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# Effectiveness and Safety of Oro-Dispersible Sildenafil in a New Film Formulation for the Treatment of Erectile Dysfunction: Comparison Between Sildenafil 100-mg Film-Coated Tablet and 75-mg Oro-Dispersible Film

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## ABSTRACT

**Background:** A new oro-dispersible film (ODF) formulation of sildenafil has been developed for the treatment of erectile dysfunction (ED) to overcome the drawbacks that some patients experience when taking the conventional film-coated tablet (FCT).

**Aim:** To assess the effectiveness and safety of sildenafil ODF formulation in patients with ED who were using the conventional FCT.

**Methods:** From May 2017 through July 2017, 139 patients with ED were enrolled. Data from penile color-duplex ultrasound, medical history, hormonal evaluation, and patient self-administered questionnaires were collected. All patients were administered sildenafil 100-mg FCT for 4 weeks. Thereafter, they underwent a 2-week washout period and subsequently took sildenafil 75-mg ODF for 4 weeks.

**Outcomes:** The International Index of Erectile Function (IIEF-15), Hospital Anxiety and Depression Scale (HADS), Patient Global Impressions of Improvement (PGI-I), and Clinician Global Impressions of Improvement (CGI-I) questionnaires were administered and severity of ED was classified as severe (IIEF-15 score $\leq 10$), moderate (IIEF-15 score 11−16), or mild (IIEF-15 score = 17−25).

**Results:** All patients completed the final protocol. Differences in mean IIEF scores for erectile function, orgasmic function, sexual desire, and intercourse satisfaction were significantly in favor of sildenafil 100-mg FCT, whereas the mean score for overall satisfaction was in favor of sildenafil 75-mg ODF. A significant difference in changes in HADS score was found from washout to final follow-up (mean difference = −0.19; $P < .01$). For the ODF formulation, the median CGI-I score was 3.5 (interquartile range [IQR] = 2.5−4.5) and the median PGI-I score was 3.0 (IQR = 2.0−4.0). The median action time was 20.0 minutes (IQR = 15.0−30.0) and the median mouth time was 60.0 seconds (IQR = 30.0−120.0).

**Clinical Implications:** The ODF formulation of a widely known drug, with the same safety and effectiveness of the FCT, was better appreciated by patients in overall satisfaction.

**Strengths and Limitations:** This is the first clinical trial to assess the efficacy of a new formulation of sildenafil in patients with ED. The limitations of the study are related to the methodology used: it was not a case-control study and the patients were not drug-naïve for ED treatment. Therefore, only the "additional" side effects of the ODF formulation compared with FCT are reported.

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**Conclusion:** The new ODF formulation is as efficient and safe as the FCT formulation and offers a new choice of treatment to specialists for more precisely tailored therapy. **Cocci A, Capece M, Cito G, et al. Effectiveness and Safety of Oro-Dispersible Sildenafil in a New Film Formulation for the Treatment of Erectile Dysfunction: Comparison Between Sildenafil 100-mg Film-Coated Tablet and 75-mg Oro-Dispersible Film. J Sex Med 2017;14:1606−1611.**



**Key Words:** Erectile Dysfunction; Impotence; Sildenafil Citrate; Therapeutics

## INTRODUCTION

Erectile dysfunction (ED) is defined as the inability to obtain or maintain an erection sufficiently rigid for achieving satisfactory sexual performance.[1] It affects nearly 50% of men older than 40 years, causing patients serious distress and prompting them to seek medical opinions they might not otherwise seek.[2]

ED has a significant impact on the quality of life of patients because it influences the self-perception and sexuality of those men and might undermine their interactions with women or potential partners.[3] Because sexual satisfaction is considered a major predictor of life satisfaction, treatment of ED would likely improve the quality of life for these patients and their partners.[4]

Many therapeutic options are available for the treatment of ED. One option is the use of phosphodiesterase type 5 inhibitors (PDE5is). PDE5is, including sildenafil, tadalafil, vardenafil, and avanafil, are currently approved for use in ED and each has an individual pharmacokinetic and side effects profile, although no significant differences in efficacy among therapies are evident.[1,5−8]

Sildenafil, the first approved PDE5i, is a safe and effective oral agent for the treatment of ED and is predominantly metabolized by cytochrome P-450 into an *N*-desmethyl metabolite (*N*-desmethyl sildenafil) that accounts for approximately 1 fifth of the drug's activity.[9,10]

Oral administration of a tablet can lead to 2 types of effects. (i) The original formulation is inconvenient for patients because water is required for the medicine to be taken. (ii) Oral administration of the tablet relies on the patient's ability to swallow the dosage safely, which could be problematic for individuals who have swallowing disorders. Dysphagia has an estimated of 22% in patients older than 50 years.[11] To overcome these drawbacks, a new oro-dispersible film (ODF) formulation was developed. It is quickly dispersed in the mouth and can be administered without water.[12]

According to the Biopharmaceutics Classification System, sildenafil is classified as a class II drug substance (high permeability and low solubility). The new sildenafil ODF formulation, developed by IBSA (Lugano, Switzerland), is approved in Europe at doses of 25, 50, 75, and 100 mg. Each sildenafil 75-mg ODF contains sildenafil citrate 105.3 mg, equivalent to sildenafil 75 mg, in the form of a rectangular, flexible, opaque, light-blue film measuring 40 × 45 mm, whereas each sildenafil 100-mg film-coated tablet (FCT) contains sildenafil citrate 140.4 mg, equivalent to sildenafil 100 mg. A previous study compared the 2 treatments with the same active substance but with different dosages and different formulations. It was a non-inferiority study of the 2 treatments for effectiveness, not for bioequivalence.[13] The ODF formulation is an innovative patented product developed in accordance with EP 1689374 (self-supporting films for pharmaceutical and food use) and WO 2014/049548 (ODFs with quick dissolution times for therapeutic and food use).[13]

We evaluated the efficacy and safety of the sildenafil ODF formulation in patients with ED who were taking the conventional sildenafil FCT.

## METHODS

From May 2017 through July 2017, we enrolled 139 patients with a history of chronic ED. The etiology of ED was determined, in all cases, by a standard protocol involving penile color-duplex ultrasound, complete medical history, hormonal evaluation, and patient self-administered questionnaires on sexual function. We measured serum concentrations of follicle-stimulating hormone (normal range = 1.5−8.0 IU/L), prolactin (3.0−18 ng/mL), thyroid-stimulating hormone (0.3−5.5 mIU/L), luteinizing hormone (1.8−12 IU/L), and total testosterone (2.7−18 ng/mL).

Inclusion criteria were heterosexual men younger than 75 years, presence of ED evaluated through the International Index of Erectile Function (IIEF), sexual intercourse at least 2 times per week, an Eastern Cooperative Oncology Group (ECOG) scale of performance status score no higher than 1, absence of moderate or severe cardiovascular diseases, and moderate ED according to penile dynamic Doppler examination. All patients enrolled in the study were eligible for first-line therapy of ED based on PDE5i, according to European Association of Urology, American Urological Association, and International Society for Sexual Medicine guidelines. Exclusion criteria were being unable or unwilling to provide informed consent, an IIEF score lower than 16, presence of unstable coronary artery disease (ECOG score > 1), sexual intercourse no more than 1 time per week, concomitant use of nitrates in any form, and known hypersensitivity to sildenafil or its components. Men with ED based on neurogenic, hormonal, or anatomic conditions and those who underwent previous surgical treatment of the penis or pelvic area were excluded from the study.