Administration of Medicinal Products by Non-Medical Personnel

Report August 2013

Paul Maltby on behalf of BNMS 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 not 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 (2013)

[* 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
Potasium iodide	Iodine-labelled RPx

Potasium 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

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 Apprehension - Commonly

	Psychiatric disorders **Special senses disorders**	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)
		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

	General disorders **Application site**	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 H_2-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 H_2-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** **Cardiac 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 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:**	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.
	Antibacterials:	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: Antihypertensives	Enhanced sedation or respiratory and cardiovascular depression with sedative antihistamines.

	Antipsychotics **Antivirals:** **Anxiolytics:** **Other drug interations**	Enhanced hypotensive effect, enhanced sedative effect with alpha blockers and possibly moxonidine. 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. 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. Enhanced sedation or respiratory and cardiovascular depression with other anxiolytics. 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	

	Reproductive **Respiratory** **Skin** **Urinary:**	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. Changes in libido, gynaecomastia. Rarely, respiratory depression and apnoea, particularly with high dosage. Skin reactions. 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:**	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.
	Entacapone:	The effects of Dobutamine concentrate may be enhanced by entacapone.
	Beta-blockers:	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 (see section 4.4 Special warnings and precautions for use).
Contraindications		Hypersensitivity to dobutamine, sodium metabisulphite or any of the other ingredients. Phaeochromocytoma.
Adverse Reactions		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.
	Immune system disorders:	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:	Bolus doses of intravenous furosemide may induce flushing, sweating, tachycardia and variations in blood pressure in patients receiving chloral hydrate or triclofos.
	Neuromuscular blocking agents:	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:**	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.
	Immune system disorders:	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

	Metabolism and nutrition disorders:	dehydration, especially in elderly patients. Severe fluid depletion may lead to haemoconcentration with a tendency for thromboses to develop. 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.
	Psychiatric/Nervous system disorders:	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.
	Eye disorders:	Visual disturbances, blurred vision.
	Ear and labyrinth disorders:	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 disorders:	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.
	Vascular disorders:	Hypotension and orthostatic hypotension may occur, especially in patients taking other medications which lower blood pressure. Allergic vasculitis has been reported very rarely.

	Gastrointestinal disorders:	Nausea, vomiting, diarrhoea and dry mouth may occur but are not usually severe enough to necessitate withdrawal of treatment.
	Hepatobiliary disorders:	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 subcutaneous tissue disorders:	Skin and mucous membrane reactions may occasionally occur eg pruritis, urticaria, other rashes or bullous lesions, erythema multiforme, exfoliative dermatitis and purpura.
	Musculoskeletal disorders:	Serum calcium levels may be reduced, muscle spasms or muscle weakness may indicate electrolyte disturbances. In very rare cases tetany has been observed.
	Renal and urinary disorders:	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.
	General disorders:	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:** **Anti-arrhythmics:** **Antibacterials:** **Antidepressants, anxiolytics, hypnotics:** **Antipsychotics:**	enhanced sedative and hypotensive effects. There may be delayed absorption of mexiletine. The opioid analgesic papaveretum has been shown to reduce plasma ciprofloxacin concentration. The manufacturer of ciprofloxacin advises that premedication with opioid analgesics be avoided. 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. 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 (see also biliary tract disorders 4.4 Special Warnings and Precautions), 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 (see also 4.9 Overdose). The commonest side-effects of morphine are nausea, vomiting, constipation, drowsiness and dizzines. 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: **Skin:** **Urinary:**	blurred or double vision or other changes in vision, miosis. pruritus, urticaria, rash, sweating. Contact dermatitis has been reported and pain and irritation may occur on injection. 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) C_{max} and AUC_{τ} 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**	Headache - common Dizziness, paraesthesia, somnolence, insomnia and vertigo - uncommon Reversible mental confusion, agitation, aggression, depression and hallucinations, predominantly in severely ill patients – rare
	Endocrine	Gynaecomastia - rare
	Gastrointestinal	Diarrhoea, constipation, abdominal pain, nausea/vomiting and flatulence – common Dry mouth, stomatitis and gastrointestinal candidiasis – rare
	Haematological	Leukopenia, thrombocytopenia, agranulocytosis and pancytopenia – rare
	Hepatic	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 **Skin** **Other**	Impotence - rare Rash, dermatitis and/or pruritus, urticaria - uncommon Photosensitivity, bullous eruption erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis (TEN), alopecia - rare 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:** **Children (6 months to 18 years):**	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 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 H_2-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 secrection: 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 H_2 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	Rare: Skin Rash.

	Tissue Disorders **Musculoskeletal and Connective Tissue Disorders** **Renal and Urinary Disorders** **Reproductive System and Breast Disorders**	Very Rare: Erythema multiforme, alopecia. Very Rare: Musculoskeletal symptoms such as arthralgia and myalgia. 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:		Sincalide for Injection
Nuclear Medicine Procedure		Hepatobiliary Imaging
Usual clinical use	**Adults:** **Children (6 months to 18 years):**	Kinevac (Sincalide for Injection) may be used: (1) to stimulate gallbladder contraction, as may be assessed by contrast agent cholecystography or ultrasonography, or to obtain by duodenal aspiration a sample of concentrated bile for analysis of cholesterol, bile salts, phospholipids, and crystals; (2) to stimulate pancreatic secretion (especially in conjunction with secretin) prior to obtaining a duodenal aspirate for analysis of enzyme activity, composition, and cytology; (3) to accelerate the transit of a barium meal through the small bowel, thereby decreasing the time and-extent of radiation associated with fluoroscopy and x-ray examination of the intestinal tract. Safety and effectiveness in children have not been established
Relevant Pharmacological action		When injected intravenously, sincalide produces a substantial reduction in gallbladder size by causing this organ to contract. The evacuation of bile that results is similar to that which occurs physiologically in response to endogenous cholecystokinin. The intravenous (bolus) administration of sincalide causes a prompt contraction of the gallbladder that becomes maximal in 5 to 15 minutes, as compared with the stimulus of a fatty meal which causes a progressive contraction that becomes maximal after approximately 40 minutes. Generally, a: 40 percent reduction in radiographic area of the gallbladder is considered satisfactory contraction, although some patients will show area reduction of 60 to 70 percent. Like cholecystokinin, sincalide stimulates pancreatic secretion; concurrent administration with secretin increases both the volume of pancreatic secretion and the output of bicarbonate and protein (enzymes) by the gland. This combined effect of secretin and sincalide permits the assessment of specific pancreatic function through measurement and analysis of the duodenal aspirate. The parameters usually determined are: volume of the secretion; bicarbonate concentration; and amylase content (which parallels the content of trypsin and total protein). Both cholecystokinin and sincalide stimulate intestinal motility, and may cause pyloric contraction which retards gastric emptying.
Drug Interactions		No data available
Contraindications		The preparation is contraindicated in patients hypersensitive to sincalide and in patients with intestinal obstruction.
Adverse Reactions	**General disorders**	Reactions to sincalide are generally mild and of short duration. The most frequent adverse reactions were abdominal discomfort or pain, and nausea; rapid intravenous injection of 0.04 mcg sincalide per kg expectably causes transient abdominal cramping. These phenomena are

		usually manifestations of the physiologic action of the drug, including delayed gastric emptying and increased intestinal motility. These reactions occurred in approximately 20 percent of patients; they are not to be construed as necessarily indicating an abnormality of the biliary tract unless there is other clinical or radiologic evidence of disease. The incidence of other adverse reactions, including vomiting, flushing, sweating, rash, hypotension, hypertension, shortness of breath, urge to defecate, headache, diarrhoea, sneezing, and numbness was less than 1 per cent; dizziness was reported in approximately 2 per cent of patients. These manifestations are usually lessened by slower injection rate.
Typical dose range used in nuclear medicine procedure	**Adult** **Children**	For prompt contraction of the gallbladder, a dose of 0.02 mcg sincallde per kg (1.4 mcg/70 kg) is Injected intravenously over a 30- to 60-second interval; If satisfactory contraction of the gallbladder does not occur in 15 minutes, a second dose, 0.04 mcg sincalide per kg, may be administered. Safety and effectiveness in children have not been established.
Preparation		Sincalide for injection may be stored at room temperature prior to reconstitution. To reconstitute, aseptically add 5 mL of Sterile Water for Injection USP to the vial; any additional dilution should be made with Sodium Chloride Injection USP, 0.9%. The solution may be kept at room temperature and should be used within 24 hours of reconstitution, after which time any unused portion should be discarded.
Administration	**Intravenous injection**	Several protocols for the administration of sincalide have been published. (eg SNM Practice Guideline for Hepatobiliary Scintigraphy 4.0 in Journal of Nuclear Medicine Technology. Vol. 38 • No. 4 • December 2010). The SPC states that it may be injected intravenously over a 30- to 60-second interval; If satisfactory contraction of the gallbladder does not occur in 15 minutes, a second dose, 0.04 mcg sincalide per kg, may be administered. To reduce the intestinal side effects (see ADVERSE REACTIONS), an intravenous infusion may be prepared at a dose of 0.12 mcg/kg in 100 mL of Sodium Chloride Injection USP and given at a rate of 2 mL per minute; alternatively, an intramuscular dose of 0.1 mcg/kg may be given. When Kinevac (Sincalide for Injection) is used in hepatobiliary imaging nuclear medicine procedures, images are usually taken at five-minute intervals after the injection. For visualization of the cystic duct, it may be necessary to take images at one-minute intervals during the first five minutes after the injection.

Approval

August 2013 by the British Nuclear Medicine Society Professional Standards Committee

Review

Date for Review/Update August 2014

Comment	Date	Version	Reviewer
Initial draft first posted	January 2010	V1	Dr. M. Palmer
Revised	August 2013	V2	Mr P Maltby
Last Revised			