

THE SHEFFIELD AREA PRESCRIBING COMMITTEE

Shared Care Protocol For Treatment of Male Erectile Disorder

Clinicians are reminded that the prescriber is responsible for monitoring the patient on the medication being prescribed

Devised by:

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ENDORSED BY THE SHEFFIELD AREA PRESCRIBING GROUP

Date Approved: November 2007

Review Date: July 2010

Dear Dr

Re: (Patient's Name
Date of Birth
Address)

Your patient has been established on treatment with medication.

This treatment can be prescribed by GPs under the Traffic Light System under the "shared care" arrangements.

I enclose a copy of the shared protocol/This protocol can be obtained from www.porterbrookclinic.org.uk (delete as appropriate).

This shared care protocol has been approved by the Sheffield Area Prescribing Committee and the Sheffield LMC.

Please will you undertake to prescribe for your patient.

IMPORTANT REMINDER

The prescribing doctor is responsible for monitoring the patient on the medication being prescribed

I will assume your willingness to help unless you inform me otherwise

Yours sincerely

Background information

Sexual Function

Erectile function is dependent on the confluence of vascular, neurological, endocrine/metabolic, medication/drugs, psychological and psychiatric, emotional and socio-cultural factors. The prevalence of sexual dysfunction is often established from community studies. It is generally considered that erectile dysfunction (formerly known as impotence) has a prevalence of between 7% - 12% with a positive age correlation. Surveys have attempted to establish aetiological factors and it is generally accepted that hospital outpatient surveys are biased dependent upon the department that a patient is referred to and assessed within. Whilst many have an identifiable organic aetiology — and ED may be the sentinel marker of underlying disease, including factors related to the metabolic syndrome (including diabetes mellitus), there will often be psychological factors (particularly in the younger age group and with secondary disorder). As with many medical conditions, the psychological reaction to physical impairment may lead to a detriment in overall function.

Aetiology of Male Erectile Disorder (MED)

Primary erectile disorder is rare and may occur in states of hypogonadism, or deep intrapersonal conflict.

Secondary erectile disorder is much more common. Patients with disease states such as diabetes mellitus show a prevalence rate of around 60% with the disorder affecting both vascular and neurological systems. Disease states like hypertension and atherosclerosis may gradually impair vascular function to the pelvis. Neurological disorders are less common but include spinal cord trauma (both lower motor neurone and upper motor neurone lesions) and multiple sclerosis.

The one year and lifetime prevalence for major depressive disorder is 8% and 13% for males, and 13% and 21% respectively for females. Nearly 90% of depressed patients will have a degree of inhibited sexual desire and difficulties with arousal (obtaining an erection in men).

Additionally, medications that are prescribed for many of the above disorders are in themselves likely to interfere with the mechanisms of sexual arousal. Drugs that commonly interfere are anti-hypertensive agents (including diuretics), anti convulsants

and most psychotropic drugs. In particular the newer group of anti-depressants, the selective serotonin re-uptake inhibitors have a greater tendency to influence arousal (up to 75% impairment). Other drugs that can interfere with arousal are anti-histamines, anti-androgens, cimetidine and some de-congestants.

The Clinical History, Examination and Investigation of MED

In distinguishing between organic, pharmacological and psychological sexual dysfunction, the sexual history is crucial. Factors suggestive of psychogenic origin are the ongoing presence of erections on awakening or during the night as well as during the day in spontaneous circumstances. A gradual onset is more likely to be suggestive of organic impairment. Problems of desire typically suggest either psychiatric disorder or endocrinological problems. In addition to a comprehensive psychosexual history, a medical and psychiatric screening should occur. Physical examination is helpful in reassuring patients but less than 5% of examinations will reveal underlying evidence of disease states. Laboratory studies involves estimation of blood glucose, testosterone and lipids. Further parameters are necessary if the testosterone is low (gonadotrophins, albumin and SHBG). Prolactin measurement is indicated with desire symptoms. More definite diagnostic investigations can occur in the hospital out-patient setting including response to intra cavernous injections. Rigi-Scan and DIR monitoring of erectile rigidity capacity during provocative and/or nocturnal readings (particularly helpful in differentiating between neurological, psychological and vascular disorder), Doppler ultrasound studies (when vascular symptoms predominate) and NEVA monitoring can be performed at the Porterbrook clinic. GSA is helpful for suspected nerve conduction pathologies.

Management of Erectile Disorder

Psychological Factors

Where marked psychological factors are evident, it is considered good practice and most appropriate to offer either individual or couple relationship therapy when patients will accept this form of treatment. Many men will not come with their partners or do not wish to engage in psychological treatments. Under these circumstances, physical treatments may be given which may allow patients to engage with their therapist/doctor at subsequent consultations. Failure to recognise and treat psychological disorders will often mean a failure of physical treatments over time. The value of brief counselling alongside physical treatments has been found to reduce the drop out rate from oral and injection therapy. (Gruenwald et al 2006). Liaison with the menopause clinic, or an offer to the female partner to attend the clinic at some stage may be appropriate in some cases (if the patient is in agreement to contact being made).

Treatment of major psychiatric disorder, in particular depression, will invoke consideration for the use of an anti-depressant and/or a referral to a Community Mental Health Team.

Organic Factors

The physical treatments can be summarised as oral medications (sildenafil, vardenafil, tadalafil and yohimbine), and intracavernous injections of vasoactive agents (alprostadil, papavarine, phentolamine and Invicorp), intra urethral pellets of alprostadil (MUSE), vacuum devices/penoscrotal rings and other miscellaneous treatments. With the exception of yohimbine, most of these treatments have an effectiveness rate of between 50% and 90%. However, patient acceptability is crucial and the high drop out rates from some treatments may be failure to discuss motivation and preference with patients in advance. Lifestyle advice may be necessary for many patients.

First Line Treatments

Oral treatments

Sildenafil

With the licensing of sildenafil (Viagra®), physicians are now able to offer men with ED an effective oral agent for their problem. The improvement in erectile capacity has been shown to be 83% in spinal cord injury, 76% in depression, 68% in hypertension, 61% following TURP, 57% in diabetes mellitus and 43% after radical prostatectomy. The patient must not receive organic nitrates in any form concurrent with this treatment. Cardiovascular status should be assessed prior to initial prescription, especially in the older man. The correct dose can usually be ascertained with 8 x 50mg tablets (see clinic patient leaflet) although up to 10 doses may need to be tried before concluding a non-response to sildenafil. In certain situations (including men with impaired hepatic or renal function, or over 65 years of age) a lower starting dose of 25 mg is recommended.

Tadalafil

Tadalafil (Cialis®) allows physicians and men with ED a further choice of highly effective oral agents. In a broad population of men with ED 84% of men reported an improvement in erectile function. The improvement in erectile capacity has been shown to be 88% in spinal and cord injury, 81% in depression, 82% in hypertension, 83% in men with DV disease, 75% in diabetes mellitus, and 71% in radical prostatectomy (with residual erectile function). Clinical pharmacology studies have shown that co-administration of tadalafil with a high fat meal does not alter the systemic exposure, maximum plasma concentrations and rate of absorption of tadalafil. Therefore, food restrictions are not required by patients before or after administration of tadalafil. Unlike other oral therapies this efficacy can last up to 36 hours after taking the tablet. This broad period of responsiveness may allow men to separate taking the tablet from the sexual act and, therefore, offer more spontaneity and sexual confidence from the sexual act. Tadalafil must not be taken with organic nitrates or nitric oxide donors and the cardiovascular state of patients should be assessed prior to initial prescription. The starting dose is 10mg and may be increased to 20mg if efficacy is insufficient. These dosing instructions do not need to be changed for different patient groups, though no data exists for 20mg in men with impaired hepatic or renal function.

Vardenafil

Vardenafil (Levitra®) is the most pharmacologically potent of the currently available PDE5 inhibitors and exhibits high selectivity for the PDE5 enzyme. Vardenafil has been studied in a wide variety of patient populations with ED and has been shown to have a high level of efficacy. One study has shown that 87% of patients achieve erections hard enough for vaginal penetration with the first dose. Continued efficacy is observed with subsequent doses. Vardenafil has also been shown to be effective in men with ED and various comorbidities, including diabetes, cardiovascular risk factors, radical prostatectomy, depression and spinal cord injury. The absorption of vardenafil is rapid and is unaffected by a normal meal or by alcohol. Most men will respond within 25-60 minutes of tablet ingestion, but a proportion will respond earlier than this. Duration of responsiveness post dosing is variable but studies have shown that some men can have an effect up to 12 hours after dosing. As for the other PDE5 inhibitors, vardenafil is contra-indicated in men taking any form of nitrate or nitric oxide donor. The usual recommended starting dose of vardenafil is 10mg. Based on efficacy and tolerability, the dose can be titrated up to 20mg or down to 5mg.

The wholesale and NHS prices for the PDE5 inhibitors are shown below.

(Prices correct at the time of printing)

NHS Price — Vardenafil					
Pack	NHS Price	Wholesale Price Ex VAT	Pack	NHS Price	Wholesale Price Ex VAT
4 x 5mg	£19.49	£16.59	8 x 5mg	£39.00	£33.19
4 x 10mg	£26.13	£22.24	8 x 10mg	£52.25	£44.47
4 x 20mg	£27.61	£23.50	8 x 20mg	£55.21	£46.99

NHS Price — Sildenafil					
Pack	NHS Price	Wholesale Price Ex VAT	Pack	NHS Price	Wholesale Price Ex VAT
4 x 25mg	£19.49	£16.59	8 x 25mg	£39.00	£33.19
4 x 50mg	£24.99	£21.27	8 x 50mg	£49.98	£42.54
4 x 100mg	£27.61	£23.50	8 x 100mg	£55.21	£46.99

NHS Price — Tadalafil		
Pack	NHS Price	Wholesale Price Ex VAT
4 x 10mg	£24.30	£24.99
4 x 20mg	£24.30	£24.99
8 x 20mg	£58.72	£49.97

Second Line Treatments

Yohimbine

Other oral treatments, which are not currently licensed for use in ED, are yohimbine and phentolamine, and the Specialist Services occasionally prescribe these where other agents have proved ineffective.

ICI & MUSE

Intracavernous injection involves educating and instructing patients to inject a 30 gauge needle into one of the corpus cavernosal bodies and inject a solution into the corpus. All patients are trained by a physician or nurse and observed before being allowed to take medication home. The dose is graduated dependent on aetiology with low starting doses in psychological and neurological impairment. The most common prescription is for alprostadil (Caverject, Viridal Duo). Alternative agents are becoming available including Moxisylyte (which like sildenafil is a facilitator and does not automatically cause erection). Once a patient is confident in the use of self-injection the ongoing prescription of the drug can be repeated by the General Practitioner. It is prudent that either the General Practitioner or the initiating clinic offer annual assessment of the penis to ensure no complications ensue (in particular fibrotic nodules in the body of the shaft). All patients are advised of the dangers of priapism and information is provided in the product notes with each preparation.

Poor respondents to licensed preparations may necessitate treatment with other agents (or a combination of such medications) including papaverine and phentolamine and/or VIP (e.g. InviCorp). Normally these prescriptions would be issued by the Hospital Clinic where experience is available in using combination therapies. Often the prescription is on a named-patient basis pending a full product license in the UK.

Intraurethral application of alprostadil (MUSE—Medicated Urethral System for Erection) is an alternative preparation for this effective prostaglandin. Again patient instruction and monitoring of technique is essential for good clinical results.

VCD

Vacuum constriction devices have been available as an effective treatment and have been described since 1874. As with injections, the device is demonstrated to the patient and a loan device offered for several weeks whilst the patient decides if they find the

device acceptable and effective. Instructional videos are available for the patient to take home as well. Normally, patients will purchase a device from the manufacturer, if they are satisfied with the response.

By placing the cylinder over the penis and pumping a vacuum, an engorged condition is created producing a full erection without pain or discomfort. To maintain the erection after the cylinder is removed, a constriction ring is placed at the base of the penis. This can be left in place for up to 30 minutes. Vacuum therapy is a safe and effective treatment for erectile dysfunction and is 90% successful. It is especially recommended for use where drug treatment is not acceptable.

Vacuum Therapy Systems are available on prescription under Schedule 2. Several systems are available and can be prescribed on the FP10 prescription forms.

The prescriber must endorse the face of the form with the reference SLS and the patient will pay the usual prescription charge. They are manufactured in the UK to ISO 9001 standard and carry a CE mark. Most come with a 2 year manufacturing guarantee and, if purchased, come with a money back guarantee if not entirely satisfied. (Check with each company for specific details).

Farnhurst Medical Ltd	01403 752775	www.farnhurst-medical.com
Owen Mumford	01993 812021	www.medicalshop.co.uk
iMEDicare Ltd	0208 207 562	www.iMEDicare.eu
Medi Plus	01494 551200	www.mediplus.co.uk
EuroSurgical Ltd	01483 456007	www.eurosurgical.co.uk
Genesis Medical	020 7284 2824	www.genmedhealth.com
Mediwatch	01788 547888	www.mediwatch.com

The Royal Hallamshire Hospital offers both a one month loan system and a technical support clinic once a month for patients requiring advice or assistance with any devices.

Surgical

For younger patients with arterial insufficiency, and for older patients with minimal or no response to the above treatments, further investigations and the opinion of a urological surgeon is sought regarding suitability for pelvic surgery or penile implants.

Androgens

For patients requiring treatment with testosterone supplementation (estimated to be 10-20%) initial treatment will be initiated in the outpatient clinic typically with three weekly or three monthly intra muscular injections or daily transdermal patches or gel or buccal pastilles. Many cases of non-response to PDE5i can be improved by the correction of testosterone delivery (Greco et al 2006). Many patients suffer dermatological reactions with the patches and so injections or gel are the usual form of treatment. Again, once a dose has been established the injectable preparation can continue to be given by the Practice Nurse in the primary care setting or the patient instructed in the technique. Alternatively, some patients may prefer to have insertion of testosterone pellets, which are replaced every four to six months in the hospital clinic setting. Ongoing screening (endocrinological, hepatological and haematological) as well as prostate review are essential and should be undertaken by the prescriber on a yearly basis in accordance to current guidelines (see www.issam.org).

Shared Care Arrangements: Eligible Groups

These guidelines have been influenced by advice issued by the DoH. Following an appropriate assessment of the needs of the man/couple, for the following groups of men, drug treatments can be prescribed on a NHS FP10 prescription from 1 July 1999.

a) Specified conditions:

<i>Diabetes mellitus</i>	<i>Multiple sclerosis</i>
<i>Parkinson's disease</i>	<i>Poliomyelitis</i>
<i>Prostate cancer</i>	<i>Prostatectomy</i>
<i>Radical pelvic surgery</i>	<i>Renal failure treated by dialysis or transplant</i>
<i>Severe pelvic injury</i>	<i>Single gene neurological disease</i>
<i>Spinal cord injury</i>	<i>Spina bifida</i>

b) Previous prescriptions:

All men receiving a course of NHS drug treatment for erectile dysfunction from their GP on or before 14th Sep 1998.

c) Additionally, there is the concept of severe distress:

For men who are caused 'severe distress by impotence'; it is proposed that NHS treatment should be available in exceptional circumstances only after a specialist assessment in a hospital. However, the general practitioner should be satisfied that the man is suffering from 'impotence' and that this impotence is causing him severe distress. For 'severe distress' to be determined, it is the advice of the DoH that the following criteria be taken into account: that there is significant disruption to normal social and occupational activity, marked effect on mood, behaviour, social and environmental awareness and marked effect on interpersonal relationships. The patient will receive the treatment through the specialist service (see appendix A).

For all other men, pharmacological treatment and devices are available on private prescription:- If a patient is in agreement, a GP may write a private prescription (without charge to the patient for writing the prescription—schedule 2) for any pharmacological treatment, or device.

It is anticipated that in most cases, and unless there are contra-indications to the contrary, that after assessment the first line treatment will be a trial of an oral agent listed above.

Specialist Services

It is suggested that where a man with ED does not have eligibility as listed above (a or b), AND where a trial of sildenafil to 100mg has been unsuccessful (up to 10 doses may be required), and preferably other oral agents on the formulary,

OR where the general practitioner would either:

- Value a second opinion or advice for further management of a non-responding man to a PDE5,
- Or prefer a patient to be instructed in the use of a particular technique,
- Or requests a loan of a VCD
- Or is seeking guidance for further investigations to be carried out.
- Or requests an assessment for psychosexual or relationship therapy
- Or considers the presence of both ED and severe distress

That a referral to one of the specialist services is appropriate.

From June 1999, the two main providers of services for men with erectile disorder in Sheffield have been offering an integrated assessment and treatment service for MED (and other sexual and relationship problems). Partnership arrangements have been established to ensure that patients referred to either of the two main centres for sexual dysfunction in the city will receive a common and in-depth assessment of the problem(s) and the opportunity for treatment appropriate to their condition. The Andrology Service of the Directorate of Urology at the Royal Hallamshire Hospital will seek referral of predominantly organic cases and the Porterbrook Clinic will seek referrals of predominantly psychogenic cases. For patients where the GP considers evidence of 'severe distress', referral should be to the service where the anticipated underlying aetiology is likely to be best managed. Both services offer an integrated package with multi-disciplinary teams offering physical and psychological therapies. Additionally patient care is improved by easy cross-referral between sites as appropriate (particularly for further investigations e.g. RigiScan, ultrasound and surgical opinion). We hope to extend clinics within primary care in due course. There is now in place close liaison with endocrine and diabetic specialities at Northern General Hospital and Royal Hallamshire Hospital sites for advice as necessary.

Any referral to the Porterbrook Clinic or Andrology Service at the Royal Hallamshire Hospital would be greatly assisted by providing the following information:

- Brief outline of the present problem
- Medical, surgical and psychiatric history
- Currently prescribed medication
- Any previous treatments (and responses) for sexual/relationship disorder
- Exclusion of diabetes mellitus (fasting blood sugar)
- Blood results for total testosterone

What we can offer

After a comprehensive assessment, patients will be offered and instructed in the use of the most appropriate and preferred treatment option(s). This will include oral agents, injectable agents and vacuum devices. This may, for reasons of time, involve a request for the GP to prescribe the agent. In the case of oral medications, the appropriate dose can be determined with an initial prescription from the clinic of 8 x 50mg tablets (sildenafil), or 10mg tablets (vardenafil or tadalafil) (see our clinic leaflets), or a lower starting dose as clinically indicated. Second line treatments will be offered as appropriate and acceptable to the man (and his partner). If he is deemed to suffer with severe distress, the prescription will be made available through the specialist service. We aim to ensure that the man (and his partner) are satisfied with their chosen treatment before advising the general practitioner (or other referrer) on arrangements for continuing prescriptions and after care. Ideally, this will be provided in the primary care setting. Treatment information leaflets are freely available for all patients, both in the clinic and on our website (www.porterbrookclinic.org.uk). We will discharge the patient from the clinic with four treatment doses of their chosen agent (unless they choose the option of telephone follow-up by the clinic). Where the man satisfies the criteria of eligibility, a prescription for the chosen drug can be prescribed by the general practitioner on the basis of an average of one treatment per week but this amount may be higher in certain situations. Where the patient does not have such eligibility for exemption from charges, the cost of the prescription must be borne by the individual patient.

References

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9. Greco E A, Spera G & Aversa A. (2006) Combining testosterone and PDE5 inhibitors in erectile dysfunction: Basic rationale and clinical evidences. *European Urology*, 50, 940-947

Useful Telephone Numbers

Services for sexual problems	Contact/Staff	Telephone No.
Porterbrook Clinic		
		0114 271 6671
Full assessment and diagnostic and treatment service for sexual problems	Consultant: Dr Kevan R Wylie Service Co-ordinator: Julie Fitter Staff Nurse: David Steward	0114 271 8674
Royal Hallamshire Hospital		
Andrology Department Full assessment and diagnostic and treatment service for ED	Consultant: Dr Kevan R Wylie Specialist Nurse Practitioners: Trish Allen & Debbie Davies-South	0114 271 3334 0114 271 2928
Specialist Services for: Genito Urinary Medicine <i>Self-referral possible</i>	Consultant: Prof. George Kinghorn	0114 226 1368
Diabetes	Diabetes Specialist Nurse: Lesley Brady	0114 226 8698
Pharmacy Department	Directorate Pharmacist: Ross McManus	0114 271 3644
Endocrinology	Consultant: Prof. Richard Ross	0114 2713990
Gynaecology Jessop's Wing	Lead Gynaecologist: Mr Andrew Faraks	0114 226 8167
<i>For patients wishing psychosexual services on a self-referral basis</i>		
Family Planning Services (Central Clinic)	Associate Specialist Dr Anita Taylor	0114 271 6815
Northern General Hospital		
Specialist Services for:		
Spinal Cord Injuries	Consultant: Mr Paul Tophill	0114 271 5659

Other support Agencies:

RELATE Services

0114 249 3979

SDA

The Sexual Dysfunction Association provides support for patients with erectile disorder and their partners

Tel: 0870 774 3571

www.sda.uk.net

BASRT

The British Association for Sexual & Relationship Therapy offer lists of accredited sexual and relationship therapists as a further alternative for psychotherapeutic support and intervention

Tel: 0208 543 2707

www.basrt.org.uk

IPM

Institute of Psychosexual Medicine

Tel: 0208 580 0631

www.ipm.org.uk

BSSM

The British Society for Sexual Medicine

Tel: 0154 343 2757

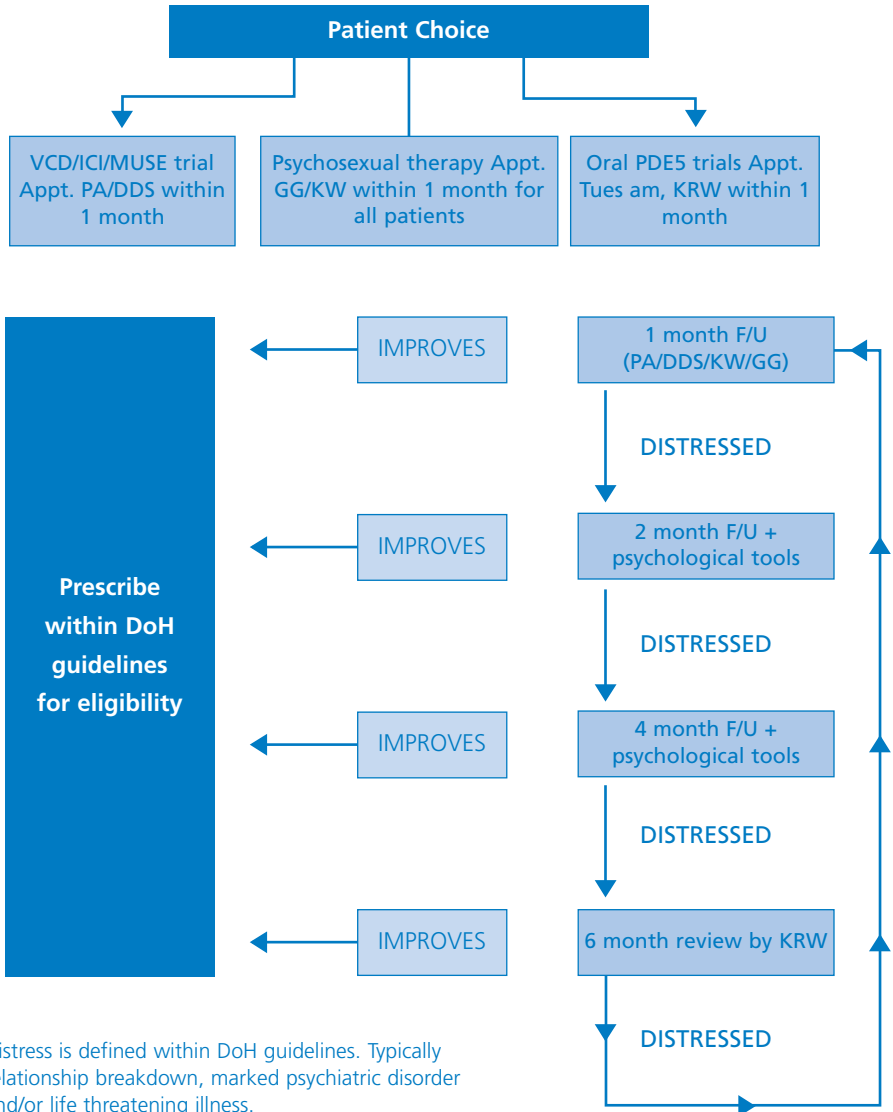
www.bssm.org.uk

Declaration

The printing and distribution of this protocol has been made possible thanks to donations from Bayer Pharmaceuticals and Eli Lilly and Company Ltd.

Appendix A

Example of Assessment and Management of Severe Distress at Andrology Service



Distress is defined within DoH guidelines. Typically relationship breakdown, marked psychiatric disorder and/or life threatening illness.

