NIHR | Innovation Observatory

HEALTH TECHNOLOGY BRIEFING JANUARY 2020

DermaSys for erectile dysfunction

NIHRIO ID	27051	**NICE ID**	10268
Developer/Company	Futura Medical Developments Ltd	**UKPS ID**	653315

Licensing and market availability plans	Currently in phase III clinical trials.

SUMMARY

DermaSys is in clinical development for treating erectile dysfunction (ED), which is the inability to achieve or maintain a penile erection sufficient for satisfactory sexual performance. ED is very common, particularly in men over the age of 40 years. It can be caused by any number of physical and psychological factors. Any abnormality involving the nervous, circulatory or hormonal systems, whether due to medication or disease, may affect the ability to develop and sustain an erection. Although ED is a benign disorder, it may affect physical and psychosocial health and may have a significant impact on the quality of life of sufferers and their partners.

DermaSys is a drug delivery technology platform that provides rapid and targeted local delivery of active pharmaceutical ingredients (API) at therapeutic levels to the required site of action. If licensed, DermaSys will provide an additional treatment option for patients with ED.

PROPOSED INDICATION

First-line treatment of erectile dysfunction (ED).[a]

TECHNOLOGY

DESCRIPTION

DermaSys is a drug delivery technology platform that provides rapid and targeted local delivery of API at therapeutic levels to the required site of action. Application of gel with API leads to a combination of solvents including volatile solvents. Then volatile solvents evaporate, leaving the remaining solvent supersaturated with API. This, in turn, derives API through the tissue and then API penetrated the skin rapidly offering rapid penetration or sustained release.[1] GTN promotes vasodilation through local absorption into penile vasculature, minimising systemic uptake. The GTN is absorbed into the penile blood system and is converted to nitric oxide, which has the effect of relaxing muscles surrounding the corpus cavernosa and dilating the penile arteries. This allows the corpus cavernosa to engorge with blood and following sexual stimulation, an erection occurs.[2]

DermaSys is currently in clinical development for the treatment of ED. In the phase III clinical trial (NCT03813992) participants received topical gel containing 0.2% (w/w) glyceryl trinitrate (GTN) and incorporates DermaSys doses ranging from 0.6mg-1.8mg when needed (PRN) up to twice daily.[3,a]

INNOVATION AND/OR ADVANTAGES

DermaSys is versatile and bespoke technology that can be tailored to suit the specific active compound being used and the therapeutic indication. Such drug delivery technology platform offers an optimised profile in terms of dose, onset time and duration of effect as well as an improved safety profile reducing the risks of side effects due to a lower systemic uptake. It is indicated that DermaSys incorporating topical gel GTN facilitate rapid absorption and effective delivery through the skin which translates into a fast onset of action (within 5-10 minutes).[2,4]

DEVELOPMENT STATUS AND/OR REGULATORY DESIGNATIONS

DermaSys does not currently have a Marketing Authorisation in the EU/UK for any indication.

- DermaSys is also in development for a number of disease states including pain relief.[5]

PATIENT GROUP

DISEASE BACKGROUND

Erectile dysfunction (ED) is the inability to get or keep an erection firm enough to have sexual intercourse. It is also sometimes referred to as impotence.[6] Normally, an erection occurs when the arteries carrying blood to the penis widen, allowing more blood to flow in, and the veins carrying blood away from the penis are compressed, restricting blood from flowing out.[7] The

[a] Information provided by Futura Medical Developments Ltd on UK PharmaScan

penile erection results due to an appropriate combination of neurological, vascular and hormonal systems on phallic tissues.[8] Any abnormality involving the nervous, circulatory or hormonal systems, whether due to medication or disease, may affect the ability to develop and sustain an erection. ED prevalence increases with age and is also a marker of significantly increased risk of coronary artery disease, stroke and all-cause mortality.[9,10]

The main risk factors for ED include medical conditions particularly diabetes or heart problem, using tobacco, obesity, injuries, psychological conditions (such as stress, anxiety, or depression), drug and alcohol use, prolonged bicycling, certain medical treatments (prostate surgery or radiation) and medications (antidepressants, antihistamines and medications to treat high blood pressure, pain or prostate cancer).[11]

The common signs and symptom of ED include difficulty in getting an erection, softer erections, erections that do not last long enough for satisfactory sex, less girthy erections and reduced penile sensitivity.[12] ED may cause stress, cause relationship problems or affect an individual's self-confidence and has a significant negative impact on the quality of life of both the affected individual and his partner.[11,13]

CLINICAL NEED AND BURDEN OF DISEASE

Several large epidemiological studies have shown a high prevalence and incidence of ED worldwide.[14] Approximately 150 million men worldwide are estimated to be affected by ED and likely to double by 2025.[15]

In a study conducted in 2001-2002, the age-standardised prevalence of ED was reported in the UK by 17.8%.[16] In another international study (covering UK, France, Netherlands, South Korea) with a UK site (Birmingham), in men aged 40-79, ED prevalence was estimated (based on Sexual Function Inventory responses) as 21.1% across all sites and 27.3% specifically at the UK site. When assessed by self-reported ED (yes/no) responses, the prevalence was 16.6% across all sites and 20.5% at the UK site.[17]

Applying these estimated prevalence rates for the UK to the UK mid-year 2018-2019 population estimates for men aged 40 to 79 years would equate to a potentially affected population ranging between 2,607,863 (17.8%) and 3,999,700 (27.3%) men.[18] The estimates for men who have ED aged 18-70 years could not be identified from published literature.

PATIENT TREATMENT PATHWAY

TREATMENT PATHWAY

A variety of options exist for treating ED. The cause and severity of the condition and underlying health problems are important factors in choosing the best treatment option.[11] The recommended approach for the management of ED is a combination of drug treatment and lifestyle changes (including regular exercise, reduction in body mass index, smoking cessation and reduced alcohol consumption).[9]

Medications may not work or may not be a good treatment option for an individual. If this is the case, other treatments include the use of penis pumps (vacuum constriction device), penile implants and blood vessel surgery.[11]

CURRENT TREATMENT OPTIONS

An oral phosphodiesterase type-5 inhibitor (PDE5i) is the first-line drug treatment for ED, regardless of the cause. These drugs act by increasing the blood flow to the penis. They do not initiate an erection, sexual stimulation is required. The choice of oral PDE5i depends on the frequency of intercourse and response to treatment. A patient with ED should receive six doses of an individual PDE5i at the maximum dose (with sexual stimulation) before being classified as a non-responder. Intracavernosal, intraurethral or topical application of alprostadil (prostaglandin E_1) is recommended as second-line therapy under careful medical supervision.[19]

According to the British Society for Sexual Medicine (BSSM)/NICE and American Urological Association (EAU) guidelines, the following PDE5i's are recommended as first-line treatment for individuals with ED (provided there are no contraindications):[20]

- Sildenafil
- Vardanafil
- Tadalafil
- Avanafil (EAU only)

BSSM/NICE recommends using alprostadil available in the UK as an intracavernous injection, intraurethral application, and topical cream as a second-line treatment option and for all guidelines (BSSM, NICE and EAU), third-line treatment consists of the insertion of a penile prosthesis. This can be either a two or three-piece inflatable penile prosthesis.[20]

PLACE OF TECHNOLOGY

If licenced, DermaSys will offer an additional first-line treatment option for ED.

CLINICAL TRIAL INFORMATION

Trial	**FM57,NCT03813992; A phase III, dose ranging, multi-centre, randomised, double-blind, placebo-controlled, home use, parallel group clinical trial of topically-applied glyceryl trinitrate for the treatment of erectile dysfunction, with an open-label extension** **Phase III** **Location(s): EU (not UK) and other countries**
Trial design	Randomised, parallel assignment, double blinded
Population	N= 1005; aged 18-70; males; ED more than 3 months; heterosexual relationship for at least 6 months
Intervention(s)	Patients were randomised to: MED2005 (0.2%) • MED2005 0.2% w/w gel to deliver 0.6 mg dose of GTN applied topically prior to a sexual intercourse attempt MED2005 (0.4%) • MED2005 0.4% w/w gel to deliver 1.2 mg dose of GTN applied topically prior to a sexual intercourse attempt MED2005 0.6%

	• MED2005 0.6% w/w gel to deliver 1.8 mg dose of GTN applied topically prior to a sexual intercourse attempt
Comparator(s)	Placebo vehicle: Placebo vehicle applied topically prior to a sexual intercourse attempt
Outcome(s)	• International Index for Erectile Function (IIEF) Questionnaire [Time frame: Up to week 64 of the study] • Sexual Encounter Profile (SEP) Questionnaire (Question 2) [Time frame: Up to week 64 of the study] • Sexual Encounter Profile (SEP) Questionnaire (Question 3) [Time frame: Up to week 64 of the study]
Results (efficacy)	All doses achieved all primary endpoints against baseline ($p<0.001$) throughout the 12-week period, with secondary endpoint also being met. However, no difference between study arms was detected from an efficacy standpoint.[21]
Results (safety)	Dose-dependent side-effects were seen, suggesting no formulation/administration errors.[21]

ESTIMATED COST

The cost of DermaSys is not yet know.

RELEVANT GUIDANCE

NICE GUIDANCE

- NICE interventional procedures guidance. Angioplasty and stenting to treat peripheral arterial disease causing refractory erectile dysfunction (IPG546). February 2016.

NHS ENGLAND (POLICY/COMMISSIONING) GUIDANCE

- No relevant guidance identified

OTHER GUIDANCE

- American Urological Association (AUA). Erectile Dysfunction: AUA guideline. 2018.[22]
- NICE clinical knowledge summary. Erectile dysfunction. Last revised 2017.[23]
- British Society for Sexual Medicine. Guidelines on the Management of Erectile Dysfunction in Men—2017.[14]
- European Association of Urology (EAU). Male sexual dysfunction: Erectile dysfunction and premature ejaculation. 2014.[24]
- NICE evidence summary. Erectile dysfunction: alprostadil cream (ESNM50). December 2014.
- NICE evidence summary. Erectile dysfunction: avanafil (ESNM45). August 2014.

ADDITIONAL INFORMATION

REFERENCES

1 Ralph DJ, Eardley I, Taubel J, Terrill P, Holland T. Efficacy and Safety of MED2005, a Topical Glyceryl Trinitrate Formulation, in the Treatment of Erectile Dysfunction: A Randomized Crossover Study. *J Sex Med*. 2018 Feb;15(2):167-75. Available from: https://www.ncbi.nlm.nih.gov/pubmed/29306609.

2 Futuramedical. *MED2005 is a topical gel applied directly to the head (glans) of the penis for the treatment of male erectile dysfunction ("ED").* Available from: https://futuramedical.com/what-we-do/med2005/med2005-clinical-programme/ [Accessed 12 December 2019].

3 Clinicaltrial.gov. *Clinical Trial Using Topically Applied Glyceryl Trinitrate (GTN) for the Treatment of Erectile Dysfunction. Trial ID: NCT03813992.* Available from: https://clinicaltrials.gov/ct2/show/study/NCT03813992?show_locs=Y#locn [Accessed 5 December 2019].

4 FuturaMedical. *Our Technology.* Available from: https://futuramedical.com/what-we-do/our-technology [Accessed 21 January 2020].

5 FuturaMedical. *Futura Medical is developing a portfolio of innovative products for two large markets, sexual health and pain.* Available from: https://futuramedical.com/what-we-do/our-product-development-pipeline/ [Accessed 21 January 2020].

6 Healthline. *Everything You Need to Know About Erectile Dysfunction (ED).* Available from: https://www.healthline.com/health/erectile-dysfunction [Accessed 02 December 2019].

7 emedicinehealth. *Erectile dysfunction medications.* Available from: https://www.emedicinehealth.com/understanding_erectile_dysfunction_medications/article_em.htm#what_is_erectile_dysfunction [Accessed 16 Decemver 2019].

8 Goldstein I, Goren A, Li VW, Maculaitis MC, Tang WY, Hassan TA. The association of erectile dysfunction with productivity and absenteeism in eight countries globally. *International Journal of Clinical Practice*. 2019;73(11):e13384. Available from: https://onlinelibrary.wiley.com/doi/abs/10.1111/ijcp.13384 10.1111/ijcp.13384.

9 National Insitute for Health and Care Excellence. *Erectile dysfunction.* Available from: https://cks.nice.org.uk/erectile-dysfunction#!backgroundSub:3 [Accessed 07 January 2019].

10 National Insitute for Health and Care Excellence. *Erectile dysfunction: What are the complications?* Available from: https://cks.nice.org.uk/erectile-dysfunction#!backgroundSub:5 [Accessed 07 January 2020].

11 Center for Intergrated Healthcare. *Erectile Dysfunction (ED).* Available from: https://www.mirecc.va.gov/cih-visn2/Documents/Patient_Education_Handouts/Erectile_Dysfunction_Version_3.pdf [Accessed 16 December 2019].

12 Impatient. *What are the most common erectile dysfunction symptoms?* Available from: https://www.getroman.com/impatient/erectile-dysfunction/symptoms/ [Accessed 16 December 2019].

13 Farahat TM, Maraee AH, Hegazy NN, Ismail IA. Quality of life in patients with erectile dysfunction in Shebin El Kom District. *Menoufia Medical Journal*. 2017;30(2):607. Available from: http://mmj.eg.net/article.asp?issn=1110-2098;year=2017;volume=30;issue=2;spage=607;epage=613;aulast=Farahat.

14 Hackett G, Kirby M, Wylie K, Heald A, Ossei-Gerning N, Edwards D, et al. British Society for Sexual Medicine Guidelines on the Management of Erectile Dysfunction in Men-2017. *J Sex Med*. 2018 Apr;15(4):430-57. Available from: https://www.ncbi.nlm.nih.gov/pubmed/29550461 10.1016/j.jsxm.2018.01.023.

15 Kalsi J, Muneer A. Erectile dysfunction - an update of current practice and future strategies. *J Clin Urol*. 2013 Jul;6(4):210-9. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4467226/ 10.1177/2051415813491862.

16 Moreira ED, Glasser DB, Nicolosi A, Duarte FG, Gingell C. Sexual problems and help-seeking behaviour in adults in the United Kingdom and continental Europe. *BJU Int*. 2008

Apr;101(8):1005-11. Available from: https://onlinelibrary.wiley.com/doi/full/10.1111/j.1464-410X.2008.07453.x 10.1111/j.1464-410X.2008.07453.x.
17 Boyle P, Robertson C, Mazzetta C, Keech M, Hobbs R, Fourcade R, et al. The association between lower urinary tract symptoms and erectile dysfunction in four centres: the UrEpik study. *BJU Int*. 2003 Nov;92(7):719-25. Available from: https://onlinelibrary.wiley.com/doi/full/10.1046/j.1464-410X.2003.04459.x?sid=nlm%3Apubmed 10.1046/j.1464-410x.2003.04459.x.
18 Office for National Statistics (ONS). *Population Estimates for UK, England and Wales, Scotland and Northern Ireland: Mid-2018*. Available from: https://www.ons.gov.uk/file?uri=/peoplepopulationandcommunity/populationandmigration/populationestimates/datasets/populationestimatesforukenglandandwalesscotlandandnorthernireland/mid20182019laboundaries/ukmidyearestimates20182019ladcodes.xls [Accessed 16 December 2019].
19 National Institute for Health and Care Excellence. *Erectile dysfunction.* Available from: https://bnf.nice.org.uk/treatment-summary/erectile-dysfunction.html [Accessed 17 December 2019].
20 Rai J, Terry T. Comparison of erectile dysfunction guidelines between the UK (BSSM/NICE) and Europe (EAU). *Journal of Clinical Urology*. 2018;11(2):122-6. Available from: https://journals.sagepub.com/doi/full/10.1177/2051415816688820.
21 Trinity Delta. *Futura Medical: Remarkable data from pivotal trial opens new possibilities.* Available from: https://www.trinitydelta.org/research-notes/remarkable-data-from-pivotal-trial-opens-new-possibilities/ [Accessed
22 Burnett AL, Nehra A, Breau RH, Culkin DJ, Faraday MM, Hakim LS, et al. Erectile Dysfunction: AUA Guideline. *J Urol*. 2018 Sep;200(3):633-41. Available from: https://www.auajournals.org/doi/10.1016/j.juro.2018.05.004 10.1016/j.juro.2018.05.004.
23 National Insitute for Health and Care Excellence. *Clinical knowledge summary* Last Update Date: August 2019. Available from: https://cks.nice.org.uk/erectile-dysfunction [Accessed 16 December 2019].
24 European Association of Urology. *Male sexual dysfunction: erectile dysfunction and premature ejaculation* Last Update Date: Available from: https://uroweb.org/wp-content/uploads/14-Male-Sexual-Dysfunction_LR.pdf [Accessed 16 December 2019].

NB: This briefing presents independent research funded by the National Institute for Health Research (NIHR). The views expressed are those of the author and not necessarily those of the NHS, the NIHR or the Department of Health.