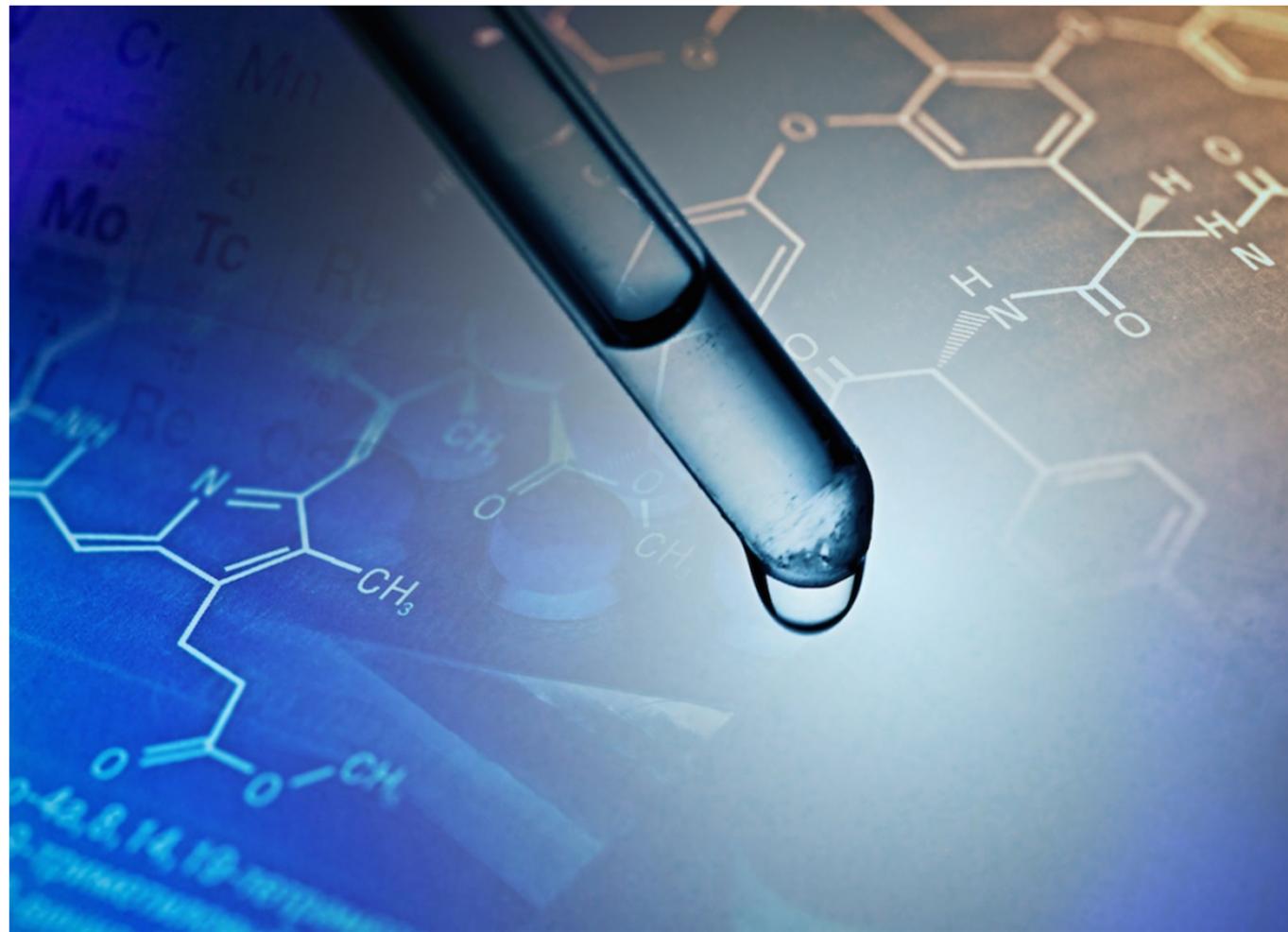




## Vaginal Dryness Treatment



*The modern  
woman needs...*



...New treatment option's

# Symptomatic Vulvo Vaginal Atrophy (VVA)

*2013 position statement of  
The North American Menopause Society (NAMS)\**



# Symptomatic Vulvo Vaginal Atrophy (VVA)

*2013 position statement of  
The North American Menopause Society (NAMS)\**

- The primary goal of treating symptomatic VVA is to alleviate symptoms.
- For the woman with symptomatic VVA unrelated to sexual activity and for whom all other causes of her symptoms have been eliminated, first-line therapies include non hormonal, long-acting vaginal moisturizers and low-dose vaginal estrogen, assuming no contraindications.

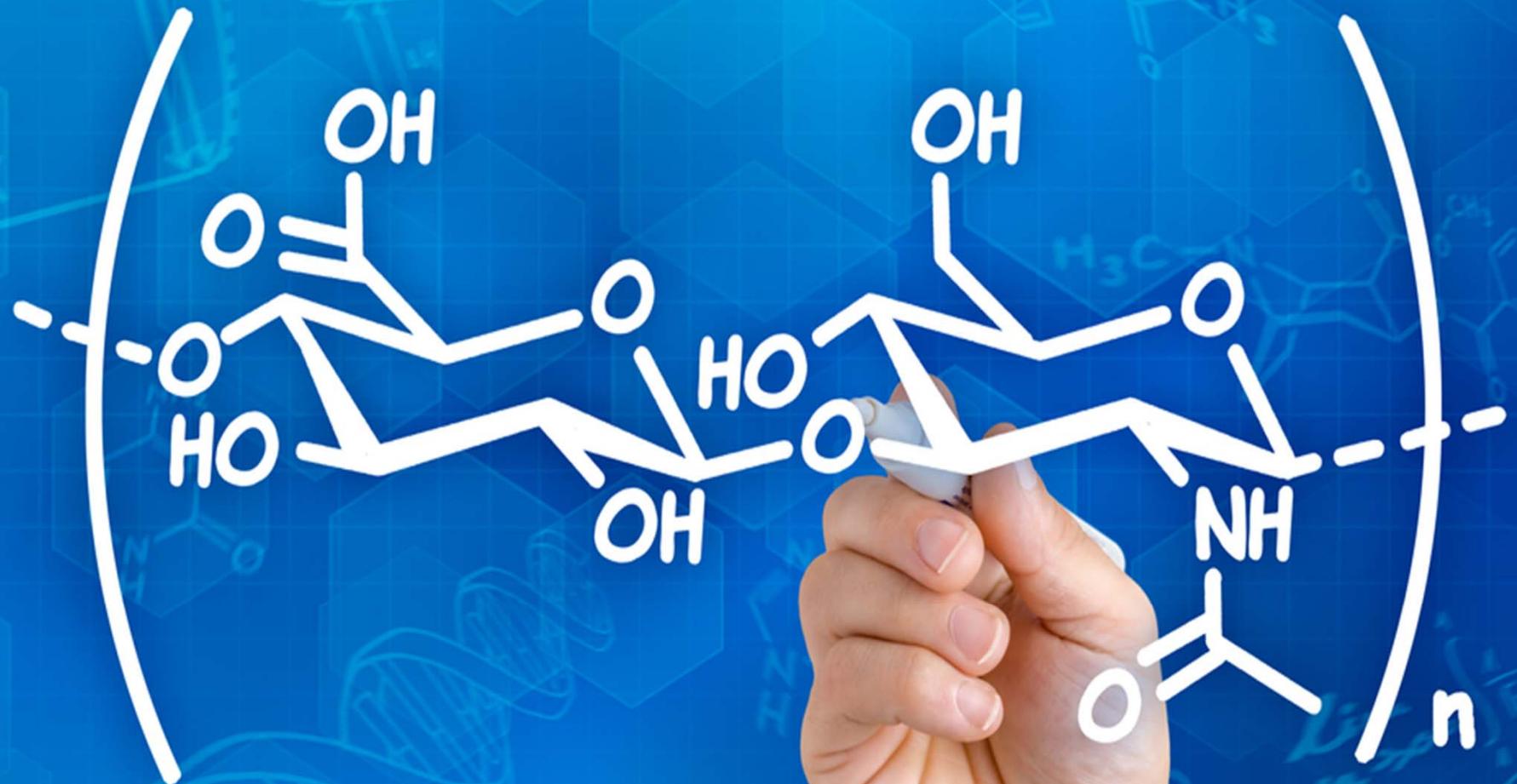
\***North American Menopause Society** . Management of symptomatic vulvovaginal atrophy: 2013 position statement of The North American Menopause Society. *Menopause: The Journal of The North American Menopause Society* 2013 Vol. 20, No. 9, pp. 888 - 902

# Main Points for Choosing the Best Lubricant Ingredients

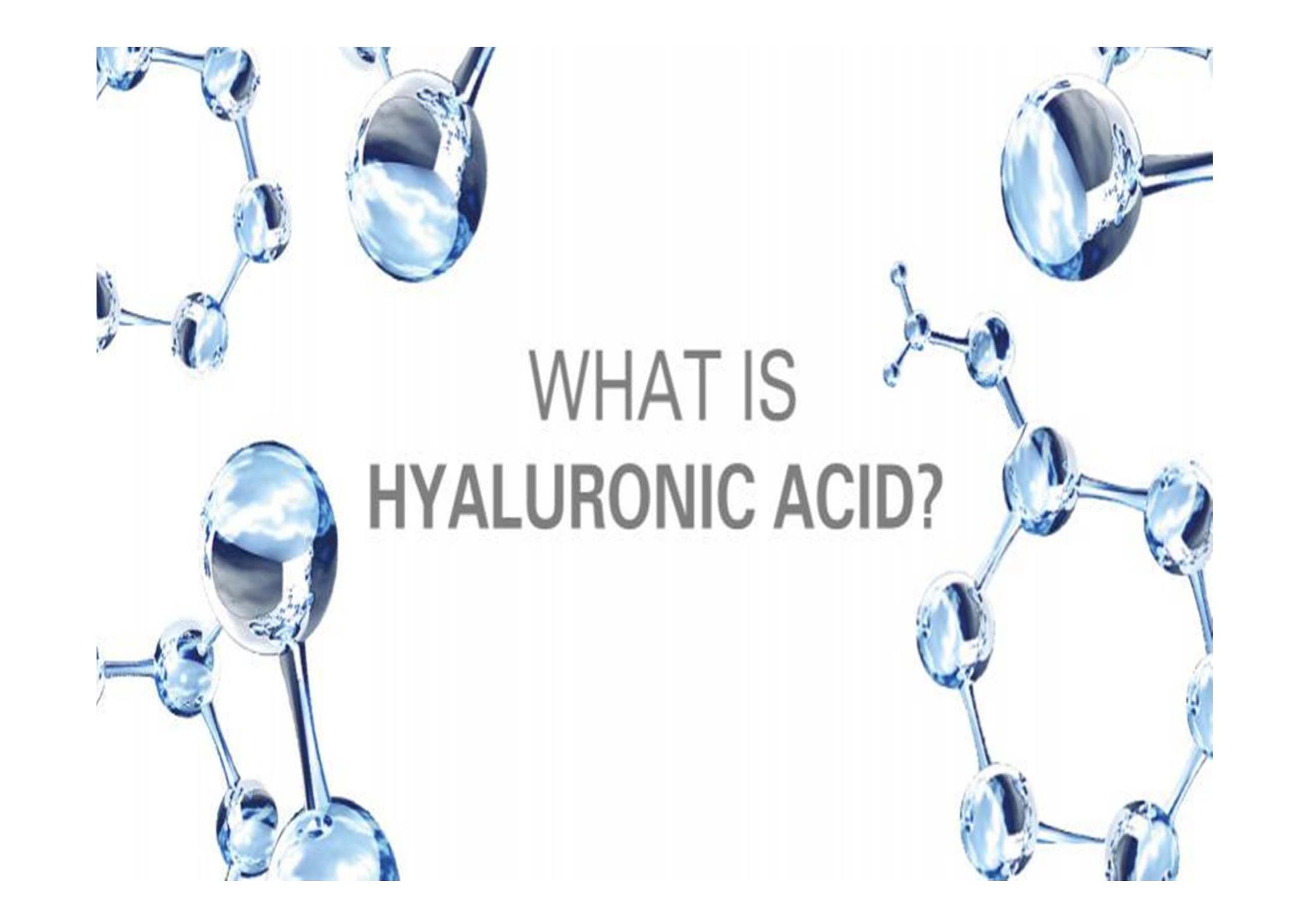


- Research into personal lubricant safety is lacking
- Women can often benefit from using an appropriate personal lubricant
- Some ingredients in personal lubricants can cause damage and erosion of surface cells lining the vagina and anus
- There is no one best lubricant for all women
- Read the label of your lubricant
- Avoid lubricants containing known irritant additives and preservatives
- Choose paraben and glycerol-free water based lubricants
- Choose additive-free silicone-based lubricants
- Avoid oil or petroleum-based lubricants

# HYALURONIC ACID





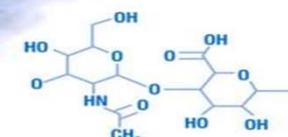
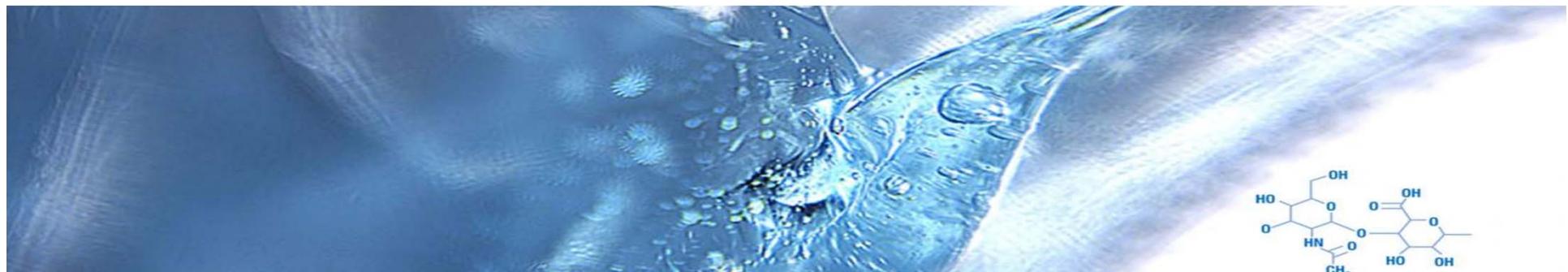


# WHAT IS HYALURONIC ACID?

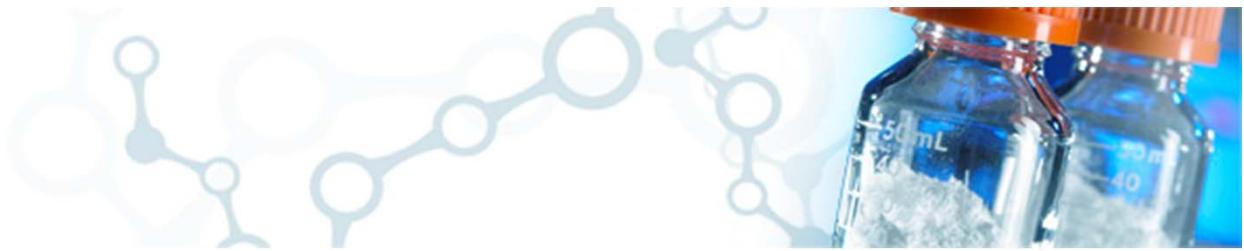


## The Discovery of Hyaluronic Acid

Though it may seem that we are just hearing about it very recently, hyaluronic acid was first discovered over 80 years ago, and has been used in various areas of medicine and cosmetology.



## Sodium Hyaluronate



- **Hialuronan** (= hyaluronic acid or sodium hyaluronate) The sodium salt of hyaluronic acid, a glycosaminoglycan consisting of D-glucuronic acid and *N-acetyl-D-glucosamine disaccharide units*.
- **Hialuronan** it's a fisiologic substrate that is widely distributed in the extracellular matrix of connective tissues in both animals and humans. It is found in high concentration in the aqueous humor of the eye, synovial fluid, skin, and umbilical cord.
- Primary medical applications include:
  - Ophthalmology,
  - Orthopedics,
  - Aesthetics,
  - Tissue Engineering, and
  - Veterinary Medicine

\*Hialuronan = *hyaluronic acid e sodium hyaluronate*. Martindale\_The Complete Drug Reference 36ed 2009

# The Discovery of Hyaluronic Acid

1934	First discovery of hyaluronic acid by German Pharmacist Karl Meyer and his assistant John Palmer, when they isolated the compound from the vitreous of bovine eyes	
1942	First commercial use of hyaluronic acid by Endre Balazs when he applied for a patent to use it as an egg substitute	
1986	The term “hyaluronan” was introduced in 1986 to conform with the international nomenclature of polysaccharides and is attributed to Endre Balazs	
1996	Hyaluronic acid was found to be helpful in the treatment of connective tissue disorders, and also to help speedup recovery of sprained ankles or joint problems in athletes; it also began being used in the cosmetics industry	
2002	Hyaluronic acid (as an injectable) was brought to the public's attention when used to treat an injury in French tennis player, Amelie Mauresmo	
2003	US Food and Drug Administration (FDA) approved hyaluronic acid as a wrinkle treatment	
Present	The effects of hyaluronic acid on different conditions continue to be studied today.	



Rooster comb  
extraction



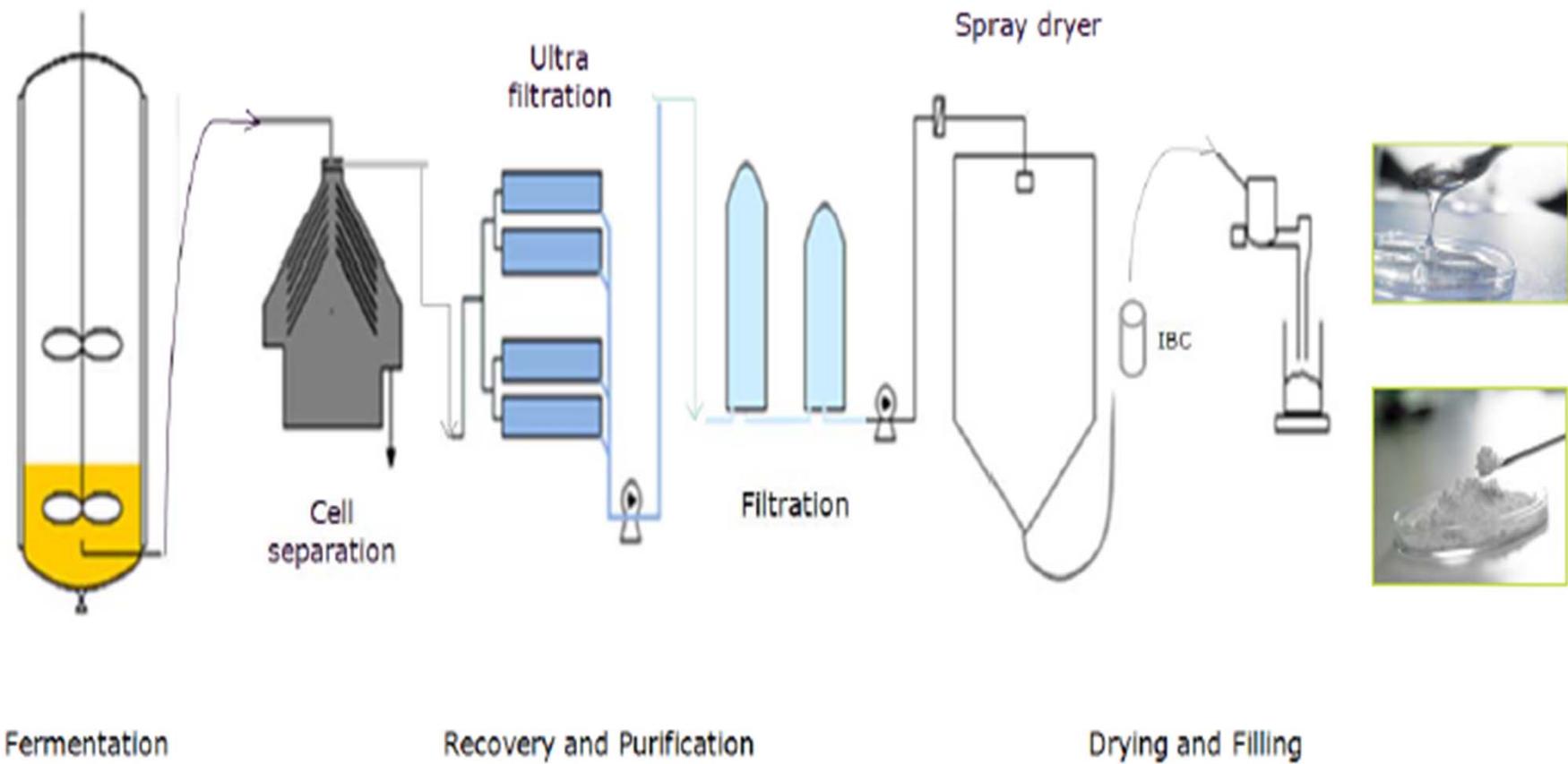
Streptococcus  
fermentation



Bacillus subtilis  
fermentation

**Sodium Hyaluronate  
Production evolution**

# Production





# Lubrinat®

Sodium Hyaluronate





Scientific support



# Clinical Study I

**Stute P. (2013)** Is vaginal hyaluronic acid as effective as vaginal estriol for vaginal dryness relief?

*Arch Gynecol Obstet. 2013 Dec;288(6):1199-201*

- The authors concluded that hyaluronic acid vaginal gel was not inferior to estriol vaginal cream in women presenting with vaginal dryness.
- They suggest using hyaluronic acid vaginal gel not only as an alternative treatment to vaginal estrogens, but also to consider its general use in women presenting with vaginal dryness of any cause.





# Clinical Study II

**Chen J, Geng L, Song X, Li H, Giordan N, Liao Q.** (2013) Evaluation of the efficacy and safety of hyaluronic acid vaginal gel to ease vaginal dryness: a multicenter, randomized, controlled, open-label, parallel-group, clinical trial.  
*J Sex Med. 2013 Jun;10(6):1575-84*

- Both hyaluronic acid vaginal gel and estriol cream are effective in the treatment of vaginal dryness.
- Hyaluronic acid vaginal gel may be considered as a valid alternative to estrogen-based treatments in relieving the symptoms of vaginal dryness.





# Clinical Study III

**Ekin, M., Yaşar, L., Savan, K., Temur, M., Uhri, M., Gencer, I., & Kivanç, E.** (2011). The comparison of hyaluronic acid vaginal tablets with estradiol vaginal tablets in the treatment of atrophic vaginitis: a randomized controlled trial.

*Archives of gynecology and obstetrics*, 283(3), 539-543.

- Two groups of postmenopausal women with atrophic vaginitis were studied. One group used estradiol vaginal tablets ( $n=21$ ) for 8 weeks, while the other group used hyaluronic acid tablets ( $n=21$ ) for 8 weeks. Outcomes consisted of the degree of vaginal atrophy, vaginal pH, vaginal maturation index, and a self-assessed 4-point scale.
- Results: Both groups had relief of vaginal symptoms, improved epithelial atrophy, decreased vaginal pH, and increased maturation of the vaginal epithelium.
- The group on estradiol did have greater improvements, however, it was determined that the hyaluronic acid vaginal tablets was effective enough to be considered an alternative treatment for those who wanted to avoid the use of a local estrogen treatment.





# Clinical Study IV

APPROVED

## Lubrinat® & Vaginal mucosa

Biocompatibility Safety Testing\*  
comprove no irritation on  
vaginal mucosa

\*according to ISO 10993-10

 <p>Rua Octávio Teixeira Mendes Sabino, 35 Vila Santa Catarina - São Paulo - SP - 04374-010 (011) 5671-7088 Fax: (011) 5671-7088 medlab@medlab.com.br</p> <p>RELATÓRIO DE ESTUDO DE IRRITABILIDADE DA MUCOSA VAGINAL MV 381991003003</p> <p></p>	<p>MASTER IND E COM DE PRODODONT E FARMACÊUTICOS LTDA. AVENIDA BEN-TE-VI, 353 - CJ. 62 MOSNA - SÃO PAULO - SP - CEP: 04624-050 FONOTEL: (11) 5671-6444 - 5622-6105 CONTATO: DRA. AMANDA YALIM</p> <p>Instalação de Teste: MEDLAB PRODUTOS DIAGNÓSTICOS LTDA. Rua Octávio Teixeira Mendes Sabino, 35 Vila Santa Catarina - São Paulo - SP fone: (011) 5671-7088 - Fax: (011) 5671-7088</p> <p>Diretora de Estudo: Paula Daniela Sabino Freitas Alves Biotécnica Rua Octávio Teixeira Mendes Sabino, 35 Vila Santa Catarina - São Paulo - SP</p>
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# Clinical Study V

APPROVED

## Lubrinat® & Penile mucosa

Biocompatibility Safety Testing\*  
comprove no irritation on penile  
mucosa

 medlab Laboratório de Análises	
Av. Octávio Teixeira Mendes Sobrinho, 35 Vila Santa Catarina São Paulo - SP - 04524-030 Tel: (011) 5271-7686 Fax: (011) 5271-7686 medlab@medlab.com.br	
RELATÓRIO DE ESTUDO DE IRRITABILIDADE DA MUCOSA PENIANA	
IMP 387961/062003	
	
MASTER IND E COM DE PROD ODONTE FARMACÉUTICOS LTDA. AVENIDA BEN-TE-VI, 333 - CJ. 62 MCEMA - SÃO PAULO - SP - CEP: 04524-030 FONE/FAX: (11) 5041-0444 - 5092-0100 CONTATO: DRA. AMANDA VALIM	
Patrocinador do Estudo:	MEDLAB PRODUTOS DIAGNÓSTICOS LTDA. Rue Octávio Teixeira Mendes Sobrinho, 35 Vila Santa Catarina - São Paulo - SP Fone: (011) 5271-7686 - Fax: (011) 5271-7686
Instalação de Teste:	Paula Daniela Sabino Freitas Alves Bióloga Rue Octávio Teixeira Mendes Sobrinho, 35 Vila Santa Catarina - São Paulo - SP
Diretora do Estudo:	

\*according to ISO 10993-10



# Clinical Study VI

APPROVED

## Lubrinat® & Skin irritation and Sensitization

Biocompatibility Safety Testing\*  
comprove no irritation skin

\*according to ISO 10993-10



1 de 25

ESTUDO CLÍNICO, MONO-CEGO, CONTROLADO, DO POTENCIAL DE  
IRRITABILIDADE E SENSIBILIZAÇÃO CUTÂNEA DE UM PRODUTO PARA  
APLICAÇÃO NA PELE  
RELATÓRIO FINAL

NOME DO PRODUTO: LUBRINAT

CÓDIGO DO PRODUTO: 051200-01

CÓDIGO DO ESTUDO: AHS-RPT-051200-01-01-15

CÓDIGO DO RELATÓRIO: AHS-RPT-051200-01-01-15-RPTV01-Rev01

DATADO RELATÓRIO: 03/03/2015

PATROCINADOR: MASTER INDÚSTRIA E COMÉRCIO DE PRODUTO DENTAL E FARMAC LTDA  
Rua Geraldo Anrade Sebastião Dado Arnuda  
35740000 – Recife – MG – Brasil

CENTRO DE PESQUISA: ALLERGISA PESQUISA DERMATO-COSMÉTICA LTDA  
Av. Dr. Romeo Tárlima, nº 452/466 – Bairro Goiabeira  
13084-791 – Campinas – SP – Brasil  
Telefone: +55 (19) 3719-8600  
Pesquisador Responsável: Dr. André Luiz Vergnani

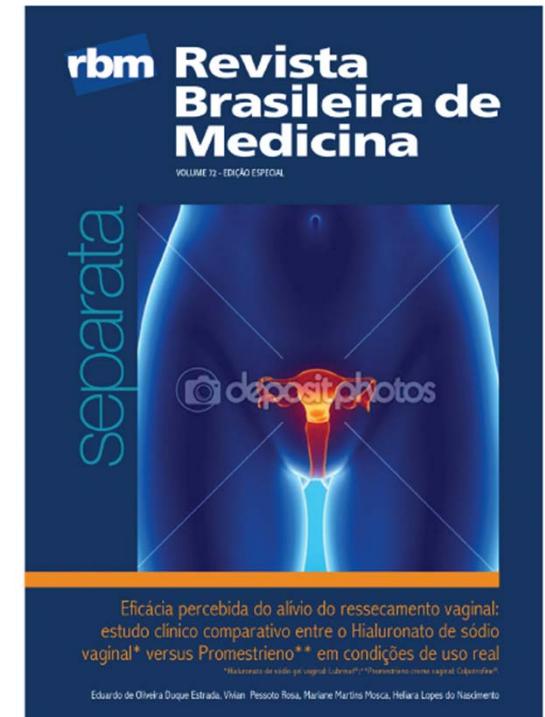


# Clinical Study VII

**Duque Estrada EO. et al.** Perceived Efficacy of the relief of vaginal dryness: a comparative clinical study between Sodium hyaluronate vaginal \* vs. Promestriene \*\* in actual use conditions.

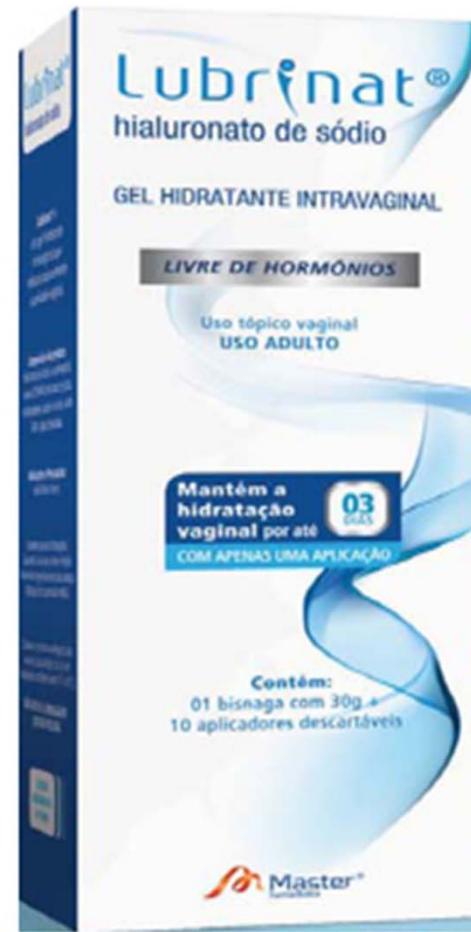
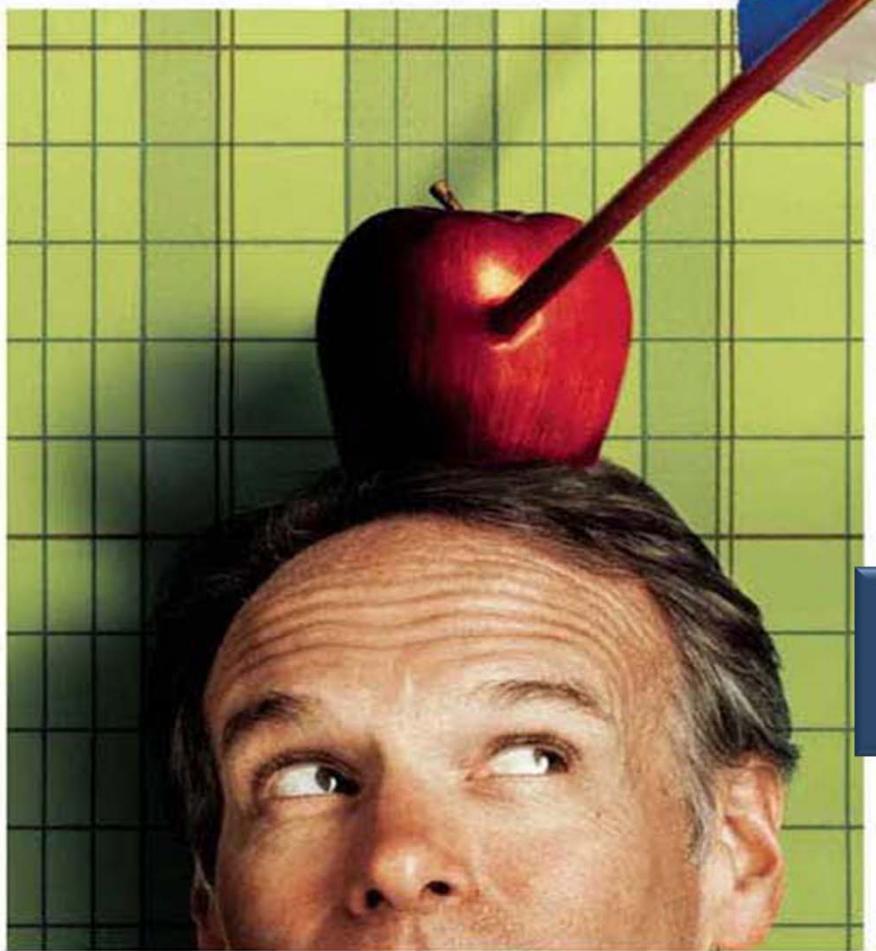
RBM Dez 2015 V 72 N 12 págs.: 103-106

- No significant difference was observed between the products regarding the attribute "on moisturizing properties to the intimate mucosa" ( $p = 0.142$ ).
- No significant difference was observed regarding the dryness of the intimate mucosa ( $p = 0.786$ ).
- No significant difference was observed regarding comfort sensation in the intimate mucosa ( $p = 0.528$ ).
- No significant difference was observed regarding the fragrance of the product ( $p = 0.088$ )
- No significant difference was observed regarding ease of application ( $p = 0.123$ )



\* Sodium hyaluronate vaginal gel: Lubrinat®

\*\* Promestriene vaginal cream: Colpotrofine®



Reps positioning



# Lubrinat®

POLIACRILIC ACID



- NATURAL SOURCE
- NO ACRYLIC
- BIOTHEC PRODUCT
- RESTORE THE NATURAL VAGINAL pH
- VAGINAL WALL CELLS REFORCE
- PROMOTES VAGINAL HEALING

- **NO NATURAL & ACRYLIC PRODUCT**
- **OLD PRODUCT - NO BIOTHEC**
- **NO ACTION ON THE VAGINAL pH**
- **NO ACTS DIRECTLY ON THE VAGINAL WALL CELLS**
- **NO PROMOTES VAGINAL HEALING**







# Lubrinat®



## UPDATE Concept (1,2)

- BIOTHEC PRODUCT
- BIOCOMPATIBILITY PROFILE
- NO PRO INFLAMMATION ACTION

## COMPROVED EFFICACY

- Long lasting vaginal moisturizer – Tissue evidence

## HISTOLOGIC EVIDENCE

- “Visible” results

1. **Zheng Shu X, Liu Y, Palumbo FS, Luo Y, Prestwich GD.** "In situ crosslinkable hyaluronan hydrogels for tissue engineering". *Biomaterials* (2004), **25**(7-8): 1339–48.
2. **Segura T, Anderson BC, Chung PH, Webber RE, Shull KR, Shea LD.** Crosslinked hyaluronic acid hydrogels: a strategy to functionalize and pattern. *Biomaterials*. 2005 Feb;26(4):359-71.
3. **(3,4,5) Estudos clínicos Lubrinat ® - MASTER**



# Lubrinat®



## Non-hormonal Safe treatment:

- Lubrinat® - It can be used associated to HRT
- Lubrinat® - It can be used associated or after CHEMOT

## Biocompatibility Safety Testing (3,4,5):

- Skin Both no irritation and Sensitization - according to ISO 10993-10
- Vaginal mucosa no irritation - according to ISO 10993-10
- Penile mucosa no irritation - according to ISO 10993-10

1. **Zheng Shu X, Liu Y, Palumbo FS, Luo Y, Prestwich GD.** "In situ crosslinkable hyaluronan hydrogels for tissue engineering". *Biomaterials* (2004), **25**(7-8): 1339–48.
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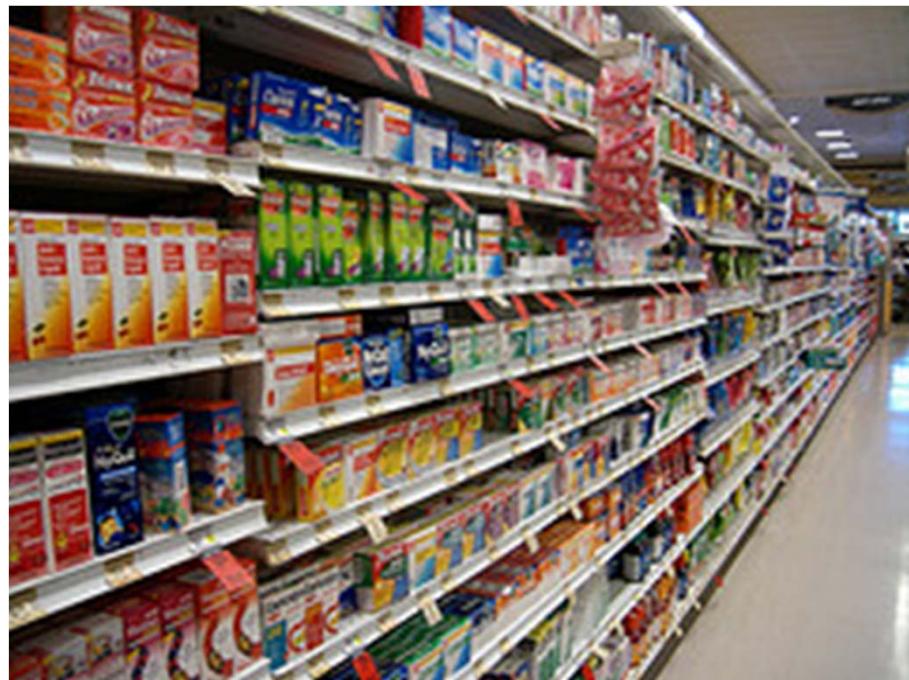
# Lubrinat®

Help your patients relieve vaginal dryness with a naturally-acting:

- Non-hormonal vaginal hydrating gel
- No additives
- No buildup or residue
- Clear and odorless
- Relief after one application (apply every three days)
- Helps to keep the natural vaginal pH balance



## Bussiness Opportunity





## Lubrinat<sup>®</sup> - Product Acquisition Opportunity

- Product by Master Farmacêutica – Brazil
- Launched & promoted by Merck in March 2016
- Substance: Sodium Hyaluronate
- Indication
  - ✓ Vaginal Hydration, Atrophic Vaginitis, Dyspareunia
  - ✓ For woman on Climacteric (Menopause), Postpartum / Breastfeeding
- Presentation
  - ✓ Box with 30g tube, with 10 disposable applicators for 30 days of treatment
- Benefits
  - ✓ Hormone Free
  - ✓ Long Lasting (Hydration for 72 hours)
  - ✓ Safety proven in Women with a history of Cancer
  - ✓ Scientific proof in important clinical trials
  - ✓ Efficacy equivalent to Estrogens threads
  - ✓ Well established among KOL physicians



## Lubrinat® Synergies With WH Portfolio

- ✓ Fast portfolio complementation once the product is already marketed and prescribed in USA/ Europe /Brazil
- ✓ Portfolio complementation with a fast growing branded product with high fit with current woman's products lines
- ✓ Portfolio complementation with a non-hormonal product (good attractiveness w/ Physicians)
- ✓ **Lubrinat** ® doesn't compete directly with hormones, but has a good commercial attractiveness of being indicated as a complement for HRT
- ✓ **Lubrinat** ® is a long lasting lubricant product which stripes dried layers maintaining humidity. There are no generics on market
- ✓ Non-Prescription product, with free price policy



# Lubrinat® - Basic Marketing Strategy

## Positioning

- Lubrinat® may be prescribed as Vaginal Hydration and a long lasting lubricant, with continuous usage and indicated to women in Climacteric, Postpartum, and others, while the common Lubricants on the market are regular OTCs indicated to non continuous usage, mostly as lubricants used prior to sexual intercourse
- Furthermore, from portfolio standpoint, Lubrinat® is promoted with similar indication as topical hormones but to be used in early stages of the same treatment, when most of physicians prefer not to prescribe hormone products.
- Lubrinat® may be used before physicians start prescribing hormones and may be kept during the treatment with hormones

## Demand Generation

- We will basically use the same current model with demand generation through Sales Reps calling on gynecologists.
- The strategy is different from the regular OTC lubricants (K-Y like) once those players generates demand mostly through mass media advertising and actions inside the POS (merchandising)