



The ROYAL COLLEGE of
OPHTHALMOLOGISTS

Ophthalmic Service Guidance

Intravitreal injection therapy

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1 Introduction

The aim of this guidance is to provide advice about performing all intravitreal injection therapy (IVT) as safely as possible, whilst supporting the requirement for innovative and efficient models of care to deal with the continuing increase in demand.

It is essential that:

- Any substance injected into the eye is sterile, and remains sterile when it enters the vitreous cavity.
- That the environment and equipment are safe and suitable.
- That staff are trained and up to date in delivering the procedure and know how to manage complications and adverse events.

This guidance is designed for easy reference. As much of the document, as is possible, is based on published evidence. In the absence of published high-quality evidence, expert consensus has been used to make recommendations.

In the UK, the most commonly treated diseases treated by IVT are neovascular age related macular degeneration (nAMD), diabetic macular oedema and retinal vein occlusion. There are important principles to be followed, both pre and post treatment, irrespective of the eye condition or product injected into the eye.

2 Staffing

Every patient having IVT should have a clear management plan and be under the care of a named consultant ophthalmologist or SAS doctor with autonomous practice rights in this area. Injections may be administered by a trainee doctor under supervision of such an ophthalmologist. Additionally, IVT administration may be delegated by a named consultant or autonomously practicing SAS doctor to appropriately trained non-medical health care professionals (HCP's) whose training and accreditation has been fully approved locally by a trust governance committee. Such non-medical delivery of care should be supported by a local policy or protocol, with recorded training and competency measures and regular clinical audit of processes and outcomes.

It is essential that the HCP giving the injection has immediate access to advice from an ophthalmologist at all times whilst giving injections and that an appropriately trained clinician is available on site to manage any very urgent complications. It should be noted that intravitreal injections performed by any HCP remains off-label for the licensed drugs and the HCP should be supported appropriately and the trust aware of this fact. For injection lists, there should be adequate nursing or healthcare assistant support to help with the procedure and to provide patient assistance.

3 Pre-injection information and consent

- Prior to treatment the patient should be counselled with full discussion and explanation of:
 - The importance of treatment
 - The treatment options
 - Why the IVT procedure is appropriate for the patient
 - What the treatment involves/what to expect/what the risks are (1,2)
 - Who is likely to give the injection. If an HCP is likely to give the injection, the patient must be advised this is off-label treatment (if appropriate)
- A relevant information leaflet or booklet, in an appropriate accessible format, should be offered to the patient/carer.
- Potentially serious risks quoted in relation to IVT should include endophthalmitis, retinal detachment, vitreous haemorrhage and cataract.
- Additional risks should be explained for specific products e.g., raised intraocular pressure/glaucoma with intravitreal steroid; systemic thrombo-embolic events with anti-VEGF medications. Floaters may occur following IVT but particularly after intravitreal implants, and may be a feature of Ocriplasmin use.
- The importance of probable repeated injections should be discussed, and the likely frequency at which these will be required, and for how long.
- Valid consent must be obtained from the patient prior to first IVT procedure; this will normally suffice for a course of treatment over at several months when the drug is licensed for IVT. However, it is recommended that local hospital consent policies are consulted for how long a time a consent form for a course of treatment is considered valid. If consent is taken in advance, before every injection the patient must be asked about any changes to their medical condition and consent should be briefly re-confirmed and those checks documented in the records. Consent should also be obtained specifically for the HCP to give the injection, if appropriate.
- If there is a change to the treatment plan, drug used, the clinical condition and/or the perceived benefit/risk to the patient, or if the drug is not specifically licensed for intravitreal usage, the change must be noted and written consent needs to be taken again.

4 Clinical setting of care

- Procedures may be carried out in theatre or, more usually, in a suitable room in an outpatient setting with full sterile precautions 3.
- For outpatient delivery, an enclosed, dedicated clean room (as defined by the local Infection Control Team) is required which only deals with clean (non-infected) cases, and is free from interruption.
- The room should be of a sufficient size to enable a patient couch for the procedure and staff access to both sides of the head of the couch. There should be storage cupboards for clinical stock and injection packs, a compliant hand wash basin or surgical trough, waste disposal bins (including sharps), a medicine fridge and computer desk/notes area.

- Ventilation to the clean room should be assured from internal systems as windows must be kept closed and there should be at least 15 air changes per hour. Any internal wall mounted air conditioning units must not direct air flow over the head of the patient couch.
- The room must have good illumination and comply with infection control requirements including a washable floor ⁴, no cloth curtains, and be in good condition e.g. no chipped paint.
- The ceiling and walls of the room should be non-particulate in nature (i.e. no dust or debris should be able to fall on to operative field during procedure) ^(3,4)
- Air inlets should not be situated above the patient head during the procedure.
- Nearby facilities for slit lamp biomicroscopy/ indirect ophthalmoscopy and viewing retinal imaging (FFA/OCT) are advantageous.
- Resuscitation facilities, based upon local risk assessment, should be available in all settings where IVT is administered ^(Appendix). As a minimum standard, all healthcare staff undertaking IVT must have evidence of up to date basic cardio-pulmonary resuscitation training.

5 Hand decontamination and masks

- The operator's hands should undergo surgical disinfection and sterile gloves should be worn. Sterile gloves should be removed between each injection.
- It is recommended that masks are worn as the operator's face is quite proximal to the operating field although this is not mandatory ⁵.
- Disinfection of hands can either involve soap and water or alcohol rub. If using alcohol rub between cases then it is recommended that:
 - first undertake a thorough scrub with antiseptic.
 - use inter-procedure alcohol rub but it must be a thorough technique with optimum alcohol surface contact time (60 seconds).
 - if using latex gloves then they must be removed and hands washed post procedure to enable latex particle removal.
 - if the injector is undertaking documentation in medical records or at computer in-between patients then best practice is to use surgical antiseptics rather than alcohol.
 - if the injector has pierced their gloves during the procedure and possibly contaminated their hands they need to wash with antiseptic.

6 Equipment requirements

- Single use topical mydriatic to achieve adequate pupillary dilation.
- (dilatation is usually recommended for adequate visualisation before and/or after the injection is given, unless otherwise contraindicated).
- Single use topical anaesthetic.
- Single use topical povidone iodine 5% solution or chlorhexidine 0.1% aqueous solution.
- Sterile surgical gloves.

- A surgical pack which may typically contain sterile dressing tray, sterile ophthalmic drape (recommended but not mandatory), sterile lid speculum, sterile mm gauge/callipers, sterile cotton buds. Buds can be used to stabilise the eye although some use sterile toothed microforceps. There are also injector devices available which may combine the functions of drape, caliper and speculum.
- Small bore injection needles are preferable e.g. 30 gauge for intravitreal injection of non-colloidal clear solutions and 27 gauge for particulate preparations e.g. triamcinolone. Special needles may be provided specifically for particular products. The injection needle length should be 12 to 15mm ($\frac{1}{2}$ to $\frac{5}{8}$ inch).

7 Pre-injection assessment/checks

- Patients should have a visual acuity measurement (preferably LogMAR) and clinical evaluation for each visit, to identify complications from previous injections and to review the appropriateness of the subsequent treatment recommended.
- As deemed necessary, pupil dilatation should be checked and a biomicroscopic examination may be undertaken prior to injection.
- Particular attention should be paid to the presence of active eyelid and/or ocular surface disease which might increase the risk of endophthalmitis.
- Intraocular pressure should be measured and documented prior, at least, to first injection. This is particularly important in patients known to have glaucoma/ocular hypertension.
- Immediately prior to every injection procedure, the correct patient identity, correct eye and marking, evidence of informed consent and the correct drug to be injected must be confirmed. Use of an ophthalmic specific mini-WHO (World Health Organisation) checklist is encouraged.

8 Pre-injection preparation

- Single use topical anaesthetic is applied to the eye.
- The operator's hands must be clean and surgical hand disinfection is essential.
- Sterile gloves should be worn.
- Pre-injection antiseptic has been shown to be effective in preventing endophthalmitis following IVT. Povidone-iodine 5% solution should be instilled on to the ocular surface and adequate time allowed (3 minutes) prior to injection [6](#).
- For patients allergic to iodine alternatives such as chlorhexidine 0.1% aqueous solution may be used [7](#).
- The routine use of a surgical drape and/or eyelid speculum is no longer considered essential [8](#) but an important principle is that the eyelid margins should always be kept away from the injection site. Disposable devices designed to facilitate intravitreal injection may be used which eliminate the need for a speculum and caliper.

- Supplemental subconjunctival anaesthetic (e.g. 1ml of 1% Lignocaine [without adrenaline]) in the area of planned IVT may be considered if using a 27 gauge or wider bore needle. In a severely inflamed eyes subtenons local anaesthetic may be necessary.

9 Injection administration

- The patient should be instructed to direct gaze away from the site of injection.
- The injection site should be marked using the mm gauge (the entry site of the needle should be 3.0-3.5 mm from the limbus in aphakic/pseudophakic patients, and 3.5-4.0 mm in phakic patients). The horizontal meridia of the globe should be avoided but any quadrant can be used, and may be changed in rotation.
- The needle/syringe pouch should only be opened immediately prior to the injection.
- If the medication is pre-loaded, the protective cap should be carefully removed from the pre-prepared syringe without twisting or turning and eject the air bubble at the top of the syringe. Care should be taken not to expel any medication. Do not draw back the plunger.
- If not pre-loaded, the medication should be prepared aseptically immediately before single usage; withdrawal is according to manufacturer's instructions. Excess medication in the syringe should be expelled through the injection needle. (This ensures that the injection needle hub is fully primed with no air therein).
- The conjunctiva may be displaced using either forceps or a sterile cotton-tipped applicator so that no direct route between vitreous and ocular surface remains before or after the injection.
- Using a bud or forceps to steady the eye (if necessary), the needle is inserted perpendicular through sclera with the tip aimed towards the centre of the globe (to avoid any contact with the posterior lens). For wide bore injections a stepped entry into the pars plana may be recommended in order to avoid leakage.
- Inject appropriate volume (maximum 0.1 ml) of therapeutic agent slowly and carefully. Be careful to avoid contact between needle shaft and lid margin.
- Remove the needle carefully. A sterile cotton-tipped applicator may be used to prevent reflux and to steady the eye. Discard syringe and needle appropriately.
- Immediately after injection, a check of light perception is advisable to ensure that the central retinal artery is perfused.
- If bilateral injections are planned at the same session, each eye must be prepared separately. A different batch of instruments must be used for each eye. Similarly, a separate batch of medication is advised for each eye.
- If intravitreal injections are given alongside other procedures, including cataract surgery, particular care needs to be taken to ensure that the correct medication is given intravitreally. This avoids unnecessary retinal toxicity.

10 Post injection management

- While small volume injections (0.05ml) are unlikely to cause a significant rise in intraocular pressure (IOP), post injection IOP should be measured in patients where there is a clinical concern of high risk (e.g. significant pre-existing visual field or optic disc compromise in glaucoma patients, narrow angles), with injection volumes greater than 0.05ml and in all cases where patients are symptomatic of pain or reduced vision immediately following injection. Clinicians should be aware that there is an increased risk of longer term raised IOP in patients undergoing regular intravitreal injections, and should monitor the IOP according to risk.¹²⁻¹⁶.
- Should high IOP resulting in non-perfusion of the central retinal artery occur, indicated by no perception of light (NPL) in the treated eye, appropriate immediate care is indicated such as an anterior chamber paracentesis or acetazolamide and digital massage. Particular care needs to be taken if the patient is phakic.
- The use of peri-injection antibiotics is no longer recommended. There is no evidence that their use reduces the risk of post-operative endophthalmitis (9,10), but there is evidence that their use can contribute to the emergence of drug-resistant pathogenic bacteria.
- Following IVT, clear printed instructions, including 24/7 emergency contact details, should be provided to the patient prior to discharge.
- Patients should be instructed to immediately report to the eye department symptoms which might indicate serious complications, particularly endophthalmitis, e.g. Increasing pain or discomfort, increased redness of the eye, or additional blurring of vision.
- Patients should be informed that some blurring of vision is common immediately post-injection; this is often described as 'seeing spots floating in the eye'. The floaters usually resolve after a few days to a week.

11 Clinical record/follow-up arrangements

- Medical records, paper or electronic, should document all relevant clinical details about each IVT episode, including batch numbers of drugs injected and the proposed arrangements for follow up.
- The follow up regimen will depend on the patient's condition and the drug injected.
- Where multiple, intravitreal injections are likely to be required, e.g. anti-VEGF injections for nAMD, it is recommended that arrangements for follow up are coordinated by a failsafe administrator to ensure that all patients receive appointments and repeat injections at the appropriate time.

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13. Sustained Elevation of Intraocular Pressure Associated with Intravitreal Administration of Anti-vascular Endothelial Growth Factor: A Systematic Review and Meta-Analysis. [Zhou Y, Zhou M, Xia S, Jing Q, Gao L. *Sci Rep*. 2016;6:39301.](#)
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13 Appendix: Resuscitation facilities for clinical settings providing intravitreal injections

1. Intravitreal therapy (IVT) is given in a variety of settings. The precise resuscitation facilities available will depend on a local risk assessment that considers:
 - a. Risk of patients having a clinical emergency.
 - b. Access to emergency help (e.g. hospital resuscitation team, ambulance service)
 - c. Training and capability of staff.
 - d. The equipment available.
 - e. Expectation of patients using the service.
 - f. The Resuscitation Council UK lists the following core standards ¹ for all clinical settings:

1. The deteriorating patient is recognised early and there is an effective system to summon help in order to prevent cardiorespiratory arrest.
2. Cardiorespiratory arrest is recognised early and cardiopulmonary resuscitation (CPR) is started immediately.
3. Emergency assistance is summoned immediately, as soon as cardiorespiratory arrest is recognised, if help has not been summoned already.
4. Defibrillation, if appropriate, is attempted within 3 minutes of identifying cardiorespiratory arrest.
5. Appropriate post-cardiorespiratory-arrest care is received by those who are resuscitated successfully. This includes safe transfer.
6. Implementation of standards is measured continually and processes are in place to deal with any problems identified.
7. Staff receive at least annual training and updates in CPR, based on their expected roles.
8. Staff have an understanding of decisions relating to CPR.
9. Appropriate equipment is available for resuscitation.

- g. Resuscitation may be required in a number of situations associated with the administration of IVT:
 - Collapse during or following an intravitreal injection, e.g. vasovagal syncope
 - Anaphylaxis to administered medication or as a result of contact with another provoking agent, e.g. latex gloves
 - Collapse unrelated to the procedure per se, but related to underlying systemic co-morbidity
 - h. All settings need to be able to call for emergency help – whether staff call a resuscitation team or the ambulance service needs to be determined locally.
Access for emergency help needs to be considered (space, access for ambulances,

patient trolleys). All staff must know how to summon help and be aware of the telephone number.

2. Training of staff:

- a. All healthcare staff must undergo resuscitation training at induction and at regular intervals thereafter to maintain knowledge and skills.
- b. Training must be to a level appropriate for the individual's expected clinical responsibilities.
- c. According to Resuscitation Council (UK) guidelines [2](#), training must be in place to ensure that clinical staff can undertake cardiopulmonary resuscitation. Training and facilities must ensure that, when cardiorespiratory arrest occurs, as a minimum all clinical staff can:
 - i. recognise cardiorespiratory arrest;
 - ii. summon help;
 - iii. start CPR;
 - iv. attempt defibrillation, if appropriate, within 3 minutes of collapse using an automated external defibrillator or manual defibrillator.
- d. Clinical staff should have at least annual updates.
- e. Training and updates that include an assessment are recommended for clinical staff.
- f. The expectation is that non-clinical staff have the resuscitation skills that would be expected from a lay person. If a lay person calls 999 in an emergency, they receive instructions from an ambulance service dispatcher whilst awaiting trained help to arrive. These instructions include starting chest compressions. Telephone guidance does not happen in hospitals unless staff dial 999, hence the expectation that all staff in an acute setting should have some basic knowledge of resuscitation.
- g. As a minimum, non-clinical staff should be trained to:
 - i. recognise cardiorespiratory arrest;
 - ii. summon help;
 - iii. start CPR using chest compressions.
- h. For all staff, a variety of methods to acquire, maintain and assess resuscitation skills and knowledge can be used for annual updates (e.g. life support courses,

simulation training, in-house training, mock-drills, ‘rolling refreshers’, e-learning, video based training/self-instruction). The appropriate methods must be determined locally. For example, training materials such as Lifesaver (www.lifesaver.org.uk), developed by the Resuscitation Council (UK), or very brief videos aimed at lay persons may be appropriate for non-clinical staff. ‘Hands-on’ simulation training and assessment is recommended for clinical staff.

- i. A system must be in place for identifying resuscitation equipment for which staff require special training, such as defibrillators and emergency suction equipment.
- j. All new members of staff must have resuscitation training as part of their induction programme. Even those who have current training require resuscitation training on induction to ensure that they are familiar with local policies and equipment.
- k. Organisations must recognise and make provision for staff to have enough time to train in resuscitation skills as part of their employment.
- l. All training must be recorded (e.g. in the organisation’s training database).

3. Suggested Minimum equipment requirement

Table 1 Airway and Breathing

Airway and Breathing		
Item	Suggested Availability	Comments
Protective equipment - gloves, aprons, eye protection	Immediate	
Pocket mask with oxygen port	Immediate	
Portable suction e.g. Yankauer	Immediate	Airway suction equipment. NPSA Signal. Reference number 1309. February 2011 According to local policy
Oropharyngeal airways sizes 3,4	Immediate	According to local policy based on risks, availability of help, and training of staff
Self-inflating bag with reservoir (adult)		

Clear face masks for self-inflating bag (size,4)		
Oxygen cylinder (CD size)		
Oxygen masks with reservoir		
Oxygen tubing		

Table 2 Circulation

Circulation		
Item	Suggested Availability	Comments
Automated external defibrillator (AED)	Immediate	According to local policy based on risks, availability of help, and training of staff
Adhesive defibrillator pads		Type of AED and location determined by a local risk assessment.
Razor		
Scissors		Spare set of pads also recommended.

Anaphylaxis kit according to organisations existing kit and policy

Notes

- a. The standard AED sign should be used in order to reduce delay in a defibrillator in an emergency www.resus.org.uk/defibrillators/standard-sign-for-aeds/
- b. All staff must have a means of calling for immediate help (e.g. internal or external landline telephone, mobile telephone with reliable signal, alarm bell).
- c. Clinical staff should be trained to use the available equipment according to their expected roles.
- d. Staff must be familiar with the location of all resuscitation equipment within their working area.
- e. Resuscitation equipment should be for single-patient use and latex-free whenever this is feasible (e.g. bag-mask devices, oxygen masks and tubing).
- f. Responsibility for checking resuscitation equipment rests with the staff at the facility where the equipment is held. This process should be designated to named individuals, with reliable arrangements for cover in case of absence. The

frequency of checks will depend upon local circumstances but should be at least weekly. Checking should be the subject of local audit.

- g. The manufacturer's instructions must be followed regarding the use, storage, servicing and expiry of equipment.
- h. A planned replacement programme should be in place for disposable equipment items that have been used or that reach their expiry date.
- i. Personal protective equipment (e.g. gloves, aprons, eye protection) must be available according to local policy.
- j. The general public expects AEDs to be available in every healthcare setting and premises where intravitreal therapy is carried out are no exception. The Department of Health Cardiovascular Disease (CVD) Outcomes Strategy promotes AED site mapping/registration, first responder programmes and ways of increasing the number of people trained in cardiopulmonary resuscitation (CPR) and use of AEDs. The Resuscitation Council (UK) recommends that all AEDs located in the community are registered with the local ambulance service, to facilitate prompt access to the nearest AED whenever one is needed.
- k. The provision of an AED enables all staff to attempt defibrillation safely after relatively little training and should be immediately available within the first few minutes of a cardiorespiratory arrest occurring. These defibrillators should have internal data storage facilities and standardised consumables (e.g. adhesive electrode pads, connecting cables). Scissors may be required to remove items of clothing from the patient.
- l. Oxygen cylinders should be of such a size to be portable easily, but must also allow for an adequate flow rate (e.g. 15 l.min^{-1}) until the arrival of an ambulance (e.g. a full 'CD' size integral valve cylinder contains 460 l of oxygen and can deliver a flow rate of 15 l.min^{-1} for approximately 30 min). Local policy should dictate whether a second cylinder is required in case the first one is at risk of running out. Published guidance from the British Thoracic Society on the use of high-flow oxygen has caused some concern and confusion regarding its safety. Current guidelines recommend that in any cardiorespiratory arrest the initial administration of high-flow oxygen (15 l.min^{-1}) is the correct course of action. If the patient regains a cardiac output and oxygen saturation levels can be measured accurately using a pulse oximeter (e.g. provided by the ambulance crew), then the concentration of inspired oxygen can be adjusted accordingly.
- m. The precise availability of equipment should be determined locally. The suggested minimum equipment requirements include recommendations on when equipment should be available:
 - i. "Immediate"- available for use within the first minutes of cardiorespiratory arrest (i.e. at the start of resuscitation)

- ii. “Accessible” - available for prompt use when need is determined by those attempting resuscitation

Further Reading

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