

The Royal College of Ophthalmologists



Commissioning Contemporary AMD Services: A guide for commissioners and clinicians

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Commissioning Contemporary AMD Services: A guide for commissioners and clinicians

Introduction

Very recently large controlled clinical trials have unequivocally demonstrated clinical efficacy for vascular endothelial growth factor therapy in preventing progressive visual loss in exudative age-related macular degeneration, a common disorder causing blindness in older people.

The Royal College of Ophthalmologists recognised the implications that these developments will have on practice in the NHS and have brought together a group with expertise in retinal disease management, health commissioning and the voluntary sector with the purpose of developing a comprehensive AMD management plan. This document which has been authored by the group describes:

- the burden of disease due to exudative AMD
- the status of the ongoing health technology assessment of VEGF inhibitors
- existing levels of service provision and referral pathways
- the significant increase in workload
- the service configuration needed to deliver VEGF inhibition therapies

It is expected that service provisions will include patients with CNV secondary to diseases other than AMD.

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Background

Age-related macular degeneration (AMD) causes severe visual loss and is the commonest cause of blindness in persons > 50years old in the western world.¹⁻⁴ Two main forms of AMD occur: dry and wet. The dry form accounts for 90%, whilst the wet form occurs in 10% of all AMD. The severe visual loss in 90% of cases is due to the wet form of AMD which is characterized by choroidal neovascularisation (CNV). CNV lesions are classified according to their location relative to the fovea, and pattern of fluorescein angiographic leakage. The majority of CNVs occur subfoveally.⁵ There is evidence that angiogenic factors, especially vascular endothelial growth factor (VEGF) and fibroblastic growth factor (FGF) play a significant role in the development and maintenance of CNV. High levels of VEGF have been demonstrated in CNV surgically excised from humans or animal experimental CNV.^{6,7}

Burden of disease due to wet AMD

It was previously estimated by research commissioned by The Macular Disease Society (MDS) that 21,000 new cases of wet AMD occurred in the UK each year.⁸ Current estimates by the Royal National Institute for the Blind (RNIB) and the National Institute for Health and Clinical Excellence (NICE) indicate there may be 26,000 patients eligible for the new anti-VEGF treatments in the UK each year (compared to 7,000 currently eligible for photodynamic therapy [PDT]).⁹

It is further estimated that 8-12% of patients with wet AMD in one eye will develop wet AMD in the second eye every year (MPSG, 1997).¹⁰

Existing service provision and referral pathways

The management of an individual patient depends on the type of wet AMD present, and its location in relation to the fovea: extrafoveal or subfoveal/juxtafoveal. Until recently, the management of wet AMD has been limited to laser photocoagulation for extrafoveal, and photodynamic therapy (PDT) for subfoveal lesions where applicable. In England and Wales the current model of care for the treatment of age-related macular degeneration (AMD) is based on the NICE Guidance (of 2003)¹¹ and the guidance for commissioners published simultaneously by The Royal College of Ophthalmologists (www.rcophth.ac.uk). With the introduction of anti-VEGF treatments in the management of wet AMD, the latter document is now obsolete and superseded by this current document.

PDT had been recommended for the treatment of wet AMD of the classic no occult (NICE 1.1), and predominantly classic (NICE 1.2) CNVs with vision of 6/60 or better. NICE made no recommendations on the treatment of occult CNV as verteporfin was not licensed for such treatment at the time of the Health Technology Assessment.¹¹ However, some Primary Care Trusts (PCTs) have commissioned the treatment with PDT of small occult which show progression.

The Department of Health Guidance (2003) relating to the NICE Guidance, i.e. the commissioning document accompanying the NICE Guidance, allowed for the treatment of CNV lesions secondary to non-AMD causes.

The current 'hub and spoke' model for the PDT service in the NHS was created so that each PDT treating centre would serve a population of approximately 1 million, with patients attending the hub unit every 3 months for PDT treatment. There are currently 56 PDT treatment centres distributed over the UK. Patients travel significant distances to receive treatment.

Assuming that PDT treatment with verteporfin is used for 100% classic and predominantly classic subfoveal lesions (NICE recommendations) this only accounts for approximately 30% of patients with wet AMD.¹² Some areas currently provide treatment for occult no classic CNVs as well, thus increasing their treatment ratio to 45% of all CNVs. The remaining lesions, minimal classic and occult, account for the 55-70% of all patients with wet AMD who are currently not treated with PDT. Since all lesions can now be treated with the new licensed anti-VEGF drugs a considerable increase in patient numbers is inevitable.

Current referral pathways recommend that for effective outcomes from PDT patients with CNV need to be seen and treated within 2 weeks. However, this view is not universally implemented. There are, therefore, significant variations in the interval between initial detection, referral and treatment depending on local circumstances.

Status of NICE HTA assessment

NICE has commenced the HTA process of evaluating new treatments for AMD. All stakeholders, including the RCOphth have made their initial submissions to NICE. Decisions are not expected till October 2007, although efforts are being made to expedite the process which may result in guidance being issued in September. Pegaptanib (Macugen) and ranibizumab (Lucentis) will be evaluated, with PDT and best supportive care as comparators. NICE has confirmed that bevacizumab (Avastin) will not be included in the appraisal as it is not licensed for treatment of AMD. NICE may, however, include it as a comparator.

The Health Service Circular (HSC) 1999/176 advises Primary Care Trusts (PCTs) to consider available evidence in order to provide funding for new treatments. This advice applies to treatments for AMD. Clinicians should, therefore, seek funding for anti-VEGF treatment from their PCTs. The aim should be the delivery of a comprehensive AMD service. The absence of NICE Guidance should not be accepted as a reason for non-funding of AMD treatments.

Anticipated workload

Given the effectiveness of anti-VEGF therapies in all types CNV lesion types¹³⁻¹⁵, the number of patients eligible for treatment will increase from 30-45% to 100% of all patients with wet AMD.

Patients receiving ranibizumab and pegaptanib will require 4 weekly and 6 weekly visits respectively. It will not be feasible to ask these patients to travel long distances for repeat treatments at these intervals. It is likely that most patients in the future will be treated with anti-VEGFs. However, a combination of PDT and anti-VEGFs may offer the possibility of less treatment revisits with good outcomes.¹⁶ If this is the case then the central unit offering PDT will need to remain.

The estimation that the incidence of wet AMD is approximately 26,000 in the UK (total population of 60 million) implies that there will be approximately 450 new cases presenting with wet AMD (of all lesion types) per million of the population each year. If it is assumed that there are approximately 135 patients/million population (with predominantly classic CNV - 30% of all wet AMD) currently treated with PDT, then there will be another 315 patients/million of the population who would require assessment and treatment with the new anti-VEGFs.

To treat all AMD CNVs will lead to a 2.25-3.3x increase in numbers of patients currently treated with PDT (depending on the particular centre and local commissioning arrangements). If the frequency of visits is 4-6 weeks intervals (cf. present 3 months) then this equates to a 2-3x the number of present patient visits.

If it is presumed that all new patients with wet AMD will be treated over the next year with PDT (135/million) and/or anti-VEGFs (315/million). The required capacity for a population of 1 million will, therefore, be

- i) PDT requiring 3.5 visits each year (135×3.5) = 472.5 appointments
- ii) Anti-VEGFs requiring 10 visits each year (315×10) = 3150 appointments.

As such a total of approximately 3,622 appointments are required in the first (transition) year to look after all patients with wet AMD per million of population. This is in addition to patients who are in year 2 of treatment with PDT ($3 \times 135 = 405$). This equates to approximately a 6-9 times increase in the present AMD workload. This increase will need to be balanced against the difference in time, if any, that it takes to undertake each PDT.

However, if all new patients with any lesion type of CNV are offered anti-VEGF therapy in year 1, there will be 4,500 appointments required in that first year. This is in addition to 405 appointments for patients who are in year 2 of treatment with PDT.

For the second year, it is anticipated that 450 or more new patients/million population will present with wet AMD. (This translates into new 4,500 appointments). These will be managed alongside patients entering their second year of treatment from the previous year.

This large increased workload has significant implications on the demand for specialist investigations including retinal imaging, and vision assessment. Irrespective of the cost of the new anti-VEGF treatments, it is anticipated that the workload for AMD will increase considerably with the introduction of intravitreal therapy. This will impinge on the ability of ophthalmic departments to deliver ophthalmic services overall. Clinicians are, therefore, urged to work with managers and commissioners to make a strong case for increasing the complement of doctors, nurses, optometrists and technicians in order to cope with this workload.

There is expected to be a significant difference between the incidence of wet AMD as detected in population-based cohort studies and the number of people actually presenting, being eligible for and accepting treatment.

It is expected that over time awareness of AMD and associated treatments will improve. This should result in more people presenting earlier and at a point where the condition is treatable. Evidence from trials suggests that the earlier a patient presents for treatment the more successful the outcome.

AMD Service Specifications

- Rapid access. It is recommended that the time from referral from the primary source to initial evaluation by the retinal specialist at the AMD centre should be not more than one week. Similarly, the time from evaluation by the retinal specialist to treatment should not normally be more than one week.

- Geographical equity of access to all regions within the UK. There needs to be immediate rapid access to retinal specialists with expertise in the management of wet AMD for all patients, irrespective of geographic location. Referral pathways of wet AMD to treating specialists may vary but must be appropriate for different regions, as there may be several variations in geographic population distribution, logistics, expertise, and physician workload. The guiding principle is that no particular patient or region should be disadvantaged.

- Minimum clinical services required for effective management
 - Best corrected visual acuity assessments by optometrist or certified VA examiners
 - Stereoscopic fundus fluorescein angiography (FFA) by trained technical staff
 - Optical coherence tomography (OCT) by trained technical staff
 - Treatment initiated within a week of assessment
 - Appropriate facilities for IVT injection
 - Appropriate capacity for follow up, monitoring and retreatment

Distribution of AMD treatment centres

The determination of AMD service providers will be decided by commissioners and PCTs and not by The Royal College of Ophthalmologists or any of its committees. However, it is the responsibility of the College to outline the best option for such service provision.

Given the above assumptions the ideal model for provision of services will be to build on the network model currently in existence for PDT, but with most of the anti-VEGF injections devolved to the referring units. Variations in population eg rural compared to urban will determine the actual demand for treatment. Local variations, therefore, will be important in determining the distribution of treatment centers.

Whereas the delivery of PDT was based on a 'hub and spoke' model, it is recommended that a 'Regional Network' model should be used for the delivery of anti-VEGF treatments. This would allow a number of local hospitals to work together and share resources and expertise.

Each Regional Network will have an administration centre to support all units – the centre and all other (peripheral) units served. This option is based on the assumption that there is local retinal expertise with particular reference to AMD management, and that the minimum equipment requirements are met.

Dedicated AMD clinics must be available in the local hospital, with facilities similar to those in the network centre. Clinical sessions need to be made available for medical retinal experts at the regional centre to read images from other (feeding) centers involved in each of the networks, and provide advice on such images/patients to specialists in these units. These sessions will essentially be 'Virtual Clinics'. There has to be an appropriate imaging and electronic transmission infrastructure for such a system to work adequately. Standards of investigation, diagnosis and decision pathways in each network will be audited regularly.

It is envisaged that the centers included in each regional network would closely liaise closely regarding data collection. Provided there is adequate NHS data transference capability the decision to treat new cases will be made locally. Patients requiring combination treatment with PDT would, however, still need to attend the central unit.

In order to ensure continuity of service, assuring that patients with wet AMD do not lose vision because of treatment delays, it is expected that the ophthalmologists running the AMD Service in any one provider unit would not normally be away simultaneously. However, when this is impossible patients with wet AMD may have to travel further than usual (to other centres within the Network) for their assessment and treatment. Commissioners should ensure that reliable alternatives are available to cover such occasions.

The alternative model requires all patients with wet AMD must attend a regional Macular Specialist Centre (previously PDT Centres) for confirmation of diagnosis and initial treatment. Patients from other hospitals (spoke units) may be re-referred back to the local hospital for subsequent follow-up and treatment. This option is also based on the assumption that there is local retinal expertise with particular reference to AMD management, and that the minimum equipment requirements are met. Dedicated AMD clinics must be available in the local hospital, with facilities similar to those in the network centre or hub. The repeated injections may be undertaken at the local hospital as it will significantly reduce traveling time for patients who need re-evaluation and treatment every 4-6 weeks for a minimum of 2 years. Where necessary, patients could be re-evaluated at the regional Macular Centre. However, this model has significant administrative bottlenecks and will be time consuming, although it will offer grading at diagnosis and networking.

It is recommended that data on cardiovascular and other adverse events associated with anti-VEGF treatments of AMD are collected and evaluated by The Royal College of Ophthalmologists. Funding will, however, be required from without the College.

There are a few web based angiographic reading centres in the UK currently. Voluntary use of such retinal angiographic and OCT reading centres should be encouraged.

AMD Referral Pathways

As stated above, there needs to be immediate rapid access to retinal specialists with expertise in the management of wet AMD for all patients, irrespective of geographic location. Patients should be seen by a specialist with medical retinal expertise within one week of diagnosis, and, there should be no more than one week between evaluation and treatment.

All patients suspected to have wet AMD by the optometrist, general practitioner, or other health workers should be referred directly to the nearest AMD Centre, Eye Casualty, or Eye Clinic. Optometrists may be used for 'screening' or first examination of patients suspected of having wet AMD. Referrals from the optometrist should be sent directly to an ophthalmology department, and should not pass through the general practitioner as such a route introduces unnecessary delays. Self referral or presentation to the Eye Casualty/Clinic or AMD Centre of wet AMD should be encouraged, especially in patients who have second eye involvement. Optometrists with specialist interest ('Super Optometrist') are not recommended as such pathways will introduce unnecessary delays, and misdiagnoses.

It is recommended that the time from referral from the primary source to initial evaluation by the retinal specialist at the AMD centre should not normally be more than one week. Similarly, the time from evaluation by the retinal specialist to treatment should not normally be more than one week. This means that the time from referral to treatment should not normally exceed 2 weeks.

Patient movement through the clinic

It is assumed that all new patients with CNV secondary to AMD will be evaluated in the AMD Centre, with an extended assessment of vision, retinal imaging (FFA and OCT), ophthalmological examination, and then proceed to treatment immediately at the same visit. At subsequent follow-up visits also, treatment will follow vision assessment, retinal imaging and ophthalmological assessment.

An integrated clinic for AMD patients is ideal. The pathway in such an integrated clinic will include visual assessments, OCT imaging and medical assessments at every visit, and FFA every 3 months, followed by treatments - intravitreal injections (and/or PDT 3 monthly) as appropriate.

Movement of patients through the AMD clinic depends on whether a 'ONE STOP' or 'TWO STOP' model is adopted. In a 'One Stop' Model all examinations, investigations and treatments are undertaken on the same day, whilst in a 'Two Stop' Model examinations and investigations take place on one day, followed by treatments during a separate visit. A 'one stop' model is preferable as it minimises patient visits to the clinic, especially as some of them may have to travel significant distances. This has to be balanced against the moderate increase in the total time spent by each patient at each visit.

Resource requirements in contemporary AMD service delivery in the UK

Personnel

The contemporary management of AMD requires teamwork with the retinal specialist leading each team. The most important aspect of AMD management is the prompt and correct diagnosis of the condition. Furthermore, the management of particular patients may change from time to time, including switching from one treatment to another, or multi-modality treatment. The focus of the AMD management process must, therefore, be the retinal specialist. To provide the AMD service, greater personnel resources are required both at the centre and the network units. A maximum of ten to twelve patients should be seen per clinic, i.e. not more than 20-24 patients for a 2-session day. This means that the new service cannot be delivered with existing staff levels.

Based on the national incidence of 26,000 new cases of wet AMD in the UK, it is expected that there will be 130 new cases of wet AMD each year, in a population of 300,000. If each of them requires 10 visits each year for 2 years, this equates to 1,300 visits per annum. For a 44 week working year, this implies a cohort of 30 patients per week at the end of year 1, and 60 at the end of year 2. As such 3 clinics of 10 patients per week will be required to serve a population of 300,000 in year 1, and 6 per week in year 2. (This is equivalent to 10 clinics each week for a population of 1 million in year 1, and 20 per week in year 2).

The following minimum service team would be required (for each clinical session) for a population of 300,000:

- 2 x doctors (one consultant with retinal expertise and one non-consultant)
- 2 x trained nurses
- 1 x optometrist or certified vision examiner
- 1 x ophthalmic photographer/technician
- 1 x healthcare assistant
- 1 x administrative coordinator
- 1 x data collection and management support staff
- 1x eye clinic liaison officer (ECLO)

Lead Clinician. Quality of care is of great importance. The team should be led by a consultant ophthalmologist with retinal sub-specialty expertise who runs dedicated AMD clinics, and has experience in the management of AMD. The decision to treat or not to treat must be made or reviewed, by the medical retinal expert. It is essential that the injections must be undertaken by skilled ophthalmologists with a high level of retinal expertise. The injections are potentially blinding and medical intervention may be needed.

Injections. It is recommended that the injections are performed by skilled ophthalmologists who would be familiar with and capable of treating the rare but serious complications that can arise from such injections. This in particular would include the ability to manage an anterior chamber paracentesis (the release of aqueous humour from the anterior chamber) which may need to be done in an emergency if the intraocular pressure becomes elevated after the injection and occludes the central retinal artery. In practice this will mean that these injections will need to be performed by experienced ophthalmologists.

Coordinator and administrative staff. Administrative staff are responsible for scheduling new and follow up appointments for patients attending the AMD clinics. As the number of patients will increase over current levels, and required appointments will be more frequent than those with PDT, over a period of 2 years (or more), the amount of coordination required will be significant. Collation of staff diaries is just as important. The coordinator will oversee the patient appointment system, the coordination of theatre or clean procedures room used for injections, as well as secretarial communications. An efficient service also requires good liaison with the hospital pharmacy over the supply of drugs. Data capture and management personnel are important for internal and external audits, as well as resource management.

Ophthalmic Nurses. Nurses will be required to provide, in addition to their normal roles in clinics, cannulation, injections for fluorescein and indocyanine green angiography, counseling, patient preparation for treatments including intravitreal injections, and infusions of verteporfin (Visudyne) when required. They will oversee patient recovery. Data capture and quality of life questionnaire completion may also be required. These duties will be undertaken with the assistance of healthcare assistants. The nursing staff will liaise with the hospital pharmacy over drugs required for the service.

Photographers/Ophthalmic Imaging Technicians. The ophthalmic photographer or trained ophthalmic imaging technician will be responsible for the acquisition, storage, and management of fundus photographs and angiography (3 monthly), as well as OCTs (monthly).

Optometrists/Certified Vision Assessors. Optometrists will be required for ETDRS (LogMAR) refraction at baseline, and 3-6 monthly intervals. Contrast sensitivity will be determined at baseline, and six monthly thereafter. Where training is available they may also check intraocular pressures.

ECLO. The eye clinic liaison officer will provide the vital link between AMD treatment, and rehabilitation (LVA) and support (social) services and allow better intergration of care. Patients who do not respond to treatment or present too late for treatment to be effective need direction to appropriate low vision services. The ECLO, where available, should ensure smooth transition from healthcare to social care. In hospitals without an ECLO, effective need to be in place to ensure that patients are directed to available support at a time of their choice. Specialists need to ensure that they offer patients the option of registration as visually impaired or severely visually impaired as soon as patients reach the thresholds for registration. Whilst registration remains a crucial gateway to support (low vision rehabilitation, provision vision devices, counseling, benefits etc), it is important to encourage eye health professionals to raise awareness of available support services even before patients reach the level of registration in order to maximize the chances of patients adjusting to their sight loss with minimal trauma.

Role of ISTCs. It is important to stipulate that any Independent Sector Treatment Centre (ISTC) bidding for the delivery of AMD services would have to provide a full service, including all of the elements outlined above. As the management of AMD has to be holistic rather than mechanistic, the best cost-effective and holistic service model has to be adopted. Unless ISTCs can demonstrate that they are able to deliver a full service which ensures quality treatment, avoids over-treatment, able to manage severe adverse events and ensure smooth patient movement from health to social care, where appropriate, their participation in the delivery of AMD services would be inappropriate. Furthermore, quality control, audit and teaching purposes membership of a regional network is necessary. Any ISTC wishing to deliver AMD services will have to meet all these criteria.

Capital Investment

Injection Room. It is essential to give intravitreal injections in a clean room or in theatre. However, it would be more cost effective and convenient to use a dedicated clean room in the outpatients department. Special clean room facilities for intravitreal injections need to be created in units where such facilities do not exist at present. The clean room should be separate from the consulting room.

The specifications of a clean room are detailed in the RCOphth IVT Procedure Guidelines (www.rcophth.ac.uk). The room needs to be adequately equipped, and approved by the hospital Microbiology, and Health and Safety teams. The details of such specifications should be discussed with the local health and safety representative. Any room where minor operations take place is suitable as long as infected cases are excluded.

Surgical Equipment and Consumables

IVT surgical injection packs will be required for each injection as per the IVT Guidelines (minimum: eyelid speculum, calliper, forceps) and surgical drape.

Gowning is not mandatory. However, it is recommended that masks should be worn when IVTs are administered. This is because of the close proximity of the surgeons face to the operation field, and because it allows the surgeon to continue verbal communications with the patient while maintaining a sterile field. Sterile surgical gloves must be worn after thorough hand washing.

Retinal Imaging

Retinal imaging services will need to be enhanced at all units providing AMD services. The minimum equipment required to provide a contemporary AMD service are a digital fluorescein angiography (FFA) and optical coherent tomography (OCT): OCT 3 or a later version. It should be possible to transmit images from the peripheral units to each network centre.

It is expected that all patients with wet AMD will require refraction LogMAR visual acuities, FFA and OCT at the commencement of treatment. Subsequent follow up will require monthly OCTs, and FFA at 3 months and thereafter when indicated.

Education and Training

Staff in all hospitals participating in the network will require additional specialised training. In particular this would include OCT scan interpretation, and injection technique. In addition, team members who have not undertaken these treatments will need to be trained in the techniques and logistics of running such services.

Costs

It is expected that the new treatments for AMD will cost significantly more than the current services. Such costs will include drug acquisition and administration, repeat vision assessments and fundus imaging, initially and at follow-up visits (monitoring). Additional costs may be associated with the management of injection related adverse events, and associated visual loss although these are expected to be few if the treatments are undertaken by experts.

In addition, non-drug related contemporary service development, staffing and training represent significant major costs. Significant costs are, therefore, involved irrespective of which particular drug is recommended. It is expected ALL costs will be covered where services are commissioned.

Estimated costs were based on those listed in a paper from the Cheshire and Merseyside Specialised Services Commissioning Team (Banks, 2006, 2007).^{17,18} Cost models were produced based upon information from Royal Liverpool and Broadgreen University Hospitals NHS Trust and Moorfields Eye Hospital. The prices include the costs of outpatient assessments, OCT, FFA and the intravitreal injections (including VAT). This allows the determination of costs of visits with, and without treatment. (Appendix B). Overheads and capital charges are often charged by NHS trusts in addition to pay, non-pay and drug costs, typically at a rate of 20%.

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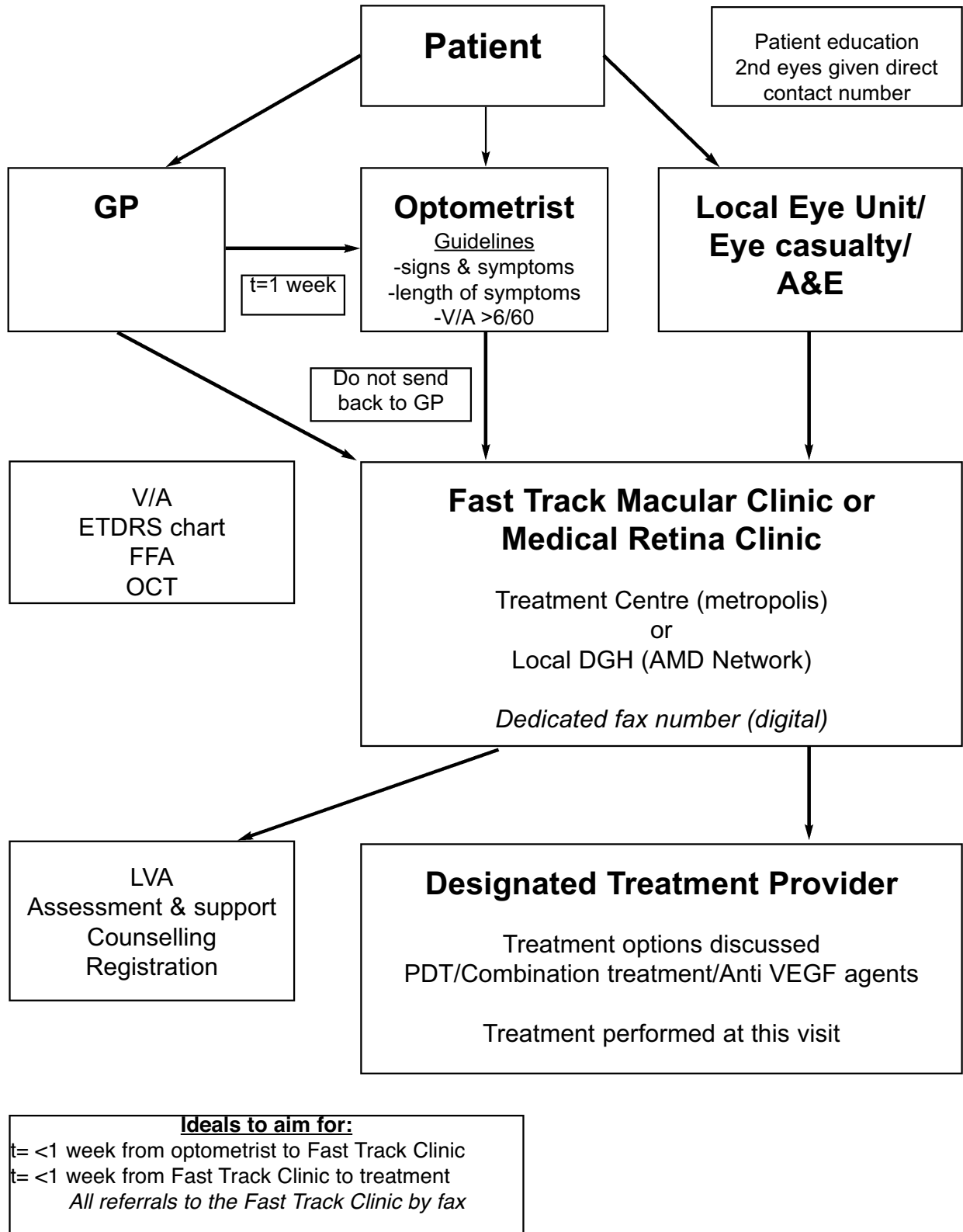
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Appendix A: AMD Referral Pathway Diagram



Appendix B: Costs
All costs are in £ sterling

	LUCENTIS		MACUGEN	
	Full assessment & treatment	Treatment (injection only)	Full assessment & treatment	Treatment (injection only)
Staffing	230.00	172.00	230.00	172.00
Band 7 management	44.00	44.00	44.00	44.00
Other drugs	8.00	8.00	8.00	8.00
Non pay costs	92.00	92.00	92.00	92.00
FFA	35.00		35.00	
OCT	14.00	14.00	14.00	14.00
Intraocular pressure	2.00	2.00	2.00	2.00
Incidentals	111.00	111.00	111.00	111.00
PTS	28.00	28.00	28.00	28.00
Total for visit	564.00	471.00	564.00	471.00
Drug (£761.20+VAT)	894.41	894.41	604.00	604.00
Sub-total	1,458.41	1,365.41	1,168.00	1,075.00
Overheads @ 20%	291.68	273.08	233.60	215.00
Cost per patient	1,750.09	1,638.49	1,401.60	1,290.00

Access rates/costs**All costs in £ sterling- based on a population of 2.4 million**

Year 1 only							
Treatment regime	Full cost (2 years)	Year 1	Year 2	100%	80%	60%	35%
Lucentis (8 Yr 1+ 6 Yr 2)*	24,501,000	14,001,000	10,501,000	24,809,304	19,853,044	14,882,782	8,680,456
Lucentis (Monthly)	42,002,000	21,001,000	21,001,000	37,213,956	29,779,565	22,324,174	13,020,684
Macugen (8 Yr 1 + 6 Yr 2)*	19,622,000	11,213,00	8,410,000	19,869,082	15,899,750	11,919,206	6,951,936
Year 2							
Lucentis (8 Yr 1+ 6 Yr 2)*				43,416,282	34,742,826	26,044,869	15,190,799
Lucentis (Monthly)				74,427,913	59,559,131	44,648,347	26,041,369
Macugen (8 Yr 1 + 6 Yr 2)*				34,770,893	27,824,563	20,858,611	12,165,888

*** Extra assessment visits or adverse events management not included**