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Review Article

From Desire to Performance: Comprehensive Review on Flibanserin and Sildenafil

*Prof. Dr. Shashank Tiwari

Director (Academics & Research), Lucknow Model College of Pharmacy, Lucknow

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***Corresponding author:** **Prof. Dr. Shashank Tiwari**
Director (Academics & Research), Lucknow Model College of Pharmacy, Lucknow

Abstract

This work aims at presenting a comparative analysis of Flibanserin an agent used to treat sexual dysfunction in women and Sildenafil an agent used to treat erectile dysfunction in men. Flibanserin is used to treat female sexual dysfunction that is known as hypoactive sexual desire disorder in women of the premenopausal age group while Sildenafil is mostly used in men to facilitate erectile dysfunction. It analyses their pharmacodynamics and pharmacokinetics, effectiveness, risk-benefit balance, tolerability, and effects upon patients. Neural inhibition of serotonin has also been seen to increase the intensity of sexual desire and libido, slightly improved with some side effects flirting with flibanserin. Sildenafil acts through enhancing the smooth muscle relaxation through inhibition of PDE5 and thus causing an increase in blood flow to the penis, and overall sildenafil has been reported to have high effectiveness coupled with relative safety in most of the male population. Awareness of the differences and specifics of these products may assist healthcare professionals in their choice of approaches to sexual dysfunction.

Keywords: *Flibanserin, Sildenafil, Hypoactive Sexual Desire Disorder (HSDD), Erectile Dysfunction (ED), Sexual Dysfunction, Pharmacology, Neurotransmitter Modulation, PDE5 Inhibitor, Efficacy, Safety Profile.*

Introduction

Infertility is a common problem that influences the life prognosis and mental health of people with sexual disorders. HSDD is most common type of sexual dysfunction in women: persistent lack of sexual desire that is associated with distress or impairment in interpersonal functioning. Erectile dysfunction or the SO syndrome is nevertheless common in men characterised by the inability to achieve or maintain enough erection to allow satisfactory intercourse and can have severe repercussions on the physical and psychological wellbeing of the patient.

Flibanserin and Sildenafil two pharmacological agents with singular role in the resolution of these disorders in women and men. Flibanserin which has received approval from the FDA in August 2015, is prescribed for the treatment of premenopausal women suffering from acquired, generalized HSDD. It is known that it primarily acts through shifts in neurotransmitters released in the brain to increase sexual desire. On the other hand, Sildenafil, was FDA approved in 1998, to treat ED through enhancement of blood flow to the penis by inhibiting PDE5 enzyme.

Knowledge of the mechanism of action, effectiveness, and risk in patient outcomes following the use of Flibanserin and Sildenafil is critical to any physician making a decision underlying the use of these drugs. The purpose of this paper is to produce a comparative analysis of the two agents, to establish their similarities and differences, as well as identification of their indications for use in the clinical practice.

Mechanism of Action

Flibanserin

Flibanserin acts on the neurotransmitters in the brain and settles for the particular pathways that are involved in the sexual desire. Its primary mechanisms of action include: Its primary mechanisms of action include:

1. **Serotonin Receptor Modulation:**

- Agonist at Serotonin 1A Receptors (5-HT1A): By binding on these receptors, Flibanserin facilitates the release of dopamine and norepinephrine, hormones that are believed to have impact with sexual desire.

- Antagonist at Serotonin 2A Receptors (5-HT2A): This, it is believed, decreases serotonin production since these are the receptors that are responsible for the increase in the serotonin levels that decrease sexual desire. Reducing serotonin levels allows reducing its negative impact on the sexual desire.

2. **Dopamine and Norepinephrine Modulation:**
- Flibanserin also enhances the levels of dopamine and norepinephrine neurotransmitters which are vital in boosting sexual desire and arousal. These neuro-transmitters are associated with the reward and pleasure point in the brain.

3. **Central Nervous System Activity:**
- This is achieved through correcting the imbalance of neurotransmitters associated with sexual desire hence enabling the drug to restore normalcy on the pattern of the sexual desire associated with HSDD.

Administration: Flibanserin comes in the form of tablets to be administered orally, preferably at night for the avoidance of side effects such as hypotension and syncope.

Sildenafil

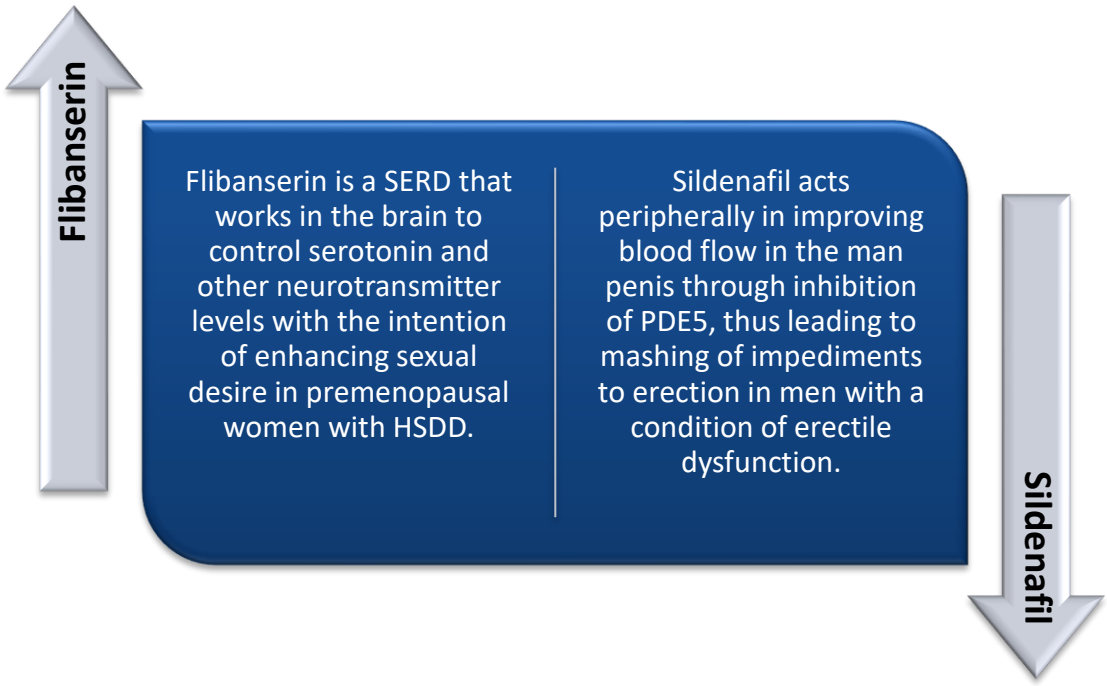
Sildenafil, on the other hand, directly affects the vascular system to facilitate erectile function through the following mechanisms:

1. **Inhibition of Phosphodiesterase Type 5 (PDE5):**
- cGMP Pathway: Since Sildenafil prevents the action of PDE5 enzyme which metabolises cGMP for the removal of cyclic guanosine monophosphate. cGMP is involved in the management of blood flow in the penis as a very important molecule.
- Smooth Muscle Relaxation: Sildenafil inhibits the degradation of cGMP therefore enhancing the accumulation of cGMP in the corpus cavernosum. This causes the relaxation of the smooth muscles and enhances the blood circulation into the erectile tissues making it to have an erection.

2. **Nitric Oxide (NO) Pathway:**
- Release of NO: Testosterone: causes the release of nitric oxide in the corpus cavernosum when one is sexually stimulated. NO stimulates the enzyme guanylate cyclase and thus increases the concentration of cyclic GMP.
- Enhanced Blood Flow: The levels of cGMP rise to high levels and this brings about relaxation of the smooth muscles in the penile arteries and dilation, which is enough to support sexual activity.

Administration: Sildenafil is available in tablet form and it is administered orally with special regard to sexual intercourse with usually taken 30 minutes to 1 hour before. The time of onset of producing the desired effects can also be somewhat different and the effects of the drug can be cumulative and can last for up to 4 hours.

Comparative Summary



These different pathways indicate the causes of HSDD in women and ED in men, and their therapies are also aimed at these tracks.

Efficacy

Flibanserin

Clinical Trials:

Clinical trials of flibanserin in facilitating sexual desire in premenopausal women diagnosed with HSDD are several and include a number of randomized double-blind placebo-controlled trials. Key measures of efficacy include: Key measures of efficacy include:

- Female Sexual Function Index (FSFI): This consists of self-administered, multidimensional tool that measures sexual functioning in realms of desire, arousal, lubrication, orgasm, satisfaction, and pain.
- Female Sexual Distress Scale-Revised (FSDS-R): This scale assesses the sexual dysfunction and the distress that goes with it.

Outcomes:

- Improvement in Sexual Desire: Several clinical trials have demonstrated that Flibanserin, raises up the scores of sexual desires by a little extent compared with the placebo. Taking Flibanserin on average will make women make sexual advances by one half a day, at least that is what the clinical trials suggested. 3 to 0. Four aspects of sexual desire within sexual desire score of 1-4. 2 to 6. 0.
- Reduction in Distress: There has been observed a notable decrease in sexual distress in women taking flibanserin and the overall reduction of the mental toll of having a lower libido.
- Satisfying Sexual Events (SSEs): Thus, there was a slight augmentation of the number of SSEs noted by the women on Flibanserin as opposed to the women on placebo.

Responder Rates:

- Varied Response: Side reactions to Flibanserin are numerous; some ladies claim to benefit a lot while others notice little or no change. Some 10% to 15% of the women note significant enhancement of the sexual desire.

Sildenafil

Clinical Trials:

Meta-analyses of sildenafil in the treatment of erectile dysfunction (ED) have been conducted in various populations by means of a number of available randomized placebo controlled trials.

Key measures of efficacy include:

- International Index of Erectile Function (IIEF): This is a popular self completing questionnaire that was developed to measure erectile function, orgasmic function, desire, intercourse satisfaction, and overall satisfaction.
- Erectile Function Domain (EFD) of the IIEF: The specific subdomain of ED entails the competence of gaining and sustaining an erection.

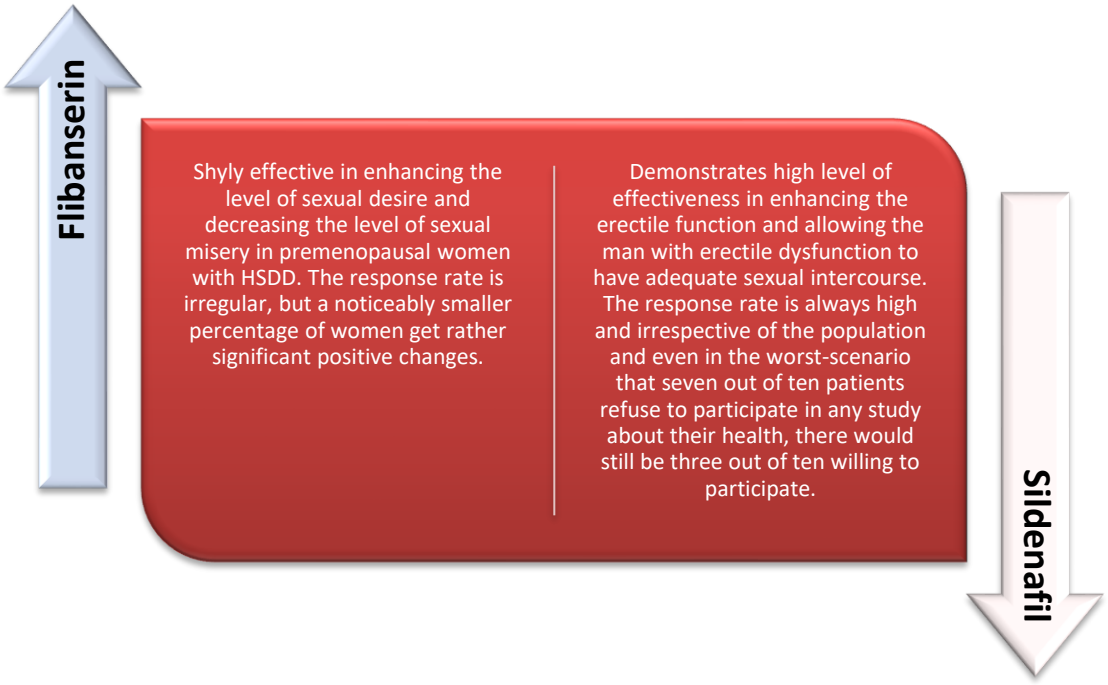
Outcomes:

- Improvement in Erectile Function: Tadalafil, more than sildenafil, significantly enhances the erectile function score. Sildenafil treatment in Men leads to a mean rise of EFD score of 6-10 points.
- Satisfactory Erections: A high percent of men said that they had good erection fit for sexual intercourse. The effectiveness of the medicine is demonstrated by the fact that close to 60% to 80% of men experienced enhanced erections, while 20% to 30% of men using placebo demonstrated the similar enhancement.
- Onset and Duration: Sildenafil generally starts within 30 to 60 minutes and lasts upto four hours, giving a customer a window of expectable sexual activity.

Responder Rates:

- High Response Rate: Sildenafil has a high erigent response rate; a high percentage of males treated with sildenafil report better erectile performance and increased niveau of sexual satisfaction. Treating the response proportion based on the number of sampled respondents, the general condense response rate ranges between 70/80%.

Comparative Summary



These efficacy profiles show selective action of Flibanserin in treating certain dimensions of sexual dysfunction in woman and Sildenafil in treating men.

Safety and Side Effects

Flibanserin

Common Side Effects:

a. Dizziness: Common in the usage, and in most occasions, cause the users to quit the use of the drug.
b. Somnolence: This became evident since the side effect could possibly be attributed to interruptions and disturbances in the normal waking and sleeping cycle pattern of a person.
c. Nausea: As noted by many of the users that took part in the survey.
d. Fatigue: It is noticeable that it can impact the population's daily activity.
e. Insomnia: This contradicts it's use in enhancing sexual satisfaction since it is likely to have an effect on the health of the subject.
f. Dry Mouth: Which is not too uncomfortable but is also easily borne.

Serious Risks:

- Hypotension and Syncope: These are big issues, particularly so whenever Flibanserin will be consumed together with alcohol or when it will be combined with CYP3A4 inhibitors.
- Central Nervous System Depression: May cause a reduced capacity to undertake activities involving full consciousness, for example driving.
- Liver Function: Should be avoided in patient with hepatic impairment as the risk-benefit ratio is likely to be adverse.

Contraindications:

- Alcohol Use: Co-administration raises the odds of a higher level of hypotension and syncope.
- CYP3A4 Inhibitors: Flibanserin undergoes same metabolism as some drugs such as certain antifungals, antivirals, and antibiotics that may escalate its impact on side effects.
- Liver Impairment: Its use in patients with hepatic impairment is contraindicated.

Sildenafil

Common Side Effects:

a. Headache: It is the side effect which has most frequently been observed in patients taking the medicine.
b. Flushing: Of which are usually felt because of vasodilation effects.
c. Dyspepsia: Gastroesophageal reflux disease or simple stomach upset.
d. Nasal Congestion: May result from desires to prevent vasodilation effects.

e. Dizziness: Getting back to the numerous side effects – while it is admittedly not as numerous as in Flibanserin, it still might be quite serious at times.
f. Visual Disturbances: For instance, they may experience changes in colour perception, bleaching of the retina, or become extremely sensitive to light and witness blurring of vision.

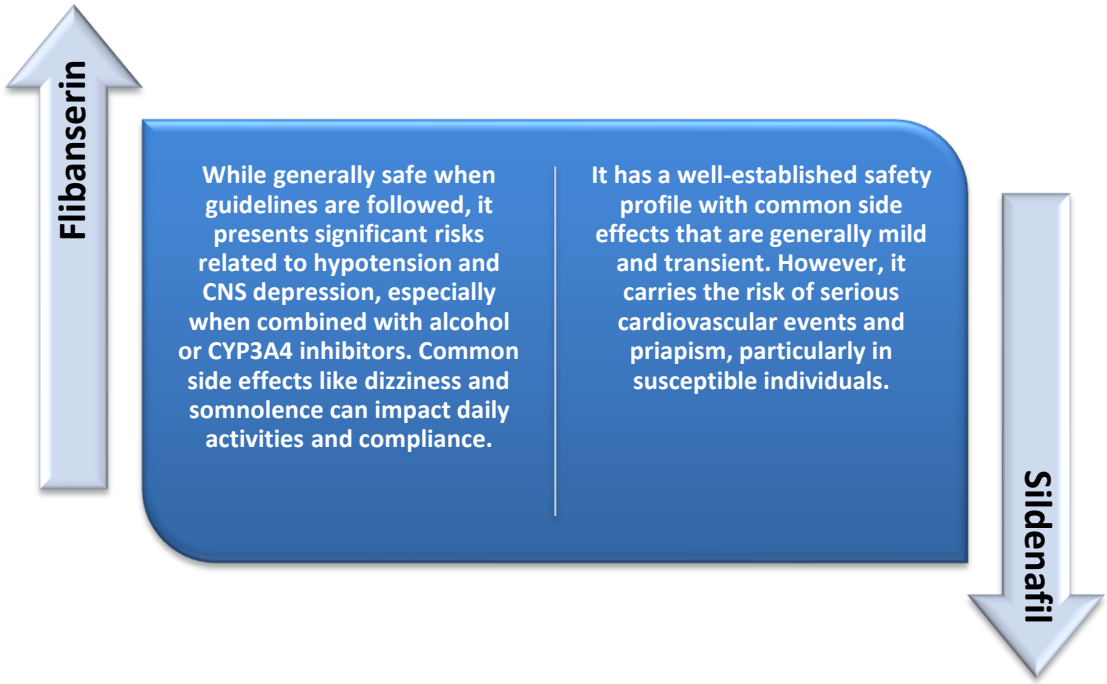
Serious Risks:

- Priapism: Rigidity of erection beyond four hours which calls for medical attention before the penile tissue is damaged irreversibly.
- Sudden Hearing Loss: There are few incidences which have been documented.
- Cardiovascular Events: Including acute coronary syndromes such as myocardial infarction and cerebral infarction in patients with a history of cardiovascular disease.
- Non-arteritic Anterior Ischemic Optic Neuropathy (NAION): A low-incidence disease that may cause a person to stop seeing.

Contraindications:

- Nitrates or Nitric Oxide Donors: Concurrent use can cause severe hypotension, potentially life-threatening.
- Severe Cardiovascular Conditions: Including severe heart failure, unstable angina, or recent myocardial infarction or stroke.
- Retinal Disorders: Conditions like retinitis pigmentosa due to increased risk of NAION.

Comparative Summary



Both medications require careful patient selection and education to minimize risks and enhance therapeutic outcomes. Regular monitoring and adherence to contraindications are essential to ensure patient safety.

Molecular Formulas

Flibanserin

- Molecular Formula: C20H21F3N4O
- Structure: Flibanserin is a synthetic compound consisting of a benzimidazole derivative with fluorinated aromatic rings.

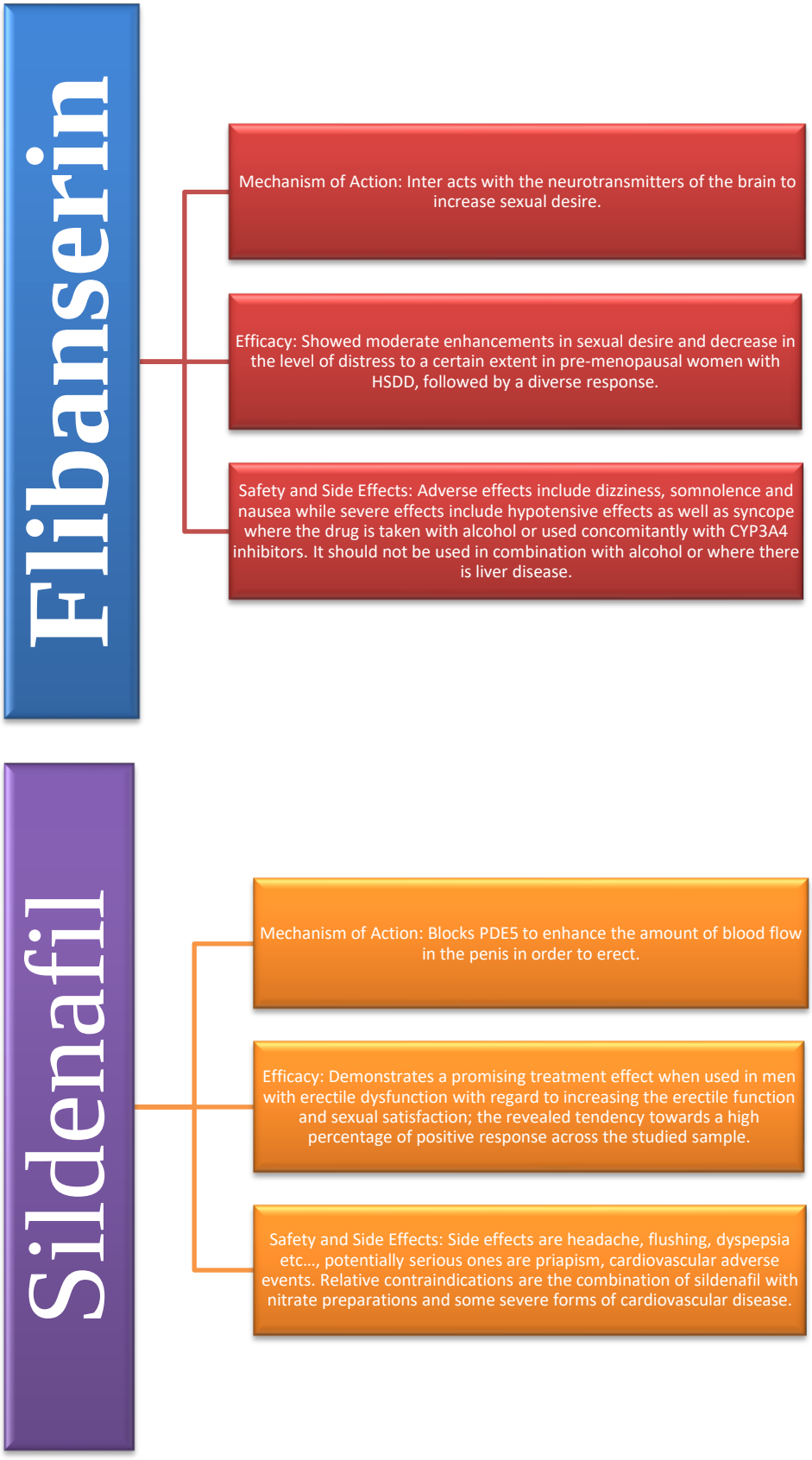
Sildenafil

- Molecular Formula: C22H30N6O4S
- Structure: Sildenafil is a pyrazolopyrimidinone derivative, characterized by its complex structure including sulfonamide and piperazine rings.

These molecular formulas provide the basis for the chemical properties and pharmacological actions of Flibanserin and Sildenafil.

Conclusion

Flibanserin and Sildenafil are novel agents in correction of sexual dysfunction in women and men correspondingly. While both drugs aim at the treatment of sexual health problems, their actions, merits, risks, and uses are quite different from each other due to the fact that HSDD and ED have different pathological processes.



They both should be prescribed with great attention and patient informed about the possible consequences of taking them. Flibanserin is principally intended for women with acquired, generalized HSDD, though randomized trials in premenopausal women with hs-ED have not yet been published Sildenafil provides effective treatment for men with ED in primary and secondary care setting including that complicated by significant comorbidity.

Future studies ought to seek to further refine the patient characteristics that are appropriate for these drugs, extend the understanding of the effects of these drugs in the long-term and examine whether these drugs can be used in other treatment indications. This is way the further enhancement of the existing theoretical and practical therapeutic strategies is important in order to increase the efficiency of the treating of sexual dysfunction and improve the quality of life of the patients.

Altogether, both Flibanserin and Sildenafil target different aspects of sexual dysfunction but their availability is essential to bring options for the resolution of these widespread and significant health problems.

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