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Fexapotide Triflutate for benign prostatic hyperplasia

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LAY SUMMARY

Benign prostatic hyperplasia (BPH) is a medical term that is used to describe enlargement of the prostate gland. It is not a cancer and is usually not a serious threat to health if well-treated. Most males aged 50 years and above develop BPH. As the prostate gets bigger, it can place pressure on the bladder and it may squeeze or partly block the tube that carries urine from the bladder out of the body. This often causes problems with passing urine and may also cause other complications such as recurrent urinary tract infections, blockage of the bladder outlet, and kidney failure.

Fexapotide Triflutate is a drug that is under development for the treatment of BPH. It is delivered through an injection directly into the prostate. It acts by shrinking the enlarged prostate tissue without damaging neighbouring tissue and nerves. With only one injection, it leads to a natural cell death within the enlarged prostate, which is believed to reduce the prostatic volume and therefore eliminate symptoms. Fexapotide Triflutate is also thought to have reduced sexual side effects and treatment of frequent night time urination when compared to existing therapies. If licensed, Fexapotide Triflutate will offer an additional treatment option for patients with BPH.

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TARGET GROUP

Benign prostatic hyperplasia (BPH)

TECHNOLOGY

DESCRIPTION

Fexapotide Triflutate (NX-1207) is an office-based pro-apoptotic protein injectable for BPH and for low grade localized prostate cancer. The drug mechanism of action is programmed natural cell death (apoptosis) selectively in prostate glands when injected intraprostatically by the transrectal route. The selective pro-apoptotic properties, which induce focal cell loss in prostate, lead to prostate volume reduction with both short- and long-term symptomatic improvement. Adjacent tissues and structures (such as nerves, bladder, rectum, urethra and periprostatic tissues) are unaffected by fexapotide triflutate.[1,2]

In phase III clinical trials, fexapotide triflutate is administered as a single intraprostatic injection of 2.5 mg.[3,4,5]

Fexapotide triflutate does not currently have Marketing Authorisation in the EU for any indication.[6] It is in phase II and III trials in the United States for prostate cancer.[1]

INNOVATION and/or ADVANTAGES

Currently available treatments for BPH including oral medications as well as invasive surgical procedures have a number of unmet needs such as reduction of the sexual side effects of current medications, and the treatment of nocturia (night time urination). Results announced by the company suggest that fexapotide triflutate positively addressed both of the unmet needs.[7] No significant safety events have been attributed to the molecule in clinical studies and no difference from placebo in number or types of related or unrelated adverse events was experienced.[2]

Fexapotide Triflutate is a drug that if licensed, will offer an additional treatment option with potentially reduced side effects for patients with benign prostatic hyperplasia.[8]

DEVELOPER

Nymox Pharmaceutical Corporation

AVAILABILITY, LAUNCH or MARKETING

In May 2017, the company stated that it filed to seek approval for marketing authorization for Fexapotide Triflutate in five European countries, comprising the Netherlands, the UK, Germany, France and Spain.[9]

PATIENT GROUP

BACKGROUND

Benign prostatic hyperplasia (BPH) or benign prostate enlargement (BPE) is a medical term that is used to describe an enlarged prostate gland. Also known as benign prostatic hypertrophy, it is a histologic diagnosis characterized by proliferation of the cellular elements of the prostate. The prostate is a small gland, located in the pelvis, between the penis and bladder. It surrounds the urethra, the tube that carries urine from the bladder out of the body. As the prostate gets bigger, it can place pressure on the bladder and it may squeeze or partly block the urethra. This often causes problems with urination. BPH is common in men over 50 years of age. It is not a cancer and is not usually a serious threat to health.[10,11,12]

The cause of BPH is unknown, but it is believed to be linked to hormonal changes as men get older. The balance of hormones in the body changes as the person gets older and this may cause the prostate gland to grow.[10]

Symptoms of BPH include: difficulty starting to urinate, a frequent and/or urgent need to urinate, difficulty of fully emptying the bladder, straining to urinate, having a weak flow of urine, dribbling, nocturia (needing to get up frequently at night to urinate), and accidentally leaking urine (urinary incontinence).[10,12]

Sometimes BPH can cause chronic bladder outlet obstruction (BOO), which may lead to urinary retention, renal insufficiency, recurrent urinary tract infections, gross haematuria (blood in the urine) and bladder calculi. End stage BOO can cause renal failure and uraemia.[12] The most important quality of life aspects reported to be most affected were sleep, anxiety and worry about the disease, mobility, leisure, daily activities, sexual activities and satisfaction with sexual relationships.[13]

CLINICAL NEED and BURDEN OF DISEASE

The prevalence of BPH increases with age and troublesome lower urinary tract symptoms (LUTS) occur in up to 30% of men older than 65 years. Around 40% of men aged 50 years have histological evidence of BPH, rising to 90% for men in their 80s.[14] Projections for the UK population and age-range changes are that the number of men in the UK aged 60-84 years will increase to 7.9 million in 2028. From a GP's perspective, these prevalence data translate to the average GP in England (with a typical list of 1,800 patients) having 50 male patients with moderate to severe LUTS, of which BPH is the most common cause.[15]

The health burden of BPH in the UK, as measured in years of healthy life lost per 100,000 men, peaks at age 75-79. The annual years of healthy life lost per 100,000 people from BPH in UK has increased by 18.0% between 1990 and 2013, an average of 0.8% a year.[16] The NHS England Hospital Episode Statistics for 2016/17 shows that hyperplasia of the prostate (ICD 10 code: N40) caused 34,567 finished consultant episodes (FCE), 32,540 hospital admissions, and 51,042 FCE bed days.[17]

PATIENT PATHWAY

RELEVANT GUIDANCE

NICE GUIDANCE

- NICE clinical guideline. Lower urinary tract symptoms in men: management (CG97). May 2010 (updated June 2015)
- NICE quality standard. Lower urinary tract symptoms in men. September 2013
- NICE interventional procedure guidance in development. Transurethral water ablation for benign prostatic hyperplasia (IPG10078). Expected publication date: TBC.
- NICE interventional procedure guidance in development. Transurethral water vapour ablation for benign prostatic hyperplasia (IPG10061). Expected publication date: TBC.
- NICE interventional procedure guidance in development. Prostate Artery Embolisation for Benign Prostatic Hyperplasia (IPG10055). Expected publication date: TBC.
- NICE interventional procedure guidance. Insertion of prostatic urethral lift implants to treat lower urinary tract symptoms secondary to benign prostatic hyperplasia (IPG475). January 2014
- NICE interventional procedure guidance. Prostate artery embolisation for benign prostatic hyperplasia (IPG453). April 2013
- NICE interventional procedure guidance. Laparoscopic prostatectomy for benign prostatic obstruction (IPG275). November 2008
- NICE interventional procedure guidance. Holmium laser prostatectomy (IPG17). November 2003
- NICE interventional procedure guidance. Transurethral electrovaporisation of the prostate (IPG14). October 2003
- NICE diagnostic guidance. Diagnosing prostate cancer: PROGENSA PCA3 assay and Prostate Health Index (DG17). June 2015
- NICE medical technologies guidance. GreenLight XPS for treating benign prostatic hyperplasia (MTG29). June 2016
- NICE medical technologies guidance. UroLift for treating lower urinary tract symptoms of benign prostatic hyperplasia (MTG26). September 2015
- NICE medical technologies guidance. The TURis system for transurethral resection of the prostate (MTG23). February 2015

NHS ENGLAND and POLICY GUIDANCE

- NHS England. The NHS England Innovation and Technology Tariff 2017 to 2019 Technical notes. Version 5.7
- NHS England. Items which should not routinely be prescribed in primary care: A Consultation on guidance for CCGs. July 2017. Version 1
- NHS England. Clinical Commissioning Policy: Urethroplasty for benign urethral strictures in adult men. July 2016

OTHER GUIDANCE

- Wu Y, Davidian MH, DeSimone II EM. Guidelines for the Treatment of Benign Prostatic Hyperplasia. US Pharm. 2016.[18]
- American Urological Association. Management of Benign Prostatic Hyperplasia (BPH). 2010 (Reviewed and Validity Confirmed 2014)[19]
- American Urological Association Education and Research, Inc. AUA Guideline on the Management of Benign Prostatic Hyperplasia: Diagnosis and Treatment Recommendations. 2003.[20]

- European Association of Urology. Guidelines on benign prostatic hyperplasia. 2002[21]

CURRENT TREATMENT OPTIONS

Treatment for an enlarged prostate gland will depend on the severity of the symptoms. The main treatments are lifestyle changes such as drinking less fizzy drinks and less alcohol, caffeine and artificial sweeteners. Also drinking less fluids in the evening, and frequent emptying of the bladder. Medications are offered when lifestyle changes are not helpful to reduce symptoms or are not suitable for the patient. Examples of these medications are:

- Alpha blockers
- Anticholinergics
- 5-alpha reductase inhibitors
- Diuretics
- Desmopressins.[10]

NICE pathways recommends offering 5-alpha reductase inhibitor to men with LUTS who have prostates estimated to be larger than 30 g or a prostate specific antigen (PSA) level greater than 1.4 ng/ml, and who are considered to be at high risk of progression (for example, older men). NICE also recommends offering a combination of an alpha blocker and a 5-alpha reductase inhibitor to men with bothersome moderate to severe LUTS and prostates estimated to be larger than 30g or a PSA level greater than 1.4 ng/ml.[22]

Patients may need catheterisation if they have difficulty in urination due to chronic renal failure. Surgery may be an option if other treatments have not worked.[10]

Most men with urinary symptoms don't need to have surgery, but it may be an option if other treatments haven't worked and the following procedures might be considered:[10]

- Transurethral resection of the prostate (TURP)
- Open prostatectomy
- Cystoplasty
- Botulinum toxin
- Implanted sacral nerve root stimulation
- Urinary diversion

EFFICACY and SAFETY

Trial	NCT00945490, NX02-0018; NX-1207 vs placebo; phase III
Sponsor	Nymox Pharmaceuticals Corporation
Status	Completed
Source of Information	Trial registry[3], Global Data[1]
Location	USA
Design	Randomized, placebo controlled
Participants	N=500; male; aged 45 years and older; American Urological Association Symptom Index (AUASI) ≥ 15; Prostate Volume ≥ 30 mL ≤ 70 mL; Qmax < 15 mL/sec based on a minimum void of 125 mL; Agree not to use any other

	approved or experimental BPH or Over Active Bladder (OAB) medication anytime during the study;
Schedule	Subjects are given a single intraprostatic injection of 2.5 mg NX-1207
Follow-up	Not reported
Primary Outcomes	American Urological Association Symptom Index (AUASI) [Time Frame: 365 days]
Secondary Outcomes	• American Urological Association Symptom Index (AUASI) [Time Frame: 90 days] • American Urological Association Symptom Index (AUASI) [Time Frame: 180 days] • American Urological Association Symptom Index (AUASI) [Time Frame: 270 days] • Peak urine flow rate (Qmax) [Time Frame: 365 days] • Peak urine flow rate (Qmax) [Time Frame: 90 days] • Peak urine flow rate (Qmax) [Time Frame: 180 days]
Key Results	Not reported
Adverse effects (AEs)	Not reported
Expected reporting date	Previously reported as May 2014.

Trial	NCT00918983, NX02-0017; NX-1207 vs placebo; phase III
Sponsor	Nymox Pharmaceuticals Corporation
Status	Completed
Source of Information	Trial registry,[4] Global Data[1]
Location	USA
Design	Randomized, placebo controlled
Participants	N=500; male; aged 45 years and older; International Prostate Symptom Score (IPSS) ≥ 15; Prostate Volume ≥ 30 mL ≤ 70 mL; Qmax < 15 mL/sec based on a minimum void of 125 mL; Agree not to use any other approved or experimental BPH or OAB medication anytime during the study;
Schedule	Subjects are given a single intraprostatic injection of 2.5 mg NX-1207
Follow-up	Not reported
Primary Outcomes	International Prostate Symptom Score (IPSS) [Time Frame: 365 days]
Secondary Outcomes	• International Prostate Symptom Score (IPSS) [Time Frame: 90 days] • International Prostate Symptom Score (IPSS) [Time Frame: 180 days] • International Prostate Symptom Score (IPSS) [Time Frame: 270 days] • Peak urine flow rate (Qmax) [Time Frame: 365 days] • Peak urine flow rate (Qmax) [Time Frame: 90 days] • Peak urine flow rate (Qmax) [Time Frame: 180 days]
Key Results	Not reported
Adverse effects (AEs)	Not reported

Expected reporting date	Previously reported as November 2013.

Trial	NCT01438775, NX02-0020; Two Doses 1-7 Years Apart; phase III
Sponsor	Nymox Pharmaceuticals Corporation
Status	Completed
Source of Information	Trial registry[5], Global Data[1]
Location	USA
Design	Single group assignment
Participants	N=192; male; aged 45 years and older; Be in good health; Received NX-1207 in a previous completed study or received NX-1207 or placebo in a concurrent U.S. study (NX02-0017 and NX02-0018) and completed their V10 (365 day) visit; Have Prostate Gland Volume ≥ 25 mL (25 g)
Schedule	A second transrectal intraprostatic injection of NX-1207 is given to subjects with BPH who previously received an injection of NX-1207 in an earlier U.S. clinical trial of NX-1207
Follow-up	Not reported
Primary Outcomes	Safety [Time Frame: 180 days]
Secondary Outcomes	• Symptomatic Improvement [Time Frame: 90 days] • Prostate Volume Change [Time Frame: 90 days] • Change in Urinary Peak Flow [Time Frame: 90 days] • Symptomatic Improvement [Time Frame: 180 days]
Key Results	Not reported
Adverse effects (AEs)	Not reported
Expected reporting date	Previously reported as January 2013.

ESTIMATED COST and IMPACT

COST

The cost of Fexapotide Triflutate is not yet known.

IMPACT – SPECULATIVE

IMPACT ON PATIENTS AND CARERS

☐ Reduced mortality/increased length of survival

☒ Reduced symptoms or disability

☐ Other

☐ No impact identified

IMPACT ON HEALTH and SOCIAL CARE SERVICES

☐ Increased use of existing services

☐ Decreased use of existing services

☐ Re-organisation of existing services

☐ Need for new services

☐ Other

☒ None identified

IMPACT ON COSTS and OTHER RESOURCE USE

☐ Increased drug treatment costs

☐ Reduced drug treatment costs

☐ Other increase in costs

☐ Other reduction in costs

☐ Other

☒ None identified

OTHER ISSUES

☐ Clinical uncertainty or other research question identified

☒ None identified

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