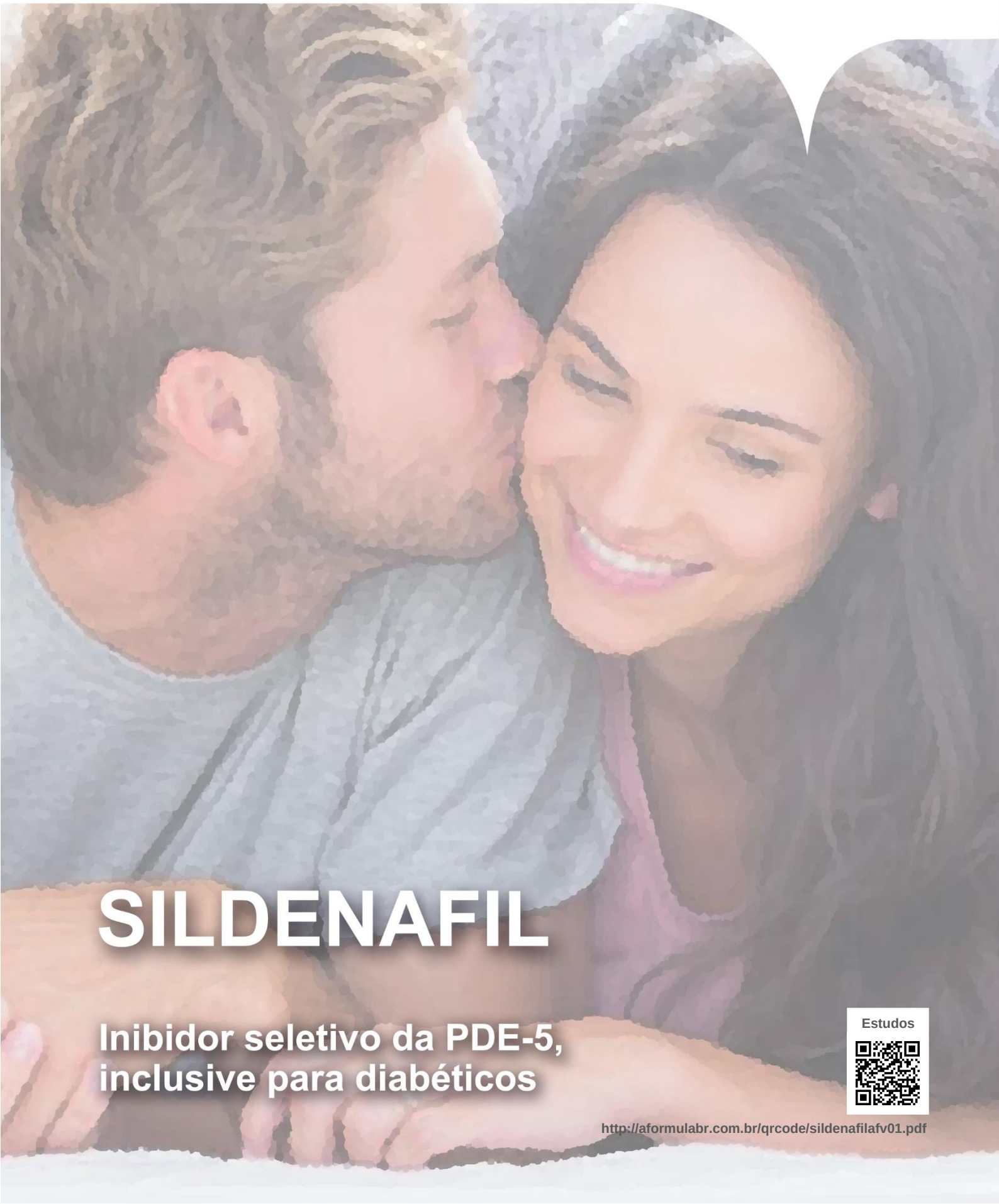
a fórmula



# SILDENAFIL

## Inibidor seletivo da PDE-5, inclusive para diabéticos

Estudos

http://aformulabr.com.br/qrcode/sildenafilafv01.pdf

a fórmula

# SILDENAFIL

**Inibidor seletivo da PDE-5, inclusive para diabéticos**

## DESCRIÇÃO

O **Sildenafil** é um inibidor seletivo da PDE-5, utilizado para melhorar a circulação sanguínea principalmente no órgão genital masculino.

## MECANISMO DE AÇÃO

O **Sildenafil** inibe a fosfodiesterase tipo 5 (PDE-5) que degrada o GMPc conservando seus níveis nos corpos cavernosos, mantendo a vasodilatação local, além de um maior influxo de sangue gerando a ereção peniana. O **Sildenafil** atua da mesma forma com a PDE-5 presente na musculatura lisa das artérias pulmonares, promovendo vasodilatação e reduzindo a hipertensão arterial pulmonar.

## INDICAÇÕES

- ✓ Tratamento da disfunção erétil e impotência;
- ✓ Hipertensão pulmonar.

## DOSE USUAL

Recomendação oral de 15 a 100mg de **Sildenafil** ao dia.

## SUGESTÕES DE FÓRMULAS

**Sildenafil**..... 20 mg
Tablete sublingual qsp..... 1 unidade

**Modo de uso**: 1 unidade, embaixo da língua ao dia.
**Indicação**: disfunção erétil.

**Sildenafil citrato**..... 10 mg
Base transdérmica/Pentravan® qsp..... 1 ml

**Modo de uso**: aplicar 1 ml na glande espalhando uniformemente até absorção completa, 5 minutos antes do ato sexual.
**Indicação**: disfunção erétil.

**Sildenafil**..... 25 mg
Doxazina..... 4 mg

**Modo de uso**: 1 dose ao dia ou conforme orientação do prescritor.
**Indicação**: disfunção erétil, LUTS (Lower Urinary Tract Symptoms), hiperplasia prostática benigna.

## PRINCIPAIS REFERÊNCIAS


BATISTUZZO, J. A O; ITAYA, M.; ETO, Y. **Formulário Médico-Farmacêutico**. 4 ed. São Paulo: Pharmabooks, 2015.

LACY F.C.; ARMSTRONG L.L.; GOLDMAN M.P.; LANCE L.L. Drug Information Handbook. **American Pharmacists Association.** Lexi-Comp. 23ª edição, 2014-2015.

# SILDENAFIL

## ESTUDOS CLÍNICOS

**Efficacy and Safety of Sildenafil by Age in Men With Erectile Dysfunction.**

INTRODUCTION: Sildenafil, an oral phosphodiesterase type 5 inhibitor, has been extensively investigated for the treatment of erectile dysfunction in randomized controlled trials. AIM: To assess the efficacy and safety of sildenafil vs placebo according to age subgroups (<65, 65-74, and ≥75 years) in 11,364 men with erectile dysfunction using pooled data from 48 randomized, double-blinded, placebo-controlled, parallel-group, flexible-dose trials. METHODS: Most trials had a 12-week treatment duration. The starting sildenafil dose was 50 mg, taken 1 hour before sexual activity, with subsequent adjustment to 100 or 25 mg based on efficacy and safety. Men taking nitrate therapy or nitric oxide donors and men with severe cardiac failure, unstable angina, or recent stroke or myocardial infarction were excluded. Efficacy analyses included all subjects with baseline and at least one postrandomization evaluation. Safety analyses included subjects who received study medication. MAIN OUTCOME MEASURES: The International Index of Erectile Function and a global assessment question ("Did the treatment improve your erections?"). RESULTS: Mean International Index of Erectile Function scores for question 3 (frequency of penetration), question 4 (maintenance of erections after penetration), and the erectile function domain were statistically significantly improved with sildenafil vs placebo for each age subgroup; orgasmic function, intercourse satisfaction, sexual desire, and overall satisfaction domain scores also were statistically significantly improved with sildenafil vs placebo. The percentage of men reporting improved erections on the global assessment question was statistically significantly higher with sildenafil vs placebo for all age subgroups; the percentage with sildenafil tended to decrease with increasing age (<65 years, 80%; 65-74 years, 69%; ≥75 years, 59%). The most common adverse events with sildenafil were headache and flushing in each age subgroup. CONCLUSION: Sildenafil is an effective and well-tolerated treatment for erectile dysfunction regardless of patient age, including men at least 75 years old.

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**[Efficacy of sildenafil citrate in men with erectile dysfunction following bilateral nerve-sparing radical prostatectomy: systematic review and meta-analysis].**

OBJECTIVE: To systematically assess the efficacy and safety of oral sildenafil citrate for post bilateral nerve-sparig radical prostatectomy (post-BNSRP) erectile dysfunction (ED). METHODS: The following keywords: sildenafil, radical prostatectomy were used to search in Medline, Pubmed, Web of Science, Cochrane Library, CNKI, WanFang Database. The title, abstract and keywords of each article were independently screened by two reviewers. Randomized controlled trials (RCT) published between 1990 and 2014 were retrieved according to our inclusion and exclusion criteria. The efficacy and safety of oral sildenafil citrate for post-BNSRP ED were systematically assessed by meta-analysis. RESULTS: Four RCTs with 320 cases were included after literature retrieval and filtering. The potency rates were 32.1% (35/109) and 11.3% (7/62) between sildenafil and placebo groups after meta-analysis and showed statistically significant differences (OR = 4.66, 95% CI: 1.79-12.11). IIEF-5 score in sildenafil group was significant higher than that in the placebo group (WMD: 4.73, 95% CI: 3.26-6.19). In subgroup meta-analysis, the potency rates in high-dose, low-dose sildenafil groups and placebo groups were 30.4% (14/46), 25.0% (10/40) and 4.5% (2/44), respectively. There were statistically significant differences between the high-dose subgroup and placebo group (OR = 9.32, 95% CI: 1.96-44.23), and the low-dose subgroup and placebo group (OR = 6.99, 95% CI: 1.43-34.22). But there was no significant difference between high-dose and low-dose subgroups (OR = 1.31, 95% CI: 0.51-3.40). CONCLUSIONS: Compared with placebo, sildenafil has considerable efficacy for erectile function rehabilitationas as a primary treatment for post-BNSRP ED. There is no significant difference between high-dose and low-dose schedule for its efficacy. However, further studies are required to optimize treatment.

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**Phosphodiesterase 5 inhibitors for the treatment of erectile dysfunction: a trade-off network meta-analysis.**

CONTEXT: Erectile dysfunction (ED) is a major health care problem worldwide and phosphodiesterase 5 inhibitors (PDE5Is) are the pharmacological treatment of choice. However, the optimal PDE5I for ED treatment is not known. OBJECTIVE: To investigate trade-offs between efficacy and adverse events for various PDE5Is in treating ED.

EVIDENCE ACQUISITION: A review was performed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Statement. Medline, Scopus, reference lists of relevant articles, and systematic reviews were searched. Eligible studies were randomized controlled trials comparing at least one PDE5I for treating ED with placebo or another PDE5I. EVIDENCE SYNTHESIS: We included 82 trials (47 626 patients) for efficacy analysis and 72 trials (20 325 patients) for adverse event analysis. In the trade-off analysis of starting dosages, sildenafil 50mg had the greatest efficacy but also had the highest rate of overall adverse events. Tadalafil 10mg had intermediate efficacy but had the lowest overall rate of all adverse events. Vardenafil 10mg and avanafil 100mg had similar overall adverse events than sildenafil 50mg but a markedly lower global efficacy. Udenafil 100mg had similar global efficacy to that of tadalafil 10mg but its overall adverse event rates were higher. CONCLUSIONS: This is the first trade-off analysis of the different PDE5Is currently available. For individuals who prioritize high efficacy, sildenafil 50mg appears to be the treatment of choice. Men wishing to optimize tolerability should take tadalafil 10mg or switch to udenafil 100mg in the case of insufficient efficacy. PATIENT SUMMARY: For patients with erectile dysfunction who wish to prioritize high efficacy, sildenafil 50mg appears to be the treatment of choice. Men who wish to optimize tolerability should take tadalafil 10mg or switch to udenafil 100mg in the case of insufficient efficacy.

**Phosphodiesterase-5 inhibitors for erectile dysfunction in patients with diabetes mellitus: A systematic review and meta-analysis of randomized controlled trials.**

BACKGROUND AND AIMS: Patients with diabetes mellitus frequently experience erectile dysfunction. This systematic review and meta-analysis were conducted to find efficacy and tolerability of phosphodiesterase 5 (PDE5) inhibitors in patients with diabetes mellitus experiencing erectile dysfunction. METHODOLOGY: Electronic searches were carried out to identify English language peer-reviewed randomized controlled trials (RCTs), which reported clinical efficacy of any PDE5 inhibitor in patients with diabetes mellitus having erectile dysfunction. Effect sizes were computed using Cohen's d, and I(2) -test was used to assess heterogeneity. Pooled mean effect sizes were computed using random-effects model. Number needed to treat (NNT), and the adverse event rates were computed. RESULTS: The systematic review included a total of 17 studies yielding 25 comparisons. Three studies were open RCTs while others were double-blind RCTs. The pooled mean effect size of any PDE5 inhibitor over placebo was 0.926 (95% confidence intervals [CI]: 0.864-0.987; I(2) =26.3). The pooled mean effect size for sildenafil was 1.198 (CI: 1.039-1.357; I(2) =0), for tadalafil was 0.910 (CI: 0.838-0.981; I(2) =33.6), and for vardenafil was 0.678 (CI: 0.627-0.729; I(2) =0). In pooled analysis, the NNT for sildenafil, tadalafil, vardenafil and any PDE5 inhibitor was 2.4, 2.6, 4.1 and 3.0 respectively. The most common side effects were headache, flushing, and nasal congestion. CONCLUSIONS: PDE5 inhibitors are effective and safe medications for the treatment of sexual dysfunction in patients with diabetes mellitus experiencing erectile dysfunction.

**Effectiveness of Phosphodiesterase 5 Inhibitors in the Treatment of Erectile Dysfunction in Patients with Spinal Cord Trauma: Systematic Review and Meta-Analysis.**

OBJECTIVE: To determine the effectiveness of the Phosphodiesterase 5 (PDE5) Inhibitors for the treatment of erectile dysfunction in patients with spinal trauma. METHODS: A systematic review and meta-analysis comparing PDE5 inhibitors versus placebo were carried out for clinical trials conducted between 1980 and 2014 that evaluated male patients older than 18 years, diagnosed with spinal cord trauma and erectile dysfunction. We designed a search strategy for Medline, CENTRAL, EMBASE and other electronic sources. Two investigators independently and blindly screened the studies for inclusion. A random effect meta-analysis was performed. RESULTS: Six studies involving 963 patients were included. Male patients over 18 years with ED attributable or subsequent to traumatic spinal cord injury (SCI) were included from these studies. In 4 of these studies, patients were randomized to the treatment group receiving sildenafil and the comparison group was placebo. Out of the remaining 2 trials, one compared tadalafil against the placebo and the other vardenafil versus placebo. The improvement on SCIs with PDE5 inhibitors was found to be large (standardized mean difference 0.71; 95% CI 0.39-1.03), with a high heterogeneity (I2 = 74.4%). CONCLUSIONS: PDE5 inhibitors are effective for the treatment of erectile dysfunction secondary to SCI.

**The effect of lifestyle modification and glycemic control on the efficiency of sildenafil citrate in patients with erectile dysfunction due to type-2 diabetes mellitus.**

OBJECTIVES: We evaluated the effect of lifestyle modifications and glycemic control on the efficiency of sildenafil citrate in patients with type-2 diabetes (T2DM) and erectile dysfunction (ED). METHODS: Eighty-three men with ED due to T2DM were included in the study. The Group 1 (n = 41) patients received lifestyle modifications (diet and exercise), and medical treatment for intensive glycemic control. In Group 2 (n = 42), in addition to the intensive glycemic control, the patients were given sildenafil citrate® 100 mg for 2-3 per weeks. The changes in ED were compared between the two groups after three months of treatment. RESULTS: The mean age was 54.9 ± 9.1 (26-75) years. An increase in the IIEF-5 scores was observed in 23 of 41 patients in Group 1 (44.2%) and 29 of 42 in Group 2 (55.8%). When the changes of the IIEF-5 scores were evaluated, the mean increase was 2.5 in Group 1, and 5.0 in Group 2 (p = 0.012). The mean IIEF changes according to the duration of diabetes were 4.8 in <5 years, 3.6 in 5-10 years and 1.6 in >10 years (p = 0.021). CONCLUSIONS: Glycemic control and lifestyle changes are not solely adequate for a better sexual function in ED due to diabetes, and sildenafil citrate should be used additionally.

**Daily use of sildenafil improves endothelial function in men with type 2 diabetes.**

Diminished vascular endothelial function results in decreased vasodilator capacity and is associated with erectile dysfunction (ED) in patients afflicted with type 2 diabetes. The current study was designed to evaluate whether daily use of sildenafil could alter endothelial function and improve penile rigidity in a group of patients with diabetic ED. A double-blind, placebo-controlled, prospective trial was conducted with 24 men with type 2 diabetes who were randomized into 2 groups: one receiving daily sildenafil (50 mg, n = 12) and the other placebo (n = 12) for 10 weeks. Erectile function was captured subjectively using the International Index of Erectile Function (IIEF-5), and endothelial function was objectively monitored via brachial artery flow-mediated dilation. Among the placebo and sildenafil groups, there were no significant differences in average patient age, time from type 2 diabetes diagnosis, duration of ED, or baseline IIEF-5 scores. Past medical histories, including smoking, alcohol consumption, hypertension, and hyperlipidemia, were also similar. At the conclusion of the 10-week trial, patients who received daily sildenafil had significantly improved erectile rigidity as captured by IIEF-5 (P < .001) and increased endothelial function via brachial artery flow-mediated dilation (P < .01). Endothelial function in men with type 2 diabetes was enhanced with daily sildenafil. Improved erectile rigidity and enhanced vascular circulation was noted after 10 weeks of daily sildenafil use.

**An open, comparative, multicentre clinical study of combined oral therapy with sildenafil and doxazosin GITS for treating Chinese patients with erectile dysfunction and lower urinary tract symptoms secondary to benign prostatic hyperplasia.**

Abstract: This study sought to investigate the clinical efficacy and safety of combined oral therapy with sildenafil and doxazosin GITS compared to sildenafil monotherapy in treating Chinese patients with erectile dysfunction (ED) and lower urinary tract symptoms secondary to benign prostatic hyperplasia (BPH/LUTS). The trial was conducted in hospitals in Beijing, Shanghai, Changsha, Wuhan and Guangzhou, five major cities in China. A total of 250 patients diagnosed with ED and BPH/LUTS aged 50-75 years, and who had International Index of Erection Function-5 (IIEF-5) scores ≤21 and International Prostate Symptom Score (IPSS) ≥10 points, were enrolled and randomly divided into Group A (168 cases; doxazosin GITS 4 mg once daily plus sildenafil 25-100 mg on demand) and Group B (82 cases; sildenafil 25-100 mg on demand). Efficacies were evaluated by IIEF-5 and IPSS scores and a quality of life (QoL) questionnaire, and adverse effects were evaluated during the treatment period. There were no statistically significant differences in mean age, and IIEF-5, IPSS and QoL scores pre-treatment between the two groups. After treatment, IIEF-5, IPSS and QoL scores were significantly improved in Group A, while only IIEF-5 scores were significantly improved in Group B compared with pre-treatment. There were no significant differences in side effects between the two groups. The results indicated that combined therapy with sildenafil and doxazosin GITS for the treatment of ED and BPH/LUTS is safe and effective compared to sildenafil monotherapy.

## REFERÊNCIAS

BALHARA, Y.P.; SARKAR, S.; GUPTA, R. Phosphodiesterase-5 inhibitors for erectile dysfunction in patients with diabetes mellitus: A systematic review and meta-analysis of randomized controlled trials. **Indian J Endocrinol Metab**. v. 19, n. 4, p. 451-461. 2015. Disponível em:< http://www.ncbi.nlm.nih.gov/pubmed/26180759>. Acesso em: 21/09/2016, às 14:45.

BATISTUZZO, J. A O; ITAYA, M.; ETO, Y. **Formulário Médico-Farmacêutico**. 5 ed. São Paulo: Pharmabooks, 2015.

CHEN, L. et al. Phosphodiesterase 5 inhibitors for the treatment of erectile dysfunction: a trade-off network meta-analysis. **Eur Urol**. v. 68, n. 4, p. 674-680. 2015. Disponível em:< http://www.ncbi.nlm.nih.gov/pubmed/25817916>. Acesso em: 21/09/2016, às 14:40.

DEYOUNG, L. et al. Daily use of sildenafil improves endothelial function in men with type 2 diabetes. **J Androl**. v. 33, n. 2, p. 176-180. 2012. Disponível em:< http://www.ncbi.nlm.nih.gov/pubmed/21680809>. Acesso em: 21/09/2016, às 16:23.

GARCÍA-PERDOMO, H.A.; ECHEVERRÍA-GARCÍA, F.; TOBÍAS, A. Effectiveness of Phosphodiesterase 5 Inhibitors in the Treatment of Erectile Dysfunction in Patients with Spinal Cord Trauma: Systematic Review and Meta-Analysis. **Urol Int**. DOI: 10.1159/000448290. 2016. Disponível em:< http://www.ncbi.nlm.nih.gov/pubmed/27509143>. Acesso em: 21/09/2016, às 14:52.

GOLDSTEIN, I. et al. Efficacy and Safety of Sildenafil by Age in Men With Erectile Dysfunction. **J Sex Med**. v. 13, n. 5, p. 852-859. 2016. Disponível em:< http://www.ncbi.nlm.nih.gov/pubmed/27114196>. Acesso em: 21/09/2016, às 14:27.

KIRILMAZ, U. et al. The effect of lifestyle modification and glycemic control on the efficiency of sildenafil citrate in patients with erectile dysfunction due to type-2 diabetes mellitus. **Aging Male**. v. 18, n. 4, p. 244-248. 2015. Disponível em:< http://www.ncbi.nlm.nih.gov/pubmed/26248034>. Acesso em: 21/09/2016, às 16:20.

LU, X. et al. [Efficacy of sildenafil citrate in men with erectile dysfunction following bilateral nerve-sparing radical prostatectomy: systematic review and meta-analysis]. **Zhonghua Yi Xue Za Zhi**. v. 95, n. 36, p. 2964-2968. 2015. Disponível em:< http://www.ncbi.nlm.nih.gov/pubmed/26814076>. Acesso em: 21/09/2016, às 14:32.

JIN, Z.; ZHANG, Z.C.; LIU, J.H.; LU, J.; TANG, Y.X.; SUN, X.Z.; SONG, W.D.; GAO, B.; GUO, Y.L.; XIN, Z.C. An open, comparative, multicentre clinical study of combined oral therapy with sildenafil and doxazosin GITS for treating Chinese patients with erectile dysfunction and lower urinary tract symptoms secondary to benign prostatic hyperplasia. Asian J Androl. 2011 Jul;13(4):630-5. doi: 10.1038/aja.2010.177. Epub 2011 May 23.Disponível em: <https://www.ncbi.nlm.nih.gov/pubmed/21602833>. Acesso em: 30 de Março de 2017.