

Vaginal and cervical irritations

New ways to bridge watchful waiting periods

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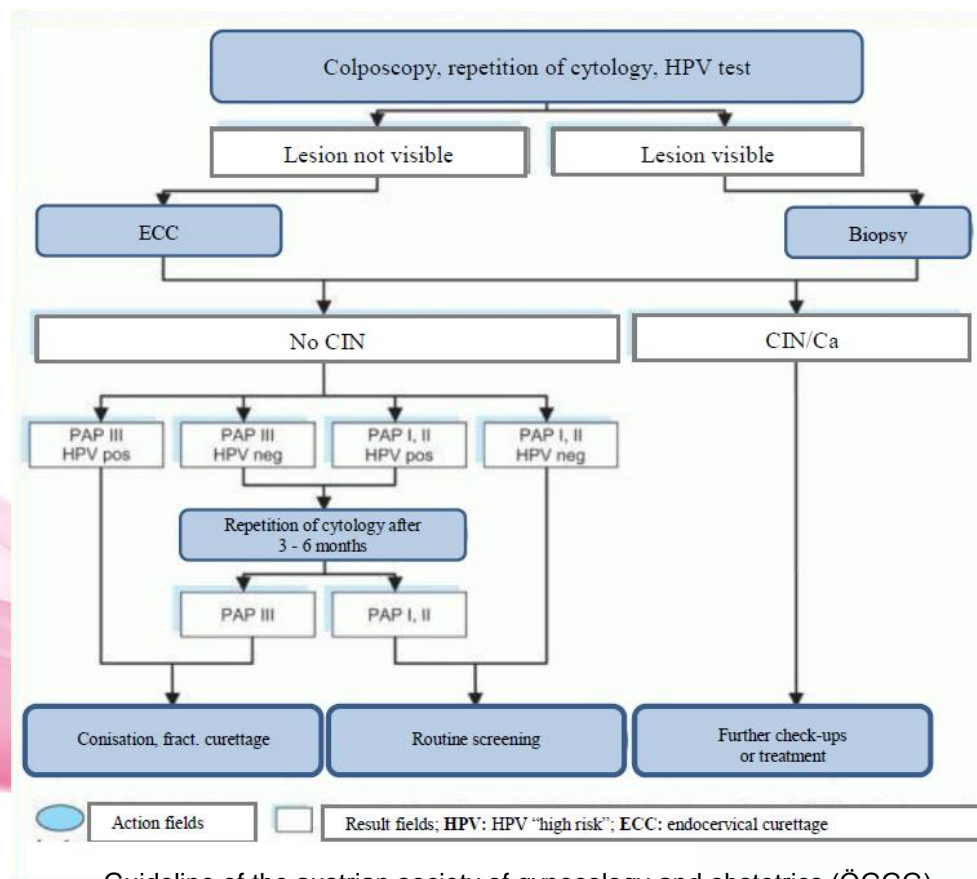
Cervical irritations – Classification systems

PAP	WHO	CIN	Bethesda	
I	Normal	Normal	Normal	
II	Reactive	Reactive	Reactive	
IIw	Atypical cells, Low grade	Atypical cells, Low grade	ASC-US, AGC	
III	Atypical squamous epithelium cells, High grade	Atypical squamous epithelium cells, High grade	ASC-US ASC-H	SeloGyn®
IIID	Minor dysplasia Moderate dysplasia	CIN 1 CIN 2	LSIL HSIL	
IIIG	Atypical glandular cells	Atypical glandular cells	AGC	
IV	Severe dysplasia	CIN 3	HSIL	
IV	Carcinoma in situ	CIN 3	HSIL	
V	Carcinoma, other malignant tumour	Carcinoma, other malignant tumour	Carcinoma, other malignant tumour	

Adapted from: Cervical Intraepithelial Neoplasia: History and Detection, L. Stewart Massad and Helen E. Cejtin.

Cervical irritations – Management of PAP III

Management of patients with PAP III without atrophy or inflammation

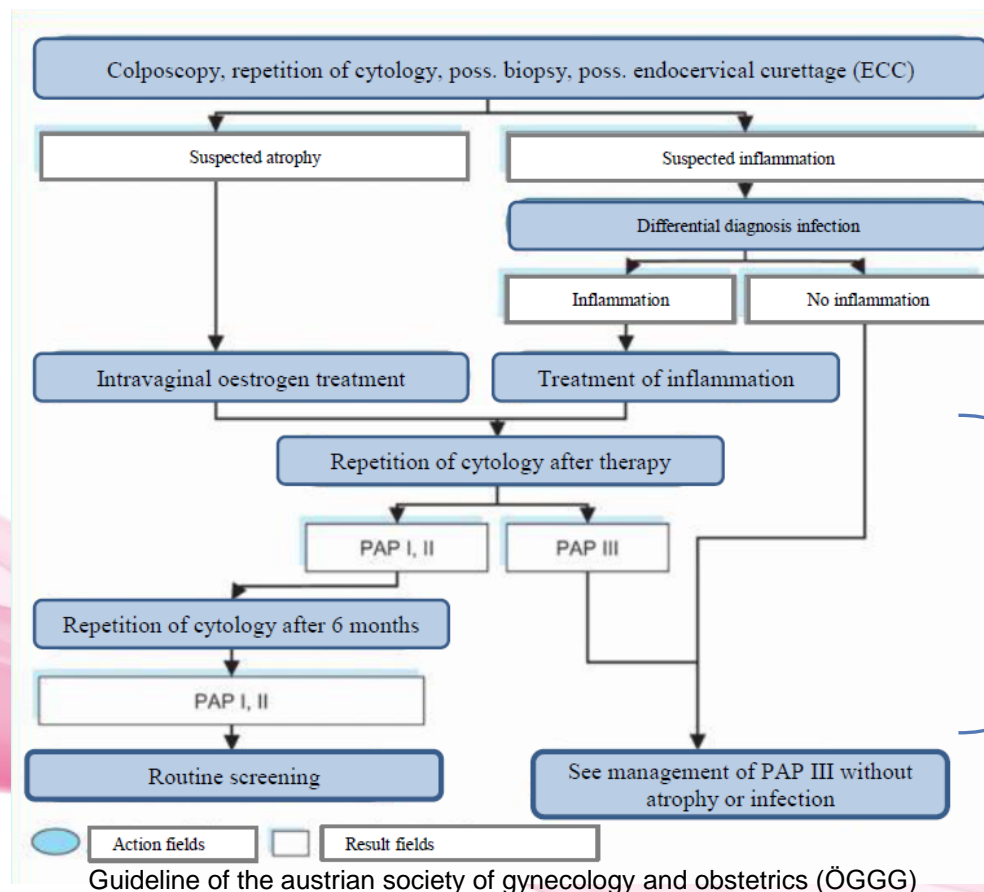


Guideline of the austrian society of gynecology and obstetrics (ÖGGG)

„watchful waiting“

Cervical irritations – Management of PAP III

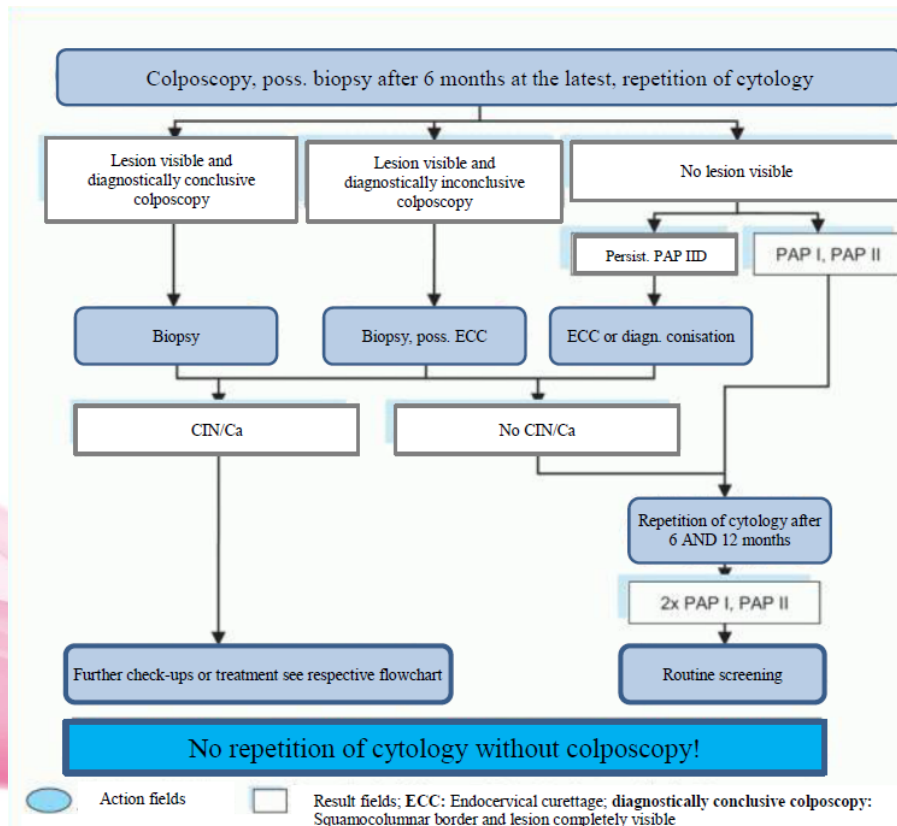
Management of patients with PAP III and suspected atrophy or inflammation



„watchful waiting“

Cervical irritations – Management of PAP IIID

Management of patients with PAP IIID



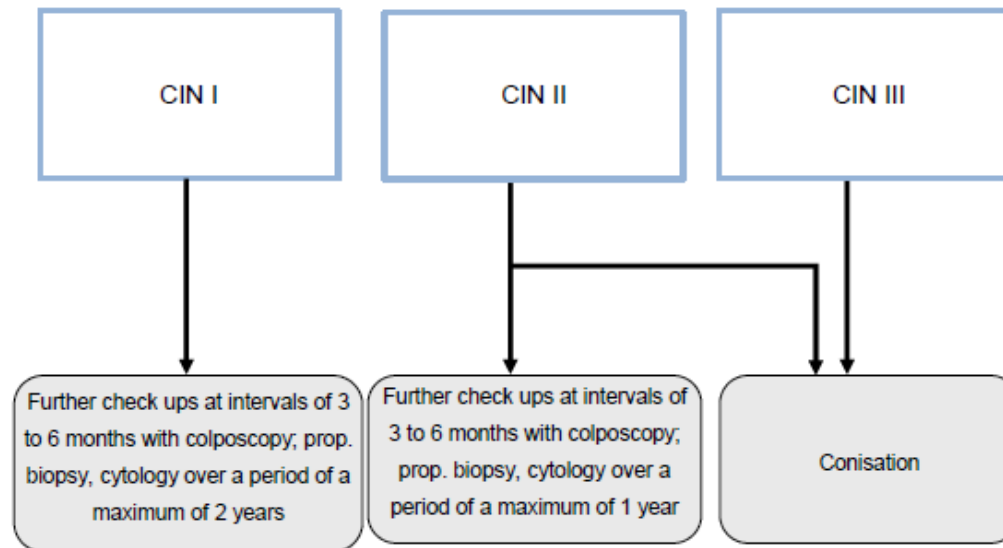
„watchful waiting“

Guideline of the austrian society of gynecology and obstetrics (ÖGGG)

Cervical irritations – Management of CIN I / CIN II

Management of patients with CIN I-III

„watchful waiting“



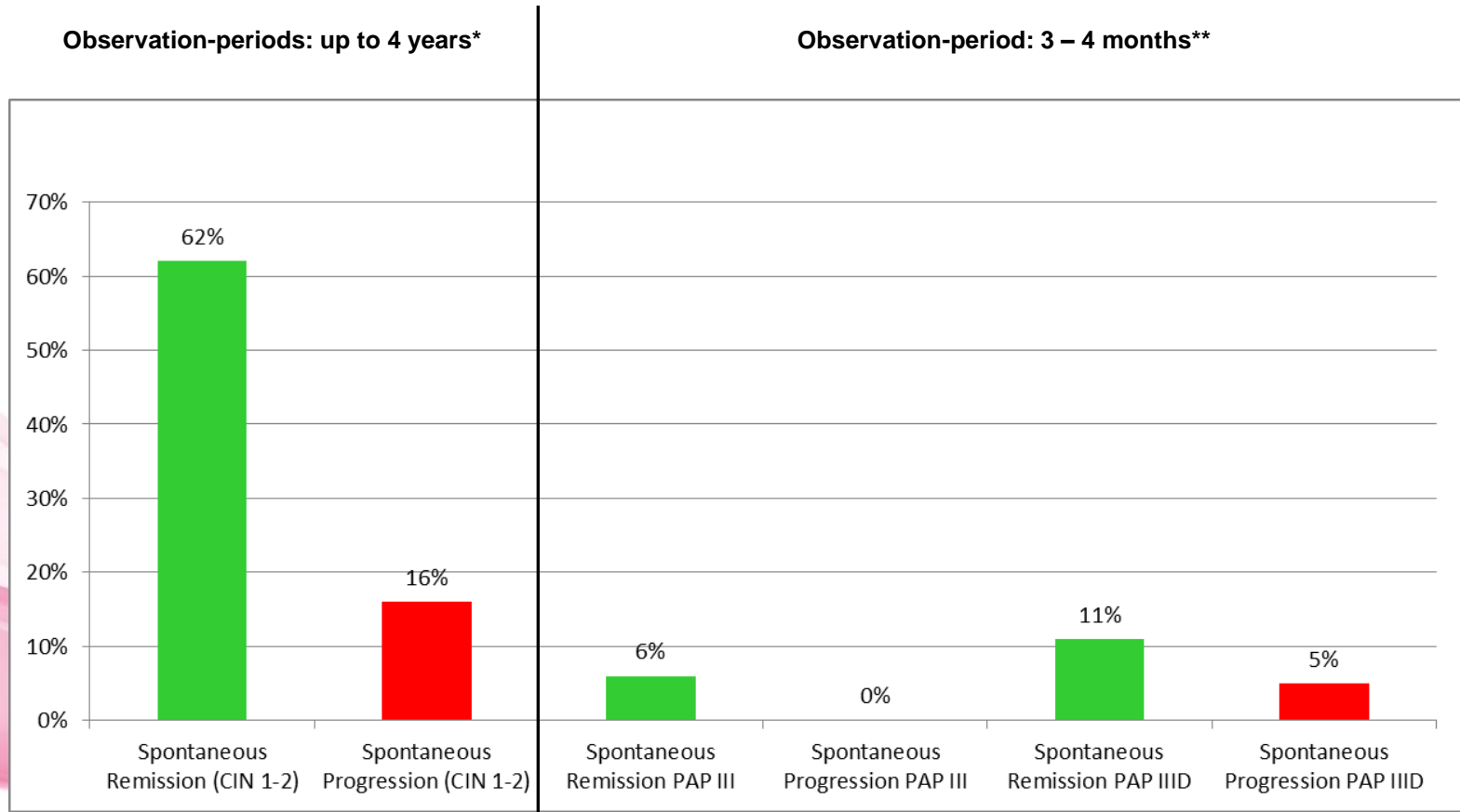
Legend:



An individual therapy is always possible: Conisation instead of control. Hysterectomy with additional indication.

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Cervical irritations - Spontaneous Remissions / Progressions



Literature:

*Bubendorfer, Zytologie in Pathologie, page 129, 2011

**Huber J. et al.: prepared for submission

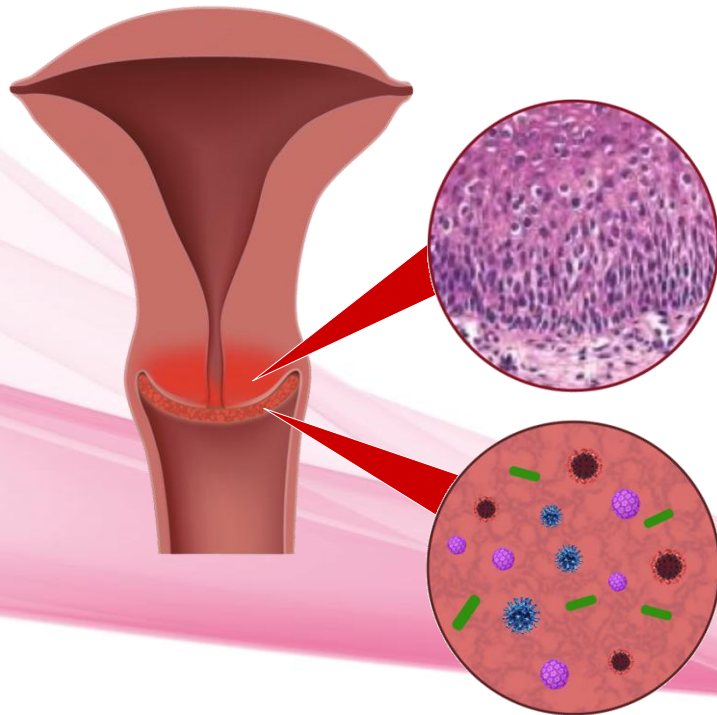
SeloGyn[®] vaginal gel – new option to bridge watchful waiting periods

Indication:

- Vaginal gel for the treatment of PAP III & PAP IIID
- PAP III & PAP IIID caused by
 - bacterial cervical irritation
 - viral cervical irritation
 - irritation of unknown origin

SeloGyn[®] vaginal gel – new option to bridge watchful waiting periods

Diagnosis:

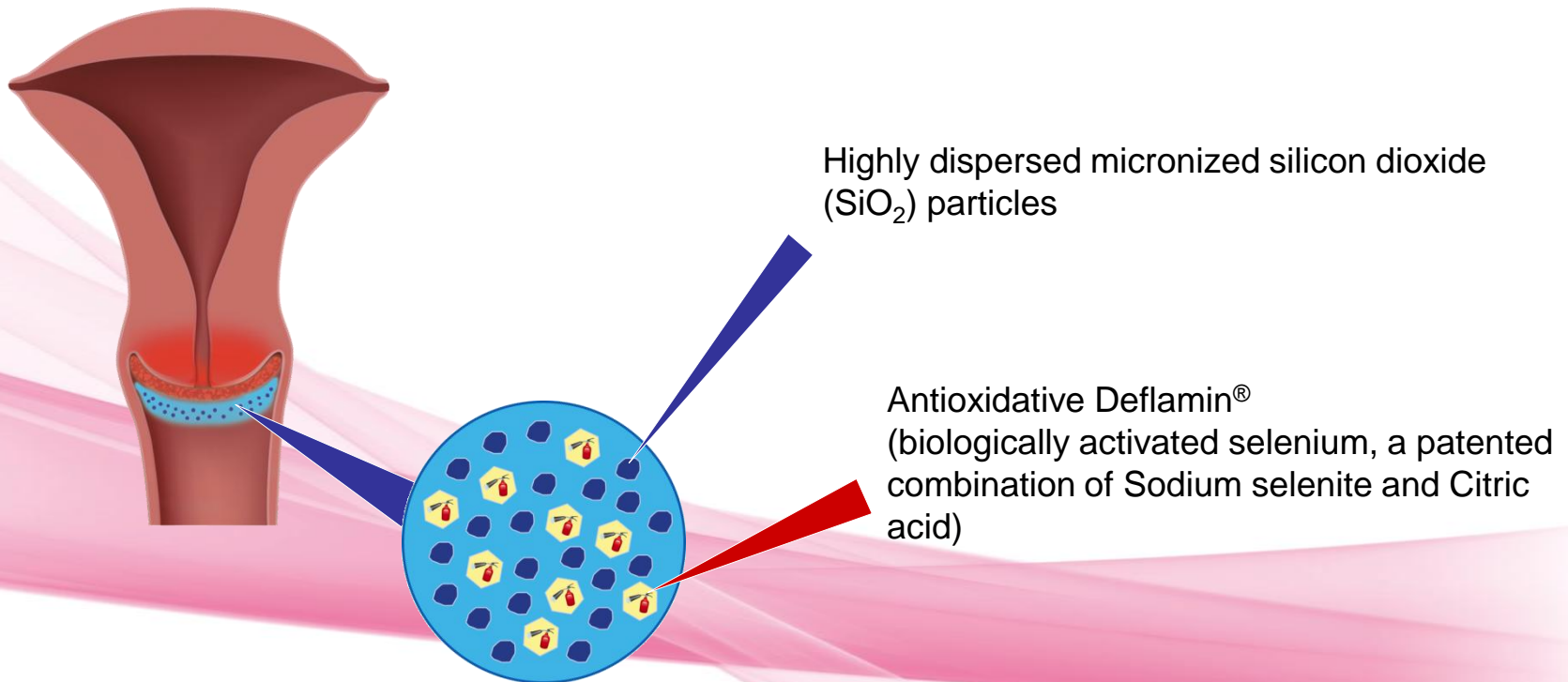


➤ Cervical epithelial irritation
(with optional partial cell changes)

- exogenically caused by
- bacteria
 - viruses
 - pro-oxidant (pro-inflammatory) particles of the vaginal secretion

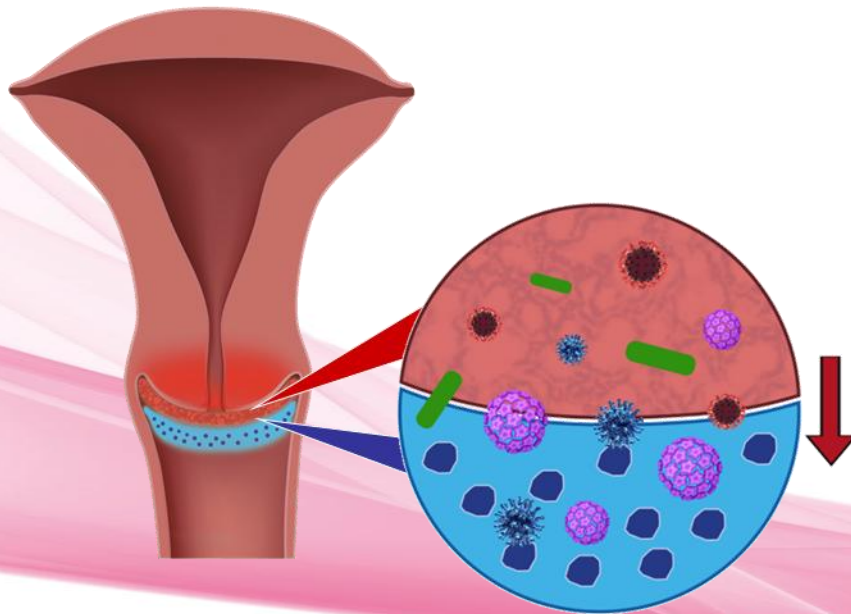
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Active components:



SeloGyn[®] vaginal gel – new option to bridge watchful waiting periods

Mode of Action: Adsorption effect

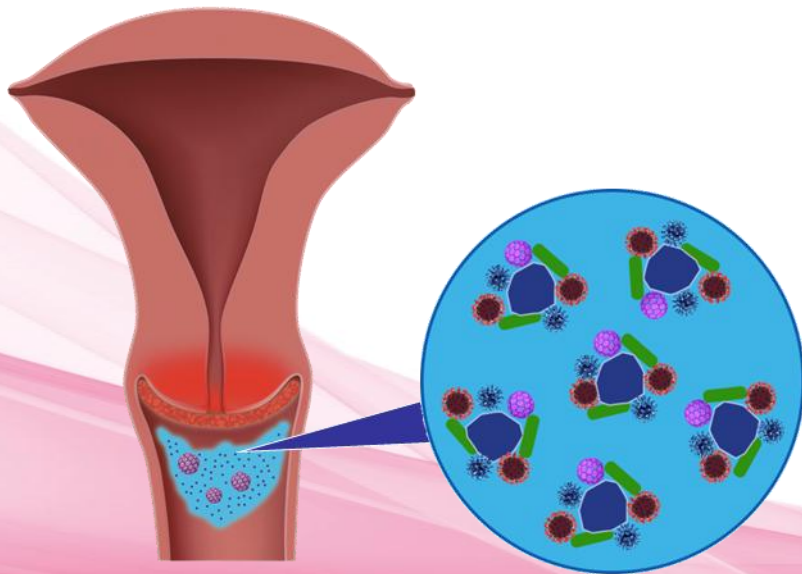


- Highly dispersed micronized silicon dioxide (SiO_2) particles adsorb pathogens from the cervical surface

The “adsorbing effect” of micronized silicon dioxide has been verified and photographically recorded through fluorescence microscopic tests by Zeta Partikel Analytik GmbH (<http://www.zeta-pa.de/>). The tests, conducted with *Staphylococcus aureus*, are extensively documented.

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Mode of Action: Binding effect

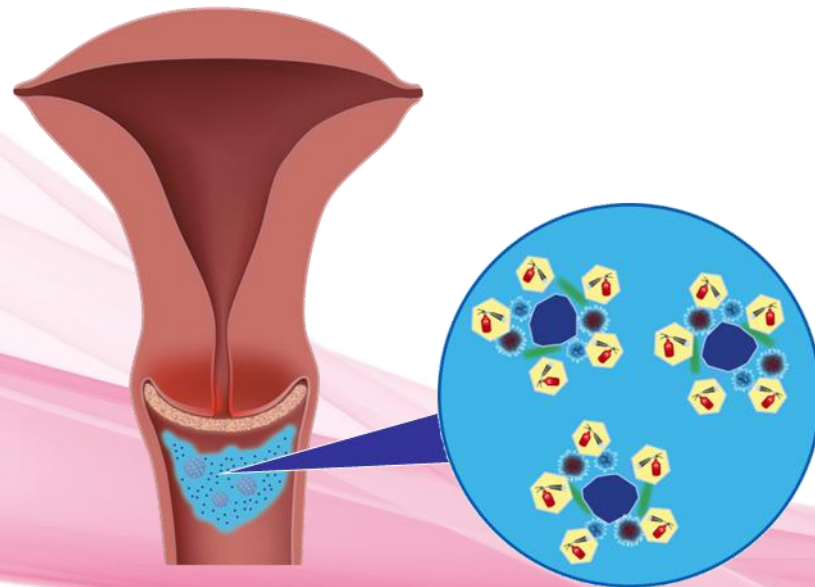


- SeloGyn[®] vaginal gel binds pathogens and inhibits their spread. This leads to a relief of the cervix epithelium.

The „binding effect“ of micronized silicon dioxide has been verified and quantified through in vitro tests using a vaginal secretion model test system by Prof. Geoffrey Lee / Friedrich-Alexander University of Erlangen (<http://www.pharmtech.uni-erlangen.de/people/lee.html>). The tests, conducted with Bovine Serum Albumin (BSA), are also described in detail and can be reviewed at any time.

SeloGyn® vaginal gel – new option to bridge watchful waiting periods

Mode of Action: Antioxidative effect



- The adsorbed and bound pathogens are now neutralized by the antioxidant properties of the patented Deflamin® formula (biologically activated selenium, a patented combination of Sodium selenite and Citric acid)

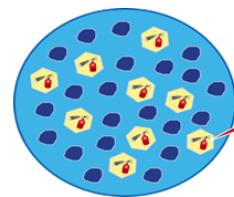
Patents:

1. "Selenium compound for the treatment of uterine inflammations"
2. "Use of aqueous selenite solutions for the manufacture of a medicament for the treatment of viral diseases and pigmented spots"
3. "Use of selenite-containing compounds to be topically or buccally administered"

The „antioxidative effect“ of Deflamin® has also been analysed gradually by Institut Prof. Dr. Georg Kurz GmbH (<http://www.institut-kurz.de/>) and showed the maximal antioxidative capacity of Deflamin® compared to other ingredients of SeloGyn®.

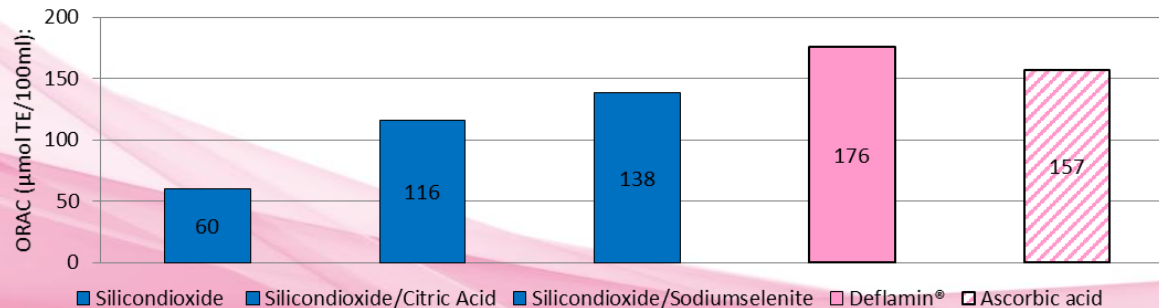
SeloGyn[®] vaginal gel – new option to bridge watchful waiting periods

DEFLAMIN[®]: highly antioxidative / anti-inflammatory properties



Antioxidative Deflamin[®]
(biologically activated selenium)

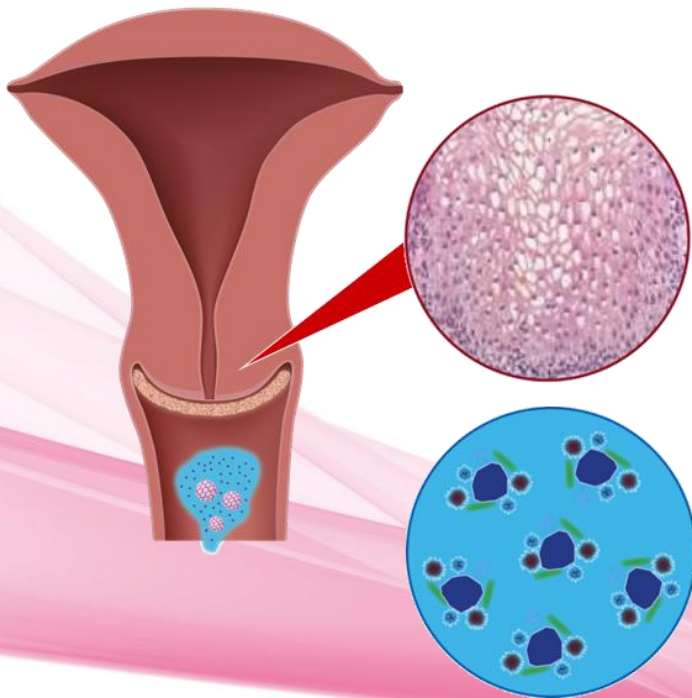
Antioxidative capacity



The „antioxidative effect“ of Deflamin[®] has also been analysed gradually by Institut Prof. Dr. Georg Kurz GmbH (<http://www.institut-kurz.de/>) and showed the maximal antioxidative capacity of Deflamin[®] compared to other ingredients of SeloGyn[®].

SeloGyn[®] vaginal gel – new option to bridge watchful waiting periods

Outcome – Relief of the cervix epithelium



- Due to the described three-step mode of action the irritated cervix epithelium is relieved, which improves the condition for a spontaneous remission.
- Elimination of the neutralized pathogens

The “Outcome” has been described by Prof. DDr. Huber <http://www.drhuber.at/> Huber J. et al.: Routine treatment of cervical PAP III and PAP III D.

SeloGyn® vaginal gel – new option to bridge watchful waiting periods

Presentation form

- Aqueous hydrocolloid gel
- 150 g suspension – gel in a vial
- 28 applicators



SeloGyn[®] vaginal gel – new option to bridge watchful waiting periods

Regulatory Status

- EEA (European Economic Area) approval / certification as Medical Device class IIa.
- Approved by TÜV SÜD / Munich as a Medical Device class IIa in the indication “Vaginal gel for the treatment of PAP III and PAP IIID” corresponding to Medical Device Directives (MDD – 93/42/EEC and 2007/47/EC).
- Approved by Turkish Ministry of Health.
- Product origin Austria.

Clinical studies - Overview

I. **Prospective / retrospective observational study: Routine treatment of vaginal and cervical irritations to bridge watchful waiting periods *)**

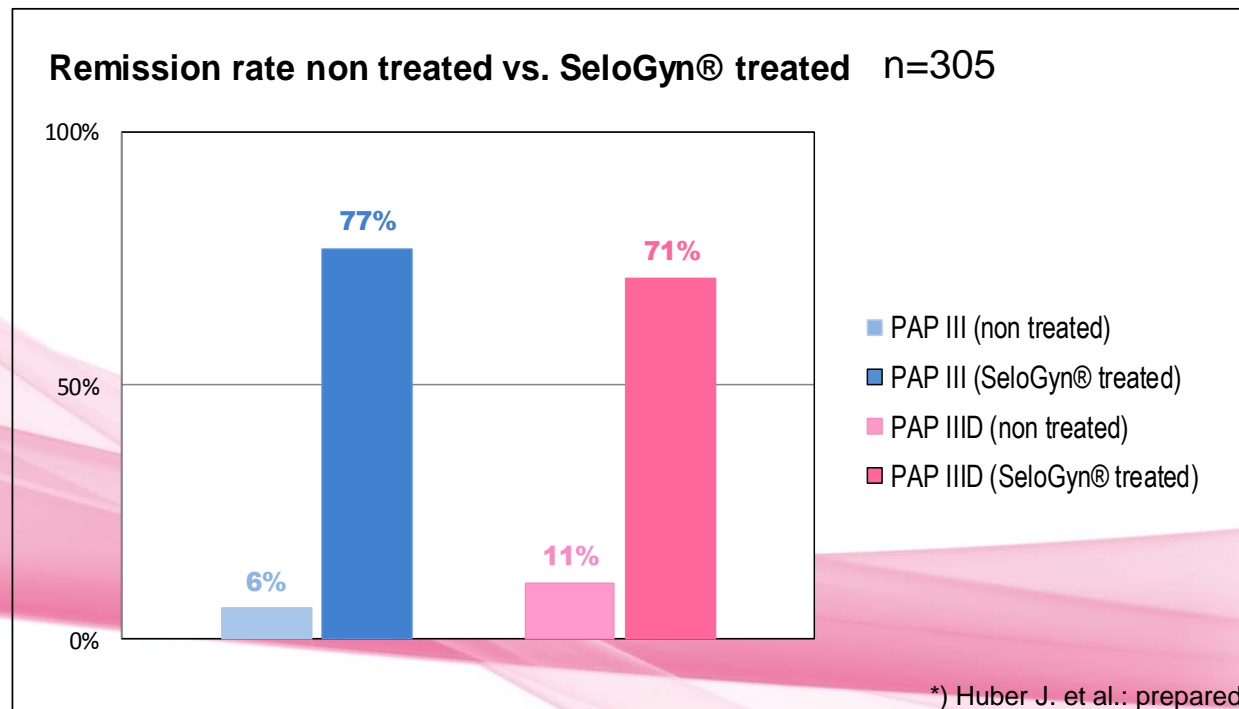
Aim of the study:	Treatment of cervical irritations <ul style="list-style-type: none">- Remission-Rates of PAP III / PAP IIID after treating with SeloGyn® vaginal gel for 3 x 28 days (prospectively)- Spontaneous Remission Rates of PAP III / PAP IIID without treatment – observation period 3 – 4 months (retrospectively)
Study centre(s):	multicentric, practitioner gynaecologists
Study type:	SeloGyn® treated patients: prospective, 182 patients
Control group:	retrospective, 123 patients

*) Huber J. et al.: prepared for submission

Clinical studies - Results

I. Prospective / retrospective observational study: Routine treatment of vaginal and cervical irritations to bridge watchful waiting periods *)

Routine treatment of cervical PAP III and PAP IIID (observation period: 3 - 4 months)



Clinical studies - Summary

I. **Prospective / retrospective observational study: Routine treatment of vaginal and cervical irritations to bridge watchful waiting periods *)**

Routine treatment of cervical PAP III and PAP IIID (observation period: 3 - 4 months)

- The rate of spontaneous remissions of 40 - 60% in case of PAP III or PAP IIID only apply for observation periods of 2 - 4 years, however in these periods also progression rates of 10 - 20% are observed.
- Shorter observation periods of 3 - 6 months only show spontaneous remission rates of **6 - 11 %**, which demonstrates the high therapeutic efficiency of SeloGyn®.
- Corresponding to actual clinical data, the therapeutic efficacy of SeloGyn® is **71-77%**, compared to 6 – 11% spontaneous remissions in the non-treated control group.

*) Huber J. et al.: prepared for submission

Clinical studies - Outcome

- I. **Prospective / retrospective observational study: Routine treatment of vaginal and cervical irritations to bridge watchful waiting periods *)**
 - **The use of SeloGyn®**
 - supports natural tendencies for remission
 - supports regeneration of irritated epithel
 - bridges the “watchful waiting” period

*) Huber J. et al.: prepared for submission

Clinical studies – Safety and Side Effects

Safety and Side Effects tests

- **Irritation Test** (BSL BIOSERVICE, 08.06.2011): SeloGyn® (test item) vs. Vaseline (control item) to New Zealand White rabbits - no indication of irritation response in the vagina with perivaginal tissue or vulva.
- **Delayed-Type Hypersensitivity Test [Guinea Pig Maximisation Test]** (BSL, 08.06.2011): SeloGyn® produced no signs of allergenic potency.
- The data analysis of the retrospective study showed that out of the documented 305 patients, 299 patients (97.4 %) reported no side effects. Only 8 patients (from 305 patients) documented a side effect.
Sodium Selenite is an ingredient of SeloGyn®. Due to a chemical reaction of sodium selenite SeloGyn® gets a slight reddish discolouration which does not impair the use of the product. This special warning is now part of the leaflet. In the retrospective study this special warning was not part of the leaflet. Due to this fact the involved women did not know that the slightly reddish vaginal discharge came from the use of SeloGyn and reported it as a side effect which it is not.
- The satisfaction with therapy was 77.6 % in the SeloGyn® group vs. 27.4 % in the non-SeloGyn® group.

Clinical studies - planned

II. Prospective, randomized, placebo-controlled double blind study

To support clinical evidence the conduction of an additional prospective, randomized, placebo-controlled double blind study with SeloGyn® is contemplated. The aforesaid clinical study is expected to start in June 2014 and should be completed in May 2015:

- 2 x 60 Patients (60 Verum / 60 Placebo)
- Study planning in coordination with Univ. Prof. Müller / University Hospital Inselspital in Bern / Switzerland.
- Prof. Müller is an expert in the field of Gynecology and Oncology
- Classification according to Papanicolaou and Bethesda (ASC-US / ASC-H)
- Improvement of PAP smear
- Improvement of histological findings (CIN1, CIN 2)
- Detection of HPV clearance
- Long term data follow up (12 months)
- Nugent score

Thank you for your attention