of iomeprol is recommended in patients with sickle cell disease. Special population Hypersensitivity to iodinated contrast media, allergic predisposition A positive history of allergy, asthma or untoward reaction during previous similar investigations indicates a need for extra caution since, as with other contrast media, this product may provoke anaphylaxis or other manifestations of allergy with nausea, vomiting, dyspnoea, erythema, urticaria and hypotension. Appropriate resuscitative measures should be immediately available. The risk of bronchospasm-inducing reactions in asthmatic patients is higher after contrast media administration, especially in patients taking beta-blockers. Hypersensitivity testing In patients with suspected or known hypersensitivity to contrast media, sensitivity test doses are not recommended, as severe or fatal reactions to contrast media are not predictable from sensitivity test. Myelomatosis or paraproteinaemias are conditions predisposing to renal impairment following CM administration. Adequate hydration and monitoring of renal function are recommended after CM administration. Cardiovascular diseases Care should be taken in severe cardiac disease particularly heart failure and coronary artery disease. Reactions may include pulmonary oedema, haemodynamic changes, ischaemic ECG changes and arrhythmias. In severe, chronic hypertension the risk of renal damage following administration of a contrast medium is increased. In these cases the risks associated with the catheterization procedure are increased. The product should be used with caution in patients with hyperthyroidism or goitre. Use may interfere with thyroid function tests. The administration of iodinated contrast media may aggravate myasthenia signs and symptoms. CNS Disorders

		Particular care is needed in patients with acute cerebral infarction, acute intracranial haemorrhage and any conditions involving damage to the blood brain barrier, brain oedema or acute demyelination. Convulsive seizures are more likely in patients with intracranial tumours or metastases or with a history of epilepsy. Neurological symptoms related to cerebrovascular diseases, intracranial tumours/metastases or degenerative or inflammatory pathologies may be exacerbated. There is an increased risk of transient neurological complications in patients with symptomatic cerebrovascular disease eg stroke, transient ischaemic attacks. Cerebral ischaemic phenomena may be caused by intravascular injection. Anticonvulsant therapy should not be discontinued. In acute and chronic alcoholism the increase in blood brain barrier permeability facilitates the passage of the contrast medium into cerebral tissue possibly leading to CMS disorders. There is a possibility of a reduced seizure threshold in alcoholics. In patients with a drug addiction there is also the possibility of a reduced seizure threshold. Patients with phaeochromocytoma may develop severe, occasionally uncontrollable hypertensive crises during intravascular administration. Premedication with an alpha and beta receptor blocker is recommended in these patients. Pronounced excitement, anxiety and pain can cause side effects or intensify reaction to the contrast medium. A sedative may be given. Renal failure In patients with moderate to severe impairment of renal function, attention should be paid to renal function parameters before re-examining the patient with a contrast media. Preventive measures include: - identification of high-risk patients; - ensuring adequate hydration before CM administration, preferably by maintaining i.v. infusion before and during the procedure and until the CM has been cleared by the kidneys; avoiding whenever possible, the administration of nephrotoxic drugs or major surgery or procedure such as renal angioplasty, until the CM has been cleared; A combination of severe hepatic and renal impairment delays excretion of the contrast medium therefore such patients should not be examined unless absolutely necessary. Diabetes mellitus 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. Children: Infants up to 1 year, especially the newborn, are particularly susceptible to electrolyte imbalance and haemodynamic alterations. Care should be taken regarding the dosage used. Elderly: There is special risk of reactions involving the circulatory system such that myocardial ischaemia, major arrhythmias and extrasystoles are more likely to occur. A combination of neurological disturbances and vascular pathologies present a serious complication. The probability of acute renal insufficiencies is higher in these people. Precautions for dedicated exams Angiography Non-ionic contrast media have less antiocoagulant activity in vitro than ionic media. Non-ionic media should not be allowed to remain in contact with blood in a syringe, and intravascular catheters should be flushed frequently to minimise the risk of clotting which, rarely, has led to serious thromboembolic complications. Intravascular administration should be performed if possible with the patient lying down. The patient should be kept in this position and closely observed for at least 30 minutes after the procedure since the majority of severe incidents occur with this time. Venography Special care is required when venography is performed in patients with thrombosis, phlebitis, severe ischaemic disease, local infection or a totally obstructed artero-venous system.
Adverse Reactions **The frequencies of undesirable effects are defined as follows:** **Very common (≥1/10), common (≥1/100),**	**General**	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. In most cases, reactions occur within minutes of dosing but at times reactions may occur at later time. Anaphylaxis (anaphylactoid/hypersensitivity reactions) may manifest with various symptoms, and rarely does any one patient develop all the symptoms. Typically, in 1 to 15 min (but rarely after as

uncommon (≥1/1000 to <1/100), rare (≥1/10,000 to <1/1000), very rare (<1/10,000) and not known (cannot be estimated from the available data)	**Nervous system disorders:** **Cardiac disorders:** **Vascular disorders:** **Respiratory, thoracic and mediastinal disorders:** **Gastrointestinal disorders:** **Skin and subcutaneous tissue disorders:** **Musculoskeletal and connective tissue disorders:** **General disorders and administration site conditions:** **Investigations:**	long as 2 h), the patient complains of feeling abnormal, agitation, flushing, feeling hot, sweating increased, dizziness, increased lacrimation, rhinitis, palpitations, paresthesia, pruritus, sore throat and throat tightness, dysphagia, cough, sneezing, urticaria, erythema, mild localised oedema, angioneurotic oedema and dyspnoea due to glottic/laryngeal/pharyngeal oedema and/or spasm manifesting with wheezing, and bronchospasm. Nausea, vomiting, abdominal pain, and diarrhoea are also reported. These reactions, which can occur independently of the dose administered or the route of administration, may represent the first signs of circulatory collapse. Administration of the contrast medium must be discontinued immediately and, if needed, appropriate specific treatment urgently initiated via venous access. 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. Uncommon: headache, dizziness Rare: presynscope Rare: bradycardia, tachycardia Uncommon: hypertension Rare: hypotension Uncommon: dyspnoea Uncommon: Nausea, vomiting

		Uncommon: Erythema, urticarial pruritus Rare: Rash Rare: back pain Common: feeling hot Uncommon: chest pain, injection site warmth and pain Rare: Asthenia, rigors, pyrexia Rare: blood creatinine increased
Typical dose range used in nuclear medicine procedure		Dependent upon type of procedure. Undertaken in accordance with local procedure
Preparation		Store below 30OC. Protect from light Product should be draw into the syringe immediately before use
Administration	**Intravenous injection**	
Drug name:		Lopamidol (Niopam); strength range 150, 200, 300, 340, 370 mg I / ml
Nuclear Medicine Procedure		X-ray contrast medium
Usual clinical use	**Adults and Children**	Iopamidol 150 X-ray contrast medium for injection, particularly in digital subtraction angiography. Iopamidol 200

		X-ray contrast medium for use in lumbar and thoraco-cervical myelography, computer tomography enhancement. Iopamidol 300 X-ray contrast medium for use in lumbar and thoraco-cervical myelography, cerebral angiography,peripheral angiography, venography, computer tomography enhancement, urography and arthrography. Iopamidol 340 X-ray contrast medium for use in peripheral arteriography, angiocardiography and left ventriculography, coronary arteriography, aortography-retrograde, selective renal arteriography, selective visceral angiography, digital subtraction angiography, computer tomography enhancement, urography and arthrography. Iopamidol 370 X-ray contrast medium for use in: Peripheral arteriography; Angiocardiography and left ventriculography; Coronary arteriography ; Aortography – retrograde ; Selective renal arteriography ;Selective visceral angiography ; Digital subtraction angiography; Urography
Relevant Pharmacological action		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.
Drug Interactions		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 day

		s 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 reinstated only after 48 hours if serum creatinine is unchanged. In emergency patients in whom renal function is either impaired or unknown, 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 receiving 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.

Contraindications		Hypersensitivity to the active substance or to any of the excipients.
Caution in Use		After the administration of the contrast medium, drugs and equipment for emergency resuscitation must be available for at least 30 minutes. 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; 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.

		. 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. 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 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. 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 haematoma/haemorrhage, history of convulsive disorder, chronic alcoholism or multiple sclerosis. Patients with these conditions have an increased risk of neurological complications. 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. 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.
Adverse Reactions **The frequencies of undesirable effects are defined as follows:** **Very common (≥1/10), common (≥1/100), uncommon (≥1/1000 to <1/100), rare (≥1/10,000 to <1/1000), very rare (<1/10,000) and not known (cannot be estimated from the available data)**	**Nervous system disorders:** **Cardiac disorders:** **Vascular disorders:** **Respiratory, thoracic and mediastinal disorders:**	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.

	Gastrointestinal disorders:	
	Skin and subcutaneous tissue disorders:	Common: headache Uncommon: dizziness, taste alteration Rare: paraesthesia
	Musculoskeletal and connective tissue disorders:	
	Renal and urinary disorders:	Uncommon: cardiac dysrhymthmias Rare: bradycardia
	General disorders and administration site conditions:	Uncommon: hypotension, hypertension, flushing
		Rare: pulmonary oedema, asthma, bronchospasm
	Investigations:	
		Common: nausea Uncommon: vomiting, diarrhoea, abdominal pain, dry mouth
		Uncommon: rash, urticarial, pruritus, erythema, sweating increased
		Uncommon: back pain Rare: muscle spasms

		Uncommon: acute renal failure Uncommon: chest pain, injection site pain, pyrexia, feeling cold Blood creatinine increased
Typical dose range used in nuclear medicine procedure		Dependent upon type of procedure. Undertaken in accordance with local procedure
Preparation		Protect from light Product should be drawn into the syringe immediately before use
Administration	**Intravenous injection**	Adequate hydration should be assured before and after administration
Drug name:		Lobitridol (Xenetix) Strength range 250, 300, 350 mg I / ml
Nuclear Medicine Procedure		X-ray contrast medium
Usual clinical use	**Adults and Children**	Iobitridol 250 whole-body CT; venography; intra-arterial digital subtraction angiography; ERP/ERCP Iobitridol 300 intravenous urography; brain and whole-body CT; intravenous digital subtraction angiography; arteriography of the aorta and lower limbs; angiocardiography; arthrography; hysterosalpingography; herniography; ERP/ERCP Iobitridol 350

		intravenous urography; brain and whole-body CT; intravenous digital subtraction angiography; arteriography of the aorta and lower limbs; angiocardiography; sialography; ERCP
Relevant Pharmacological action		Injected via the intravascular route, iobitridol is distributed in the vascular system and interstitial space. It is rapidly eliminated via urinary excretion (glomerular filtration without tubular reabsorption or secretion) in unchanged form.
Drug Interactions		Metformin in diabetics Iodinated contrast media may affect the uptake of radioactive iodine by the thyroid for several weeks. This may lead to impaired uptake in thyroid scintigraphy, and/or to a decrease in the efficacy of Iodine 131 treatment. In patients due to undergo renal scintigraphy with injection of a radiopharmaceutical secreted by the renal tubule, it is preferable to carry out this examination before an iodinated contrast agent injection. Beta-blocking agents vasoactive substances, angiotensin-converting enzyme inhibitors, angiotensin receptor antagonists. There is some evidence to suggest that concurrent use of a beta blocker is a risk factor for anaphylactoid reactions; also, hypotensive effects may be exacerbated. Moreover these drugs reduce the efficacy of the cardiovascular compensation mechanism that occurs during haemodynamic disorders. The physician must be informed about the situation and appropriate intensive care equipment must be available. Diuretics: in cases of dehydration induced by diuretics, there is an increased risk of acute renal failure, especially when using high doses of iodinated contrast media. The patient should be rehydrated before administration of an iodinated contrast medium. The risk of developing a reaction to the contrast agents is increased in the event of recent treatment with interleukin 2 (intravenous route): a skin reaction is possible, or more rarely hypotension, oliguria or even renal insufficiency. High concentrations of iodinated contrast media in plasma and urine can interfere with the in vitro determination of bilirubin, proteins and inorganic substances (iron, copper, calcium and phosphate); it is recommended that these determinations not be made within the first 24 hours following the examination.

Contraindications		Hypersensitivity to iobitridol or to any of the excipients; History of major immediate or delayed cutaneous reaction to Iobitridol injection; Manifest thyrotoxicosis. Carotid arteriography
Caution in Use		All iodinated contrast media can cause minor or major reactions that can be life-threatening. These can occur immediately (within 60 minutes) or be delayed (within 7 days) and are often unpredictable. Due to risk of major reactions, emergency resuscitation equipment should be available for immediate use. As in the case of all iodinated contrast agents, non-ionic water-soluble tri-iodinated contrast media can result in minor, severe, or fatal intolerance reactions, anaphylaxis or other manifestations of hypersensitivity which are often early and sometimes delayed. They are unpredictable but are more frequent in patients with a history of allergy (hives, asthma, hay fever, eczema, various food or drug allergies) or who have shown particular sensitivity during a previous examination with an iodinated contrast agent. They cannot be screened using iodine reaction tests or any other currently available test. Patients who have already experienced a reaction after previous administration of an iodinated contrast agent present an increased risk of experiencing a further reaction following administration of the same or possibly another iodinated contrast agent, and are thus considered to be at-risk patients. Any severe disorder of water or electrolyte balance should be corrected, especially in patients with multiple myeloma, polyuria, oliguria, hyperuricemia, as well as in small children and elderly patients. Adequate hydration must be ensured before the examination. Iodinated contrast agents can induce a transient alteration in renal function or worsen pre-existing renal insufficiency. Preventive measures include: Identifying at-risk patients, i.e. those with dehydration, renal insufficiency, diabetes, severe heart failure, monoclonal gammapathy (multiple myeloma, Waldenström’s disease), history of renal

		failure after contrast agent administration; infants below the age of one year and elderly subjects with atheroma. Hydrate when necessary using a saline solution. Avoid concomitant use of nephrotoxic drugs. If this cannot be avoided, reinforce monitoring of renal laboratory parameters. [Includes aminosides, organoplatinum compounds, high-dose methotrexate, pentamidine, foscarnet and certain antivirals (aciclovir, ganciclovir, valaciclovir, adefovir, cidofovir, tenofovir), vancomycin, amphotericin B, immunosuppressants such ciclosporin or tacrolimus, ifosfamide.] Allow at least 48 hours between two radiological examinations with injection of contrast agents, or postpone any new examination until renal function returns to baseline. Prevent lactic acidosis in diabetics treated with metformin, by monitoring serum creatinine levels. Normal renal function: treatment with metformin must be suspended before contrast agent injection and for at least 48 hours after or until normal renal function is restored. Abnormal renal function: metformin is contraindicated. In case of emergency: if the examination is mandatory, precautions must be taken, i.e. metformin discontinuation, hydration, monitoring of renal function and checking for signs of lactic acidosis. Iodinated contrast agents can be used in haemodialysed patients as the agents are removed by dialysis. Particular attention is necessary when a patient presents with both hepatic and renal insufficiency since, in this situation, the risk for retention of the contrast agent is increased. Care should be taken in renal or hepatic impairment, diabetes or in patients with sickle cell disease. Due to an increased risk of bronchospasm, special caution should be taken in patients who have suffered an asthma attack within eight days preceding the examination. After iodinated contrast agent injection, particularly in patients with a goitre or a history of dysthyroidism, there is a risk of either a flare-up of hyperthyroidism or development of

		hypothyroidism. There is also a risk of hypothyroidism in neonates who have received or whose mothers have received an iodinated contrast medium. In patients with cardiovascular disease (such as early or patent heart failure, coronaropathy, pulmonary hypertension, valvulopathy, cardiac arrhythmias), the risk of cardiovascular reactions is increased after administration of an iodinated contrast agent. Patients with phaeochromocytoma can develop a hypertensive crisis after intravascular administration of the contrast agent and must be monitored prior to the examination. Administration of a contrast agent can worsen the symptoms of myasthenia gravis.
Adverse Reactions **The frequencies of undesirable effects are defined as follows:** **Very common (≥1/10), common (≥1/100), uncommon (≥1/1000 to <1/100), rare (≥1/10,000 to <1/1000), very rare (<1/10,000) and not known (cannot be estimated from the available data)**	**Immune system disorders** **Endocrine disorders** **Nervous system disorders** **Ear and labyrinth disorders** **Cardiac disorders** **Vascular disorders** **Respiratory, thoracic and**	Adverse reactions related to the use of Xenetix are generally mild to moderate, and transient. The adverse reactions most commonly reported since marketing are feeling of warmth, pain and oedema at the injection site. The hypersensitivity reactions are usually immediate (during the injection or over the hour following the start of the injection) or sometimes delayed (one hour to several days after the injection), and then appear in the form of adverse skin reactions. Rare: hypersensitivity Very rare: anaphylactic shock, anaphylactic reaction, anaphylactoid reaction Very rare: thyroid disorder Rare: presyncope (vasovagal reaction) Rare: vertigo Very rare: hearing impaired Rare: tachycardia

	mediastinal disorders **Gastrointestinal disorders** **Skin and subcutaneous tissue disorders** **Renal and urinary disorders** **General disorders and administration site conditions** **Investigations**	Very rare: cardiac arrest, myocardial infarction (more frequent after intracoronary injection), arrhythmia, ventricular fibrillation, angina pectoris Unknown: Torsades de Pointes, coronary arteriospasm Rare: hypotension Very rare: circulatory collapse Unknown: hypertension Rare: dyspnoea, cough, tightness in the throat, sneezing Very rare: respiratory arrest, pulmonary oedema, laryngospasm, bronchospasm, laryngeal oedema Uncommon: nausea Rare: vomiting Very rare: abdominal pain Rare: angioedema, urticaria (localised or extensive), erythema, pruritus Very rare: Acute Generalized Exanthematous Pustulosis, Stevens-Johnson syndrome, Lyell's syndrome, eczema, maculopapulous exanthema (all as delayed hypersensitivity reactions) Very rare: acute renal failure, anuria Uncommon: feeling hot Rare: facial oedema, malaise, chills, injection site pain Very rare: injection site necrosis following extravasation, injection site inflammation following extravasation, injection site oedema Very rare: blood creatinine increased

Typical dose range used in nuclear medicine procedure		Dependent upon type of procedure. Undertaken in accordance with local procedure
Preparation		Store below 30oC
Administration	**Intravenous injection**	Adequate hydration should be assured before and after administration After administration of the contrast agent, the patient must be monitored for at least 30 minutes since the majority of serious undesirable effects occur within this period of time. patient must be informed about the potential for delayed reactions (up to 7 days after the examination).

Approval

June 2016 by the British Nuclear Medicine Society Professional Standards Committee

Review

Date for review/update May 2017

Comment	Date	Version	Reviewer
Initial draft first posted	January 2010	V1	Dr M Palmer
Revised	August 2013	V2	Mr P Maltby
Revised	May 2016	V3	Dr B Ellis
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