

SUMMARY INFORMATION - ZESTRA®**Topical Medicated Oil****HEALTH PROFESSIONAL SUMMARY INFORMATION**

This Product Monograph was prepared based on the approval of Zestra® for sale in Canada and is designed specifically for healthcare professionals. Contact your local Orimed representative for questions about this medication.

RECOMMENDED USE

Zestra® is approved by Health Canada for the relief of symptoms of FSAD. Specifically, its indication given by Health Canada is the following: to temporarily improve sexual desire/arousal in women suffering from female sexual interest/arousal disorder.

COMPOSITION

Route of administration	Dosage form / dosage	Active ingredients	Non medicinal Ingredients
Topical	Topical drug (oil). - 3 individual sachets: 0.8 ml per sachet - 1 multidose bottle: 12ml	Borage oil 0.45 g (Borago officinalis seed) equivalent to 23% of gamma-linolenic acid Evening primrose oil 0.3 g (Oenothera biennis, seed), equivalent to 9% gamma-linolenic acid Huo 0.005 g (Angelica pubescens root) Forskohlii 0.0005 g (Coleus forskohlii, root), equivalent to 40% forskolin	Natural raspberry, vitamin C, vitamin E.

MODE OF ACTION AND CLINICAL PHARMACOLOGY**Mechanism of Action**

- The active ingredients induce vasodilation via smooth muscle relaxation:
 - a) The gamma-linoleic acid (GLA) is metabolized in the skin into prostaglandin E1 (PGE1)¹ which increases nerve conduction and vascular smooth muscle dilation resulting in enhanced desire sensitivity and clitoral engorgement
 - b) Increases cAMP⁴

- Vasodilation effect demonstrated in normotensive subjects (low blood pressure)³
- Inside smooth muscle cells², cAMP and cGMP contributes to lowering the concentration of intracellular calcium
- Synergy Primrose & Borage:
 - a) ↑ nerve conduction
 - b) ↑ vascular smooth muscle dilatation = enhanced desire sensitivity and clitoral engorgement
- Forskolin activates the enzyme adenylate cyclase to promote the generation of cAMP^{12,13}
- Additive effect between Osthol and Forskolin (10,11)
- Osthol enhances the increase in tissue cAMP and cGMP levels induced by forskolin

In short: induction of the normal physiological response to sexual arousal process, including:

- smooth muscle vasodilation
- ↑ neurosensitivity

Known and reported side effects are rare, particularly when applied topically^{5,6,7,8,9}

1. Dines, 1996, *Prostaglandins, Leukotrienes, and essential Fatty Acids*, 55(3), 159-75.
2. Teng, 1994, *Naunyn Schmiedeberg's Archive Pharmacologie*, 349(2), 202-208.
3. Kast 2001, *Int Immunopharmacol* 1, 2197-2199.
4. Mills 1990, *Am J Physiol* 259(6 Pt 2), R1164-R1171.
5. Engler 1993, *Prostaglandins Leukot Essent Fatty Acids* 49(4), 809-814.
6. Anstey 1990, *J Dermatol Treat* 1(4), 199-201.
7. Muggli 2009, *Eur J Pediatric Dermatol* 19(1), 43-46.
8. Tolleson 1997, *Pediatr Dermatol* 14, 423-425.
9. Choi 2000, *Urology* 55, 257-261.
10. Herbaut 1996, *Eur Urol* 30(1), 60-64.
11. Horrobin 1977, *Prostaglandins* 14(1), 103-108.
12. Mulhall 1997, *J Urol* 158(5), 1752-1758.
13. Amaro-Ortiz 2014, *Molecules* 19, 6202-6219.

PHARMACODYNAMICS/PHARMACOKINETICS

Current studies on the effect of the active ingredients used in Zestra® are extrapolated to illustrate its mode of action.

Time to Induction of action: 3-5 minutes.

Duration of action (on the basis of observations in clinical trials): approximately 45 minutes.

ABOUT THIS MEDICATION

Reasons why you should use this medication:

Zestra® medicated oil is applied topically. Its formula, which does not contain hormones, is composed of natural medicinal ingredients. Zestra® is an alternative supported by clinical studies to treat women who experience a decrease in their interest and their sexual desire.

Effects of this treatment:

Zestra® reduces the symptoms in women with disorders of desire and sexual arousal. Topically applied, Zestra® increases the sensitivity of receptors and stimulates local vasodilation. By reproducing the natural process of blood flow to the vulva, Zestra® induces the process of sexual arousal, interest and, for some women, lubrication. Zestra® also increases the feelings of pleasure in women during a sexual encounter.

PRECAUTIONS & CONTRAINDICATIONS

When it should not be used:

Do not use if Zestra®:

- If you have a known hypersensitivity (allergy) to the ingredients in Zestra®
- If you are pregnant, if you are breastfeeding or trying to conceive
- If you have a vaginal infection or irritation, such as a fungal infection (yeast). If you think you have a fungal infection, see your healthcare provider to get treatment. Wait until the infection is gone before using Zestra®

Additional information on use:

- Do NOT use Zestra® with LATEX condoms, since LATEX condoms are not compatible with oil-based products. Zestra® can only be used with POLYURETHANE condoms because they are specially designed to be used with oil-based products such as Zestra®
- Zestra® does NOT assure you protection against sexually transmitted infections (STIs)
- Zestra® is NOT a contraceptive and does NOT contain spermicides
- Zestra® is NOT a lubricant

DRUG INTERACTIONS

There are no known drug interactions between topically applied Zestra® and prescribed or non-prescribed drugs.

PROPER USE OF THIS MEDICATION

Usual Dose:Apply 5 minutes before intercourse.

1. Using the Zestra® packet: tear open the packet and pour the entire contents into the palm of the hand*
Using the Zestra® MULTI-DOSE bottle: put the equivalent of 3 pumps in the palm of the hand
2. Apply the content onto the clitoris and lips of the vulva while gently massaging. See diagram. (DO NOT APPLY WITHIN THE VAGINA)
3. The first sensations should be felt after 3 to 5 minutes. The peak effect is after 10 minutes and lasts for up to 45 minutes
4. If you decide to use a personal lubricant (ex. Glide by Zestra) during your sexual encounter, it important to apply the lubricant **after** Zestra® to feel the desired effects. You **MUST** first apply Zestra® and you must leave Zestra® on for 5 minutes before applying the lubricant

OVERUSE: If too much of the product is applied, simply rinse with water. It is important not to apply too much of Zestra® to PREVENT IT GOING INSIDE the vagina. If necessary, do not attempt to perform sex. Wait until the product flows out of the vaginal cavity. It is possible that the person applying Zestra experiences some burning, it should be minor and disappear after 45 minutes. However, if you experience unusual side effects not listed, contact a health care practitioner and communicate the event to our pharmacovigilance center.

FOR MORE INFORMATION

Contact us if you have questions or comments, want more information on the product or obtain more information prepared for health professionals.

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Orimed Pharma Inc. prepared this document.

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