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INTERNATIONAL JOURNAL OF

EXPERIMENTAL & CLINICAL RESEARCH

Supplement n° 2
2016

An international survey on vulvodynia

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EXPERIMENTAL & CLINICAL RESEARCH

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An international survey on vulvodynia

Introduction

Vulvodynia is a chronic vulvar pain condition characterized by symptoms such as itching, burning, vaginal dryness, chronic pain, pain during sexual intercourse and/or during urination, which involves the vulva for more than 3 months and does not have a clearly identifiable aetiology.[1] The differential diagnosis includes infectious and inflammatory diseases, tumours, neurological diseases, trauma, iatrogenic causes and hormonal deficiencies.

Table 1 shows the 2015 Consensus terminology and classification of persistent vulvar pain according to the International Society for the Study of Vulvovaginal Diseases (ISSVD), the International Society for the Study of Women's Sexual Health (ISSWSH), and the International Pelvic Pain Society (IPPS).

Vulvodynia probably is a multifactorial condition. Many theories have been proposed to explain its aetiology, such as abnormalities in early foetal development, genetic or immune factors, hormonal factors, inflammation, infection, neuropathic changes and oxalate-rich diet. Specialists indicate that vulvodynia may be also associated with other chronic painful conditions, such as Interstitial Cystitis/Bladder Pain Syndrome. [1,3]

Key words: vulvodynia, hyaluronic acid, verbascoside, glycerophosphoinositol, carrageenan

Table 1 – Classification of vulvovaginal pain disorders

A. Pain caused by identifiable aetiology
Infectious (e.g. recurrent candidiasis, human papillomavirus, herpes)[2-3]
Inflammatory (e.g. lichen sclerosus, lichen planus, immunobullous disorders)[2-3]
Neoplastic (e.g. Paget disease, squamous cell carcinoma)[2-3]
Neurologic (e.g. post-herpetic neuralgia, nerve compression or injury, neuroma)[2-3]
Trauma (e.g. female genital cutting, obstetrical)[3]
Iatrogenic causes (e.g. post-operative, chemotherapy, radiation)[3]
Hormonal deficiencies (e.g. genito-urinary syndrome of menopause [vulvo-vaginal atrophy], lactational amenorrhoea)[3]
B. Pain occurring in the absence of relevant causes
Vulvodynia[2-3]

Vulvodynia can affect 8 to 16% of women, independently of age and ethnicity. It has a negative impact on the quality of life of patients because it interferes with sexual and daily activities. It is also associated with a huge economic burden that has a major impact on individuals, society and the healthcare system alike.[1,3-4]

Vulvodynia is classified by the site of pain and can be *"generalized"* to the whole vulva or *"localized"* to a specific area, such as the clitoris (clitoridynia) or the vestibule of the vagina (vestibulodynia).

Furthermore, based on the type of pain, vulvodynia can be *"provoked"* i.e. caused by direct stimuli, such as inserting a tampon or sexual intercourse, *"unprovoked"* i.e. spontaneous without any triggering stimuli, or have a *"mixed"* pattern.[1,3-4]

Vulvodynia is diagnosed by excluding other known aetiologies (Table 1), assessing the pain history of each patient and performing a clinical examination, as well as the evaluation of vaginal pH, fungal culture and Gram staining. The cotton swab test is the most common diagnostic procedure designed to identify areas of localized pain and to classify the level of pain (mild, moderate, severe).[1,3-4]

Many therapeutic strategies have been suggested for the management of patients with vulvodynia. These include: vulvar care measures (good skin care and vulvar hygiene practices), topical drugs (local anaesthetics, oestrogens, corticosteroids, capsaicin, antibiotics and antifungal creams, moisturizing, hydrating and lubricant creams and gels), oral drugs (tricyclic antidepressants, serotonin inhibitors, venlafaxine, gabapentin, carbamazepine, NSAIDs), injectable medications (steroids plus lidocaine, botulin toxin, interferon), pudendal nerve blocks (anaesthetics), biofeedback (self-regulation strategies for confronting and reducing pain), training and physical therapy (to relax muscles and tissues), dietary modifications (low oxalate diet), cognitive behavioural therapy and sexual counselling (stress and sexual problems), complementary and alternative therapies (acupuncture, hypnotherapy, homeopathic and Chinese therapy) and surgery (vestibulectomy, laser).[1,3]

However, studies have shown that some of these treatments are poorly effective, and there is a general consensus that no single treatment is successful in all women.

Most of the evidence on treatment of vulvodynia is based on clinical experience, descriptive studies, or Expert Consensus Reports, since there are few randomized clinical trials published on vulvodynia treatment.[3]

More recently, clinicians have recommended a therapy based on a multimodal approach, which combines oral treatment with the use of topical products, good skin care and vulvar hygiene practices.[1] Therefore, the management of vulvodynia should be tailored to the individual patient with a multidisciplinary approach, addressing both physical and psychological aspects of the disease.

The aim of this survey was to investigate the characteristics of the actual population of women with vulvodynia and its management in clinical practice across several countries worldwide, as well as to explore the potential use of new topical therapeutic approaches.

Materials and methods

A total of 167 specialists (mainly urologists and gynaecologists) from 35 countries worldwide took part in this survey. The specialists were asked to provide information on the characteristics and management of patients with vulvodynia, as well as their impression on a new product for the treat-

ment of symptoms of vulvar pain. The data collected by means of questionnaires were:

- estimated annual rate of female patients (out of the total of female patients) who consult the specialist for problems related to chronic pain in the vulvar area;
- characteristics of the typical patient with vulvodynia (age, sexual and hygiene habits, concomitant disturbances, etc);
- local treatment of vulvodynia (type of topical drug/therapy used for its management);
- medical judgement using a semi-quantitative rating scale (1 = useless and 10 = very useful) on the potential use of a new product containing hyaluronic acid (HA) (hydration, lubrication), verbascoside (natural anti-oxidant), glycerophosphoinositol choline salt (emollient and soothing action) and carrageenan (muco-adhesive action) for the treatment of symptoms accompanying vulvodynia;
- most interesting and convincing characteristics of the new product among the following: hydrating and lubricating action, action on symptoms, emollient and soothing action, anti-oxidant effect.

Demographic and treatment data were analysed descriptively and presented as a total sample across all countries and by specialty (urology and gynaecology).

Results

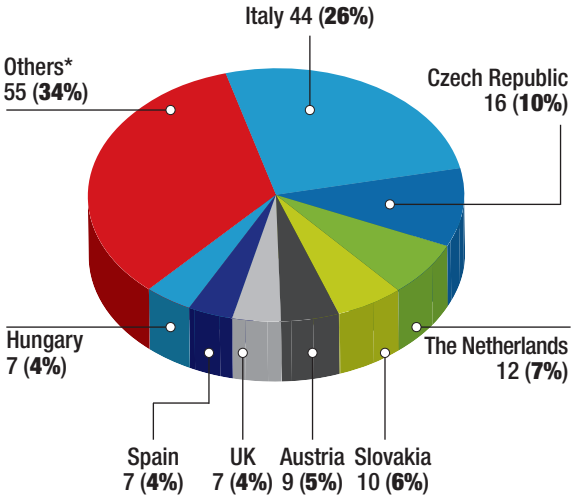
Figure 1 shows the countries involved in the survey (n = 35), as well as the specialists in each country. Italy was the country with the highest number of collected questionnaires (n = 44; 26%), followed by Czech Republic (n = 16; 10%), the Netherlands (n = 12; 7%), Slovakia (n = 10; 6%) and Austria (n = 9; 5%).

Urologists account for 61.7% of the total number of specialists involved (103/167), whereas gynaecologists represent one third of the participants (55/167, 32.9%; Figure 2).

The annual rate of female patients (out of the total of female patients) who consult physicians for problems related to chronic pain in the vulvar area is 20%.

More than 50% of patients with chronic pain in the vulvar area are over 45 years old (Figure 3).

Results show that 66.3% of women with chronic pain in the vulvar area also suffer from cystitis, 54.2% are sexually active, 48.2% suffer from vulvodynia, 38.6% have hormonal disturbances and 36.1% are prone to develop vaginal infections (Figure 4).



* Egypt 6; Algeria 5; United Arabian Emirates 4; France 3; Uzbekistan 2; Germany 2; Greece 2; India 2; Ukraine 2; Sweden 2; Switzerland 2; Argentina 1; Brasil 1; Bulgaria 1; Canada 1; South Korea 1; Danmark 1; Philipinas 1; Hong Kong 1; Israel 1; Luxembourg 1; Turkish 1; Thailand 1; Poland 1; missing data 3

Figure 1 – Countries participating in the survey, with the respective number (%) of specialists

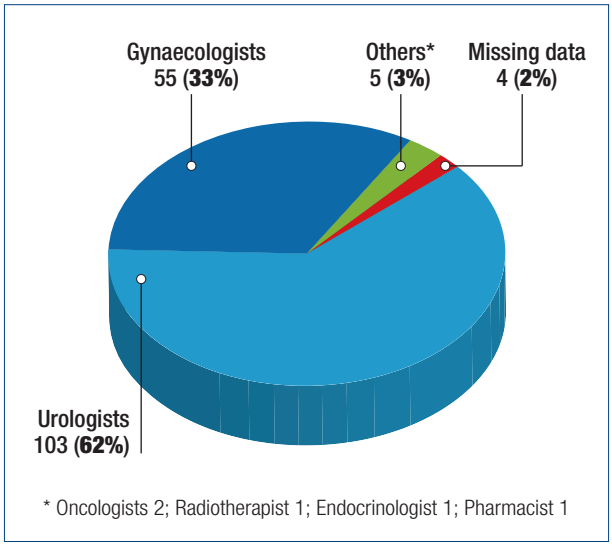


Figure 2 – Specialists attending the survey, number (%)

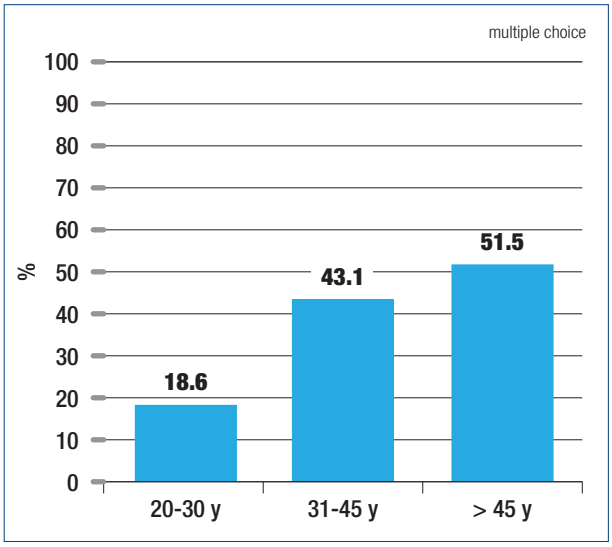


Figure 3 – Age range of female patients with chronic pain in the vulvar area

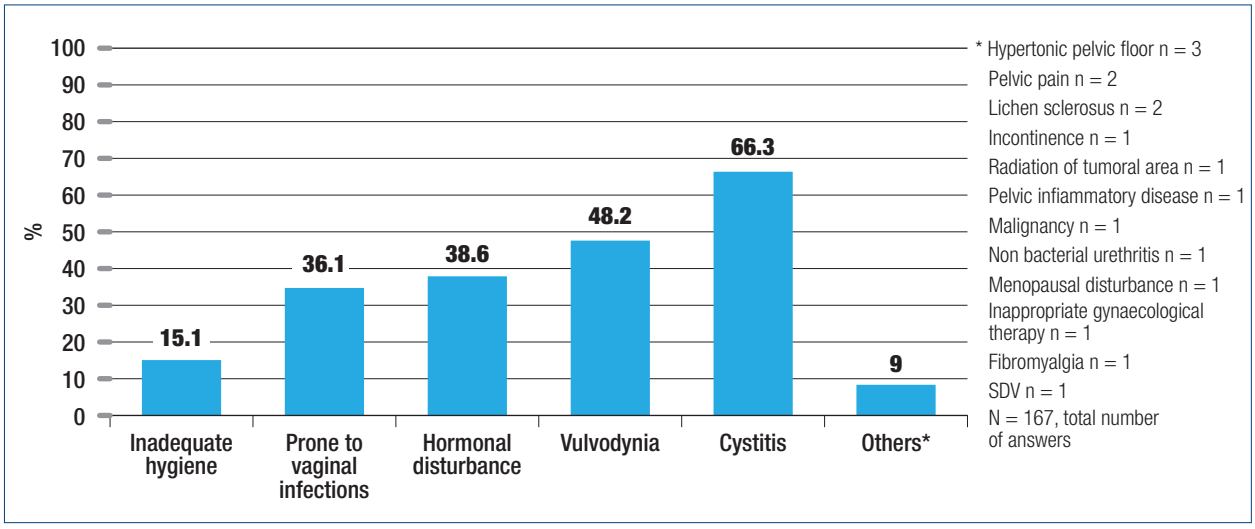


Figure 4 – Predisposing factors/concomitant causes of chronic pain in the vulvar area (average %)

Nevertheless, on average, 54.2% of these patients are described as sexually active. Regarding the treatment of vulvovaginal disorders, most of the specialists (158/167, 94.6%) suggest systemic therapy combined with topical therapy and/or other therapeutic strategies (Figure 5).

This outcome is in line with the published guidelines for the management of vulvodynia, which recommend both topical products, such as creams and gels, and systemic medications, including antidepressants and anticonvulsants, together with vulvar hygiene measures, biofeedback training and physical therapy, as appropriate.[3]

Figure 5 shows the most prescribed/suggested topical treatments by the 158 specialists interviewed. About two thirds of specialists use topical hor-

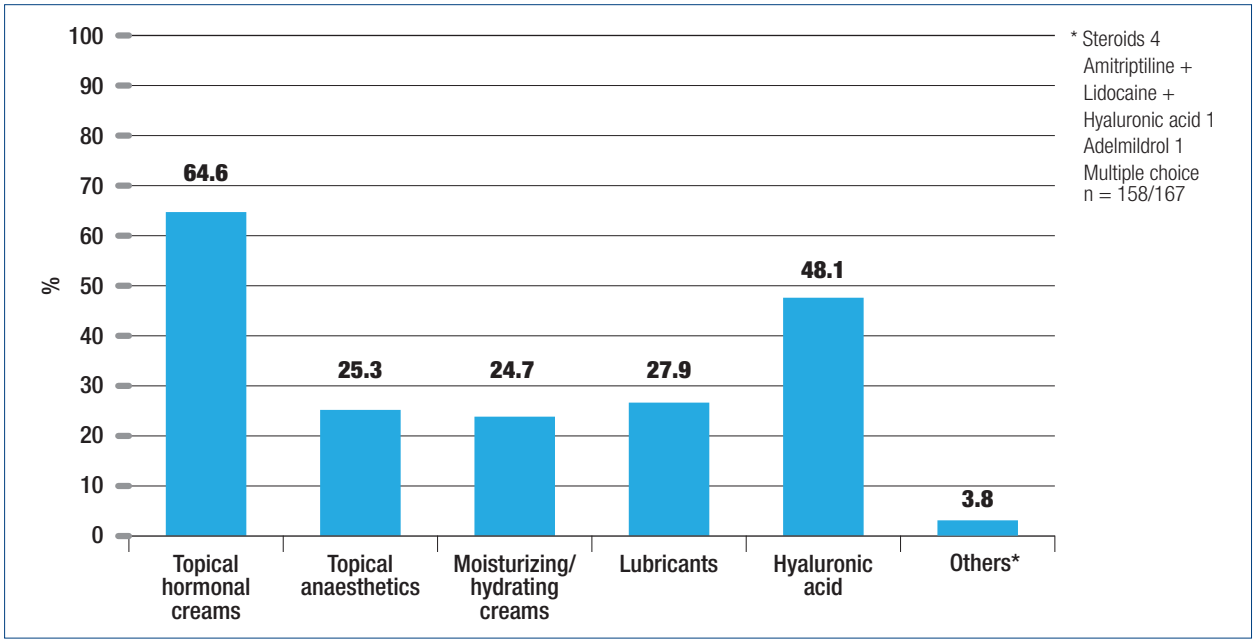


Figure 5 – Most used topical treatments for the management of patients with chronic pain in the vulvar area

monal creams (e.g., oestrogens, testosterone), and half of them HA preparations.

Topical anaesthetics (e.g., lidocaine), moisturizing/hydrating creams and lubricants are prescribed by ~ 25% of specialists.

A new product containing HA and other components was presented to physicians participating to the survey as a new therapeutic option for the treatment of vulvodynia. The general opinion was positive: the mean prescription/suggestion score was 7.2/10 in the whole population (median value 8) and at least 70% of specialists interviewed would have been willing to prescribe/suggest this new product to more than 50% of patients with chronic pain in the vulvar area (Table 2).

The most appreciated characteristics of the new topical product resulted to be its activity on symptoms (67.3%) and its hydrating and lubricant properties (46.1%). Table 3 reports the data analysis by type of specialist: urologists (n = 103) and gynaecologists (n = 55; no data reported for 9 specialists). The estimated annual rate of patients with problems related to chronic pain in the vulvar area is 25% among urologists as compared to 12.2% among gynaecologists.

Table 2 – Patient groups (out of 100 patients) potentially eligible for the prescription/suggestion of the new product for the management of chronic vulvar pain.

To how many patients would you recommend the new product (out of 100 patients)?	
Range of patients (%)	**Rate of recommendation**
0 - 20	10.8%
20 - 40	19.6%
40 - 60	22.6%
60 - 80	37.3%
80 - 100	9.8%
(N = 165/167)	Outcome: more than 2/3 of specialists would prescribe the new product to 50% or more of their patients

Table 3 – Analysis of data by specialist

		Urologists N = 103	Gynaecologists N = 55
Estimated patients with problems related to chronic pain in the vulvar area/total number of examined patients in a year			
		25%	12.2%
Age group (incidence of patients with problems related to chronic pain in the vulvar area per age groups)			
	20–30 years	14.6%	29.1%
	31–45 years	49.5%	27.3%
	> 45 years	50.5%	54.6%
Characteristics of the typical patient			
	Sexually active	50%	65.5%
	Inadequate hygiene	11.8%	23.6%
	Prone to vaginal infections	35.3%	40%
	Hormonal disturbances in place	38.2%	40%
	Suffers from vulvodynia	44.1%	60%
	Suffers from cystitis	78.4%	45.6%
Topical medication for the symptomatic treatment of vulvodynia and other vulvar pain disorders			
	Yes	92.2%	98.2%
	No	7.8%	1.8%
Main topical product suggested			
	Topical Hormonal Creams	71.6%	53.7%
	Topical Anaesthetics	23.2%	26%
	Moisturizing/Hydrating creams	17.9%	35.2%
	Lubricants	25.3%	35.2%
	Hyaluronic acid preparations	46.3%	48.15
Value of interest of the new topical product			
	Median	8/10	8/10
To how many patients would you recommend the product (out of 100 patients)?			
	0 - 20	10.8%	9.3%
	20 - 40	19.6%	13%
	40 - 60	22.6%	40.7%
	60 - 80	37.3%	24.1%
	80 - 100	9.8%	13%
Which product characteristics do you find most interesting and would convince you to prescribe it?			
	Hydrating and lubricating action	48.5%	37.7%
	Action on symptoms	64.1%	75.5%
	Emollient and soothing action	25.2%	13.2%
	Anti-oxidant action	11.7%	9.4%

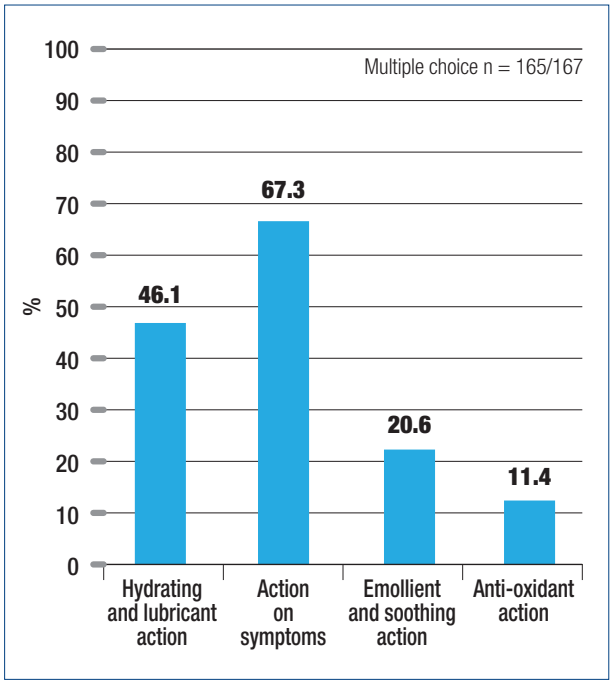


Figure 6 – Most appreciated characteristics of the new topical product

According to urologists this problem occurs more frequently in women after the age of 30 years. On the contrary, according to gynaecologists, chronic pain in the vulvar area occurs more often in women in the 20s and in patients older than 45 years. Both gynaecologists and urologists use topical therapies for the management of local vulvo-vaginal pain disorders.

The latter prefer to use more hormonal creams than gynaecologists, which in turn prescribe more moisturizing/hydrating creams and lubricants.

The use of topical anaesthetics and HA preparations is similar in the two groups of specialists. The ranking of the preferred characteristics for prescribing the product was the same in the two groups. However, the most appreciated characteristic of this product by both gynaecologists and urologists was its activity on symptoms (67.7%; Figure 6).

Discussion

Vulvodynia is a complex disorder that frequently frustrates both patients and clinicians, because available strategies are not completely satisfactory from a clinical, safety and practical point of view. For this reason, new therapeutic options are needed.

The primary goal of this survey was to collect information on the main characteristics of women with vulvodynia, as well on the current therapeutic management of the disease. Specialists, mainly urologists and gynaecologists, from several countries were involved in this survey.

The main results show that the estimated global annual rate of female patients with chronic pain in the vulvar area is approximately 20%, with a higher percentage of patients consulting urologists as compared to gynaecologists (25% vs 12.2%, respectively). Most of the women with vulvodynia that gynaecologists see are either in their 20s (at check-ups, consultations for contraception, etc.) or aged 45 years and over (consultations for menopausal disturbances and uro-gynaecological diseases). Gynaecologists have a higher number of sexually active patients with the condition.

On the contrary, the women with vulvodynia that urologists see are usually over 30 years of age (especially at consultations for urological diseases). These specialists reported a higher number of women with cystitis/interstitial cystitis.

Topical products prescribed by specialists result the most commonly used. Among these, while urologists prefer topical hormonal creams, gynaecologists prescribe more moisturizing/hydrating creams and lubricants. HA is used to the same extent by both specialists.

The second objective of this survey was to explore the potential use of a new topical product containing (HA), verbascoside, glycerophosphoinositol

choline salt (GPI) and carrageenan for the management of vulvodynia.

Due to its well-known moisturizing and lubricant properties, as well as its biocompatibility, HA has been used for the management of joint diseases, wound healing, ophthalmic surgical devices and, more recently, in cosmetic medicine.[7] HA occurs naturally in female and male genital organs: high levels have been detected in the vagina and bladder of female rats.[8] The effects of HA on the vulvar area include: restoring the vaginal mucosa and a suitable level of hydration, protection against external environment, decrease in vaginal pH, increase maturation of the vaginal epithelium, lubrication during sexual intercourse, healing of fissures and vulvar skin damage.[9-10]

To date, no studies have evaluated the efficacy and safety of HA in the management of vulvodynia.

A recently published double-blind, randomized, placebo-controlled study evaluated the efficacy and safety of topically administered HA in 36 post-menopausal women with vaginal atrophy.

The local application of HA was able to significantly reduce all the symptoms of the patients (vaginal dryness, itching, burning, vaginal atrophy, erythema) versus baseline. Compliance of physicians was rated "very good".[11]

Verbascoside is a phenylethanoid glycoside extracted from plant stem cells *(Syringa vulgaris)* with antimicrobial (especially against *Staphylococcus aureus*) and anti-oxidant (control of tissue damage related to oxidative stress) activities.[12-14] When verbascoside is combined with HA, it is able to protect this polysaccharide from oxidative degradation, improving the duration and the effect of HA.[12]

GPI, a sunflower lecithin-derived ingredient, has emollient and soothing properties. It offers reliable, long-term relief from irritation and itching. In addition, it is involved in the control of various cell functions, as well in immune and inflammatory responses.[15] Carrageenan, a naturally occurring bioadhesive polymer derived from red seaweed, which is well known for its special ability to form hydrogels, is used to provide muco-adhesive effects to the gel formulation. Thus, the main advantage is the increase in residence time of the gel on the treated area, which maximizes the synergy among the components of the product in terms of therapeutic effects.

According to the results of this survey, both urologists and gynaecologists show a potential interest in this new product for their clinical practice.

Thanks to the innovative formulation and the synergy of action of its components, the new topical product should become a valid therapeutic option in the topical market and could be recommended together with other therapies within the context of the multimodal therapeutic approach for the management of the symptoms of vulvodynia.

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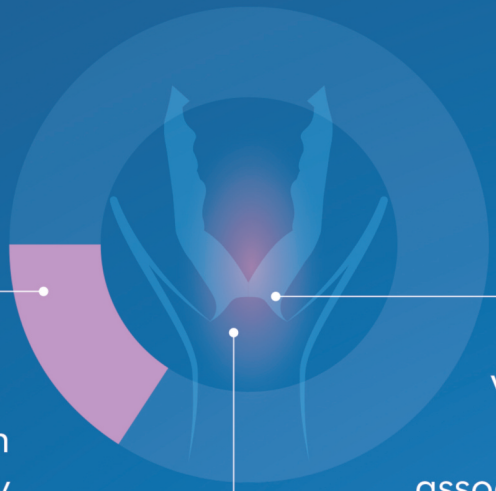
Vulvodynia

A vulvovaginal disorder

Affects up to 16% of women[1] mostly between 20 and 50 years of age[2]

Characterized by chronic vulvar pain or discomfort that impacts negatively on a woman's quality of life[1]



Vulvodynia can be associated with other conditions[3]

Nebycrom®

gel for vulvovaginal use

A new medical device based on an innovative formulation

HYALURONIC ACID (HA)

A highly purified compound obtained through a multiphase biofermentation process

VERBASCOSIDE

Phenylethanoid glycoside extracted from plant stem cells *(Syringa vulgaris)*

CARRAGEENAN

Natural bioadhesive polymer derived from red seaweed

GLYCEROPHOSPHOINOSITOL (GPI)

Sunflower lecithin-derived ingredient

PARABEN-FREE

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