



Ziwig Endotest®

A saliva test for the early and reliable diagnosis
of endometriosis

Women suffering from endometriosis, for the most part, go through a long period of doctor-hopping (over a period of 8 to 12 years on average)¹. During this time they see multiple physicians and undergo numerous tests and examinations before a diagnosis, which sometimes requires surgery, is finally reached.

A global innovation now allows women suffering from endometriosis to avoid this tortuous medical journey. A team made up of expert doctors specialized in endometriosis, engineers in artificial intelligence, and medical researchers from Ziwig, has recently developed a saliva based diagnostic test that uses Next Generation Sequencing of microRNAs.

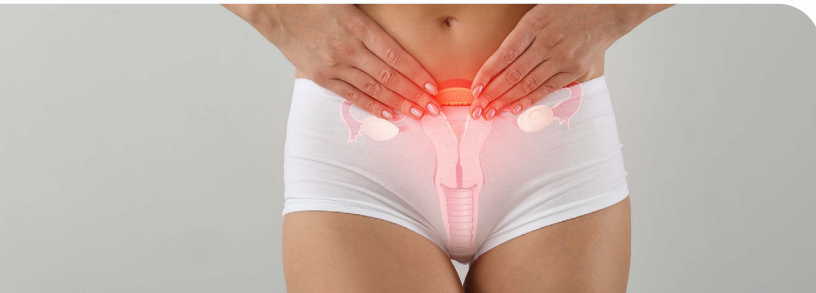


This simple and non-invasive test, called Ziwig Endotest®, allows for the early diagnosis of all types of endometriosis with a performance that exceeds that of conventional diagnostic tests²⁻⁶ (sensitivity > 95%, specificity > 95%, diagnostic accuracy AUC > 95%).

Ziwig Endotest® has been validated by one of the largest clinical trials ever carried out in this field⁶ in collaboration with 18 French centers specialized in endometriosis. The Diagnostic performance was tested firstly on blood samples⁶, and then on saliva samples⁴. This tool is set to revolutionize the diagnosis of, and the care for, endometriosis by providing a reliable and rapid diagnosis to healthcare professionals who prescribe the test.

Ziwig Endotest® has obtained the CE label.

Endometriosis, a scarcely known disease



Endometriosis affects about 10% of women of childbearing age in the Nordics, i.e. about 700 000 women. It potentially affects all women and can appear as early as from adolescence.

Endometriosis is characterized by the presence of endometrial-like epithelium and/or stroma outside of the uterine cavity (womb). The growth of these tissue fragments is frequently associated with an inflammatory process⁷. During menstruation, endometriosis lesions can react to variations in hormonal levels, leading to acute inflammation, bleeding, severe pain and many other symptoms.

Endometriosis can also be completely asymptomatic, and is sometimes diagnosed during a consultation prompted by difficulty in conceiving. In fact, a significant proportion of patients with endometriosis suffer from infertility.

Main symptoms of endometriosis:

- Severe menstrual pain
- Pain during sexual intercourse
- Pelvic pain outside of menstruation
- Pain in the right shoulder
- Digestive problems
- Intense fatigue
- Urinary disorders
- Infertility
- Pain during defecation
- Alternating diarrhea – constipation

A major impact on personal and social life



Endometriosis causes a significant deterioration in quality of life.

Pain is responsible for a disruption in sleep that induces chronic fatigue and symptoms of psychological distress (irritability, depression, etc.). This can have a significant impact on overall well-being, as well as on personal and public relationships. The repercussions of endometriosis on a patient's working life is also considerable, with a marked increase in repeated scholar or professional absenteeism.

Moreover, the persistence of pain can induce a phenomenon of **wwwwww**: pain perception thresholds decrease over time leading to the onset of chronic pain.

This can occur at any stage of endometriosis and chronic pain can persist even after lesions have been treated.

A saliva test, why and when?

Compared to current methods, Ziwig Endotest® represents a major innovation in the diagnosis of endometriosis⁹. Patient care will be greatly improved via the reduction of the average time to diagnosis from several years to a few weeks¹. Ziwig Endotest® paves the way for the early treatment of endometriosis and represents a major paradigm shift in clinical practice².

The advantages of Ziwig Endotest®:

- Clear Positive/negative result
- Rapid diagnosis
- All forms of endometriosis can be diagnosed²⁻⁶
- High reliability: close to 100% (sensitivity > 95%, specificity > 95%, diagnostic accuracy (AUC) > 95%)⁷
- Simple and non-invasive sample collection





When to prescribe the saliva test?

It is essential to remove any doubts of the possibility of endometriosis as soon as possible. The prescription of Ziwig Endotest® is intended for women between the age of 18 and 43 years with symptoms suggestive of endometriosis¹⁰.

Suggestive symptoms of endometriosis⁹:

- Chronic pelvic pain
- +/- dysmenorrhea/painful menstrual periods
- +/- deep dyspareunia/painful intercourse
- +/- dysuria/painful urination
- +/- dyschezia/painful defecation
- +/- painful rectal bleeding
- +/- haematuria (blood in urine) during menstruation
- +/- pain in the shoulder tip
- +/- infertility



Ziwig Endotest® is not intended to replace diagnosis by pelvic medical imaging. Medical imaging remains essential after diagnosis for lesion description, mapping, and classification.

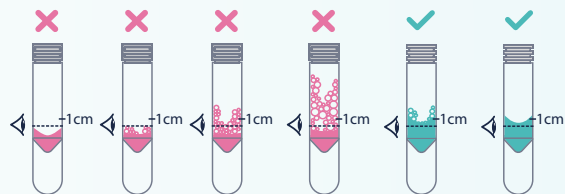
Instructions for collecting saliva samples

30 minutes before sampling:

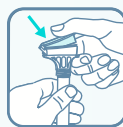
- Wash your hands
- Do not use if you are sick (infection)
- Do not eat or drink
- Do not smoke or use snuff
- Do not chew gum
- Do not wear lipstick
- Do not brush your teeth



The quantity of liquid must be sufficient and exceed the filling line by at least 1 cm (not including bubbles).



1. Spit in the funnel until the amount of liquid (without bubbles) reaches 1 cm above the filling line.



2. Close the tube tightly by pressing strongly on the funnel cap until you hear a clear click.



3. Unscrew the funnel from the tube.



4. Close the tube with the cap.



5. Shake the tube for 5 seconds.

Treatment and care

Currently, endometriosis remains without a complete cure. However, early diagnosis allows for targeted care that can slow or even stop the worsening of pain and other symptoms, thereby greatly improving patient quality of life. Furthermore, an optimized treatment strategy can be implemented in case of associated infertility.

In addition to the analgesic treatment and supportive care adapted to each patient, hormonal treatments, which are based on the use of estrogen-progestin contraceptives or progestins, aim to block menstruation. These treatments reduce the intensity of symptoms and their consequences on quality of life. As a second-line treatment, it is also possible to use GnRH analogues, with the effect of putting patients in a state of reversible menopause. This treatment is always combined with an "add-back therapy" to avoid hot flashes.

Surgical treatment is considered when medical treatments are insufficient to alleviate pain⁹. The objective of surgery is to remove or electro-coagulate endometriosis lesions and correct anatomical abnormalities caused by the disease. The procedure is most often performed by laparoscopy.

Sciences



Ziwig Endotest® uses two cutting-edge technologies: Next Generation Sequencing and artificial intelligence. Through a simple saliva sample, 109 different microRNAs are analyzed to diagnose endometriosis.

The development of a non-invasive test for the diagnosis of endometriosis has been the subject of intense medical research for many years. More than 100 biomarkers have been evaluated over the last decades. Among them, a new class of molecules first described in 1993, microRNAs, has emerged as a promising option, supported by a growing number of studies on tumors and neurodegenerative disorders.

MicroRNAs are small non-coding RNAs. They participate in gene expression: when a microRNA binds to its target, a specific messenger RNA, it blocks or stimulates its translation into protein and/or causes its destruction.

MicroRNAs are also released into the extracellular environment through different transport structures that protect them from ribonucleases. This gives them a remarkable stability. These circulating microRNAs are found in varying amounts in body fluids (blood, urine, breast milk, tears, saliva, etc.).

In recent years, there has been increasing evidence of the contribution of microRNAs in the pathophysiological mechanisms of endometriosis. A direct link has been proven between the dysregulation of certain microRNAs and the development of endometriosis lesions¹¹.

The studies on Ziwig Endotest® have been published in international peer-reviewed scientific journals.



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About Ziwig

Ziwig® is an innovative French biotech specialising in salivary RNA analysis and AI. It operates as an ecosystem at the crossroads of several medical, scientific, and digital disciplines. Ziwig® is strongly committed to disruptive innovations that support the transformation of healthcare systems towards more effective, more humane, and more accessible precision medicine.

www.ziwig.com

Acknowledgements

Ziwig®'s ambition to foster research and treatment of endometriosis and to change the way we understand this debilitating disease that affects so many women around the world, would never have succeeded without all the women and men who believed in our project.

They fought alongside us to make this innovation possible. On behalf of all those who will benefit from our progress, we thank them!



Ziwig Endotest® wins
the Prix Galien 2022

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