LIFE GENOMICS

Endometriosis: A major cause of infertility

Ziwig Endotest®

The saliva test for an early and reliable diagnosis of endometriosis

Endometriosis and infertility

Endometriosis is one of the main causes of infertility among women, and affects around one third of women with endometriosis[1].

When women have difficulty conceiving, endometriosis is often discovered by chance as part of an infertility assessment, as endometriosis can sometimes be completely asymptomatic otherwise.

Endometriosis is characterized by the development, outside the uterine cavity, of tissue similar to endometrial tissue[2]. During menstruation, these tissue fragments react to hormonal variations, leading to symptoms.

Endometriosis can affect fertility by causing changes in reproductive organs such as the fallopian tubes or ovaries as a result of inflammation, cyst formation, or by altering the uterine environment and by disturbing the hormonal balance necessary for conception.

Endometriosis affects around 10% to 15% of women of childbearing age[1,3]. It can potentially affect any woman in good health and can appear as early on as adolescence. Most women suffering from endometriosis go through a long period of medical wandering (7 years on average)[3], during which they undergo numerous medical appointments, tests and examinations before a diagnosis is made, sometimes requiring surgery.

A saliva test, why do we need one?

Ziwig Endotest® is a major scientific advancement[4,5], it enables a rapid and reliable diagnosis of endometriosis[6]. As a result, it allows for earlier targeted care with the introduction of fertility preservation, reducing the average diagnostic time from several years to just a few weeks[7]. The introduction of Ziwig Endotest® into routine clinical practice represents a major paradigm shift for patients and practitioners[7].

The advantages of Ziwig Endotest®:

Clear positive/ negative result

Rapid diagnosis

All forms and stages of endometriosis can be diagnosed[5,7-11]

High reliability: (Sensitivity >95%, Specificity >95%, Diagnostic Accuracy (AUC) >95%)[7]

Simple and non-invasive saliva sample

This simple and non-invasive diagnostic test, called Ziwig Endotest®, facilitates the diagnosis of endometriosis in cases of infertility with high reliability (sensitivity > 95%, specificity > 95%, diagnostic accuracy (AUC) > 95%)[6]. Ziwig Endotest® also enables early diagnosis of all forms of endometriosis with performance that exceeds that of conventional diagnostic tests[12] (sensitivity′ > 95%, specificity′ > 95%, diagnostic accuracy AUC > 95%[7]).

Ziwig Endotest®, is based on the Next-Generation Sequencing (NGS) of microRNAs present in saliva. It was developed by a French team of doctors specializing in endometriosis, experts in artificial intelligence and medical researchers. The diagnostic signature has been validated by the world's leading clinical studies in this field of saliva biomarkers[5,8–11], in collaboration with 18 French centers specializing in endometriosis, first in blood[11], then in saliva[9].

Ziwig Endotest® opens up new perspectives for the care of patients suffering from infertility, as part of the initial work up, thanks to a reliable and rapid diagnosis, on prescription from a healthcare professional.

By diagnosing endometriosis at an early stage, Ziwig Endotest® makes it possible to personalize the care pathway and to propose the most appropriate treatments to patients. Thereby saving time and improving chances of conception, either through medically assisted procreation or through spontaneous conception after surgery.

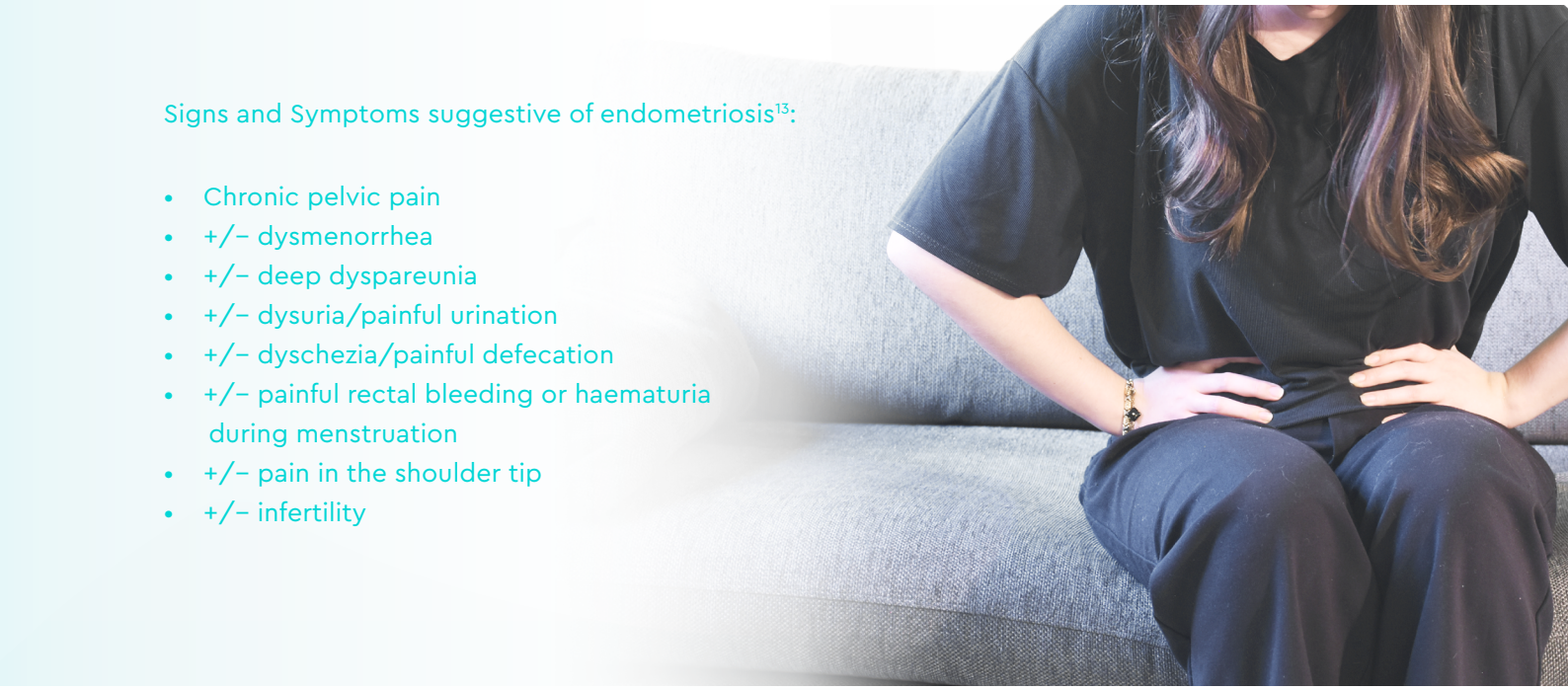
Ziwig Endotest® is CE marked.

When to prescribe Ziwig Endotest®?

Removing doubt as early as possible relative to the risk of infertility and the possibility of endometriosis saves time and helps to shorten periods of medical wandering. Ziwig Endotest® is intended for patients aged between 18 and 43 with infertility and/or who present one or more symptoms suggestive of endometriosis[13].

Signs and Symptoms suggestive of endometriosis[13]:

- Chronic pelvic pain
- +/– dysmenorrhea
- +/– deep dyspareunia
- +/– dysuria/painful urination
- +/– dyschezia/painful defecation
- +/– painful rectal bleeding or haematuria 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.

Treatment and care

The current management of endometriosis is multi-disciplinary including medical and non-medical measures and, in some cases, surgery.

The early diagnosis of endometriosis enables targeted treatment to be given from the onset of symptoms with the aim of slowing the progression of the disease and optimizing fertility care.

For professionals

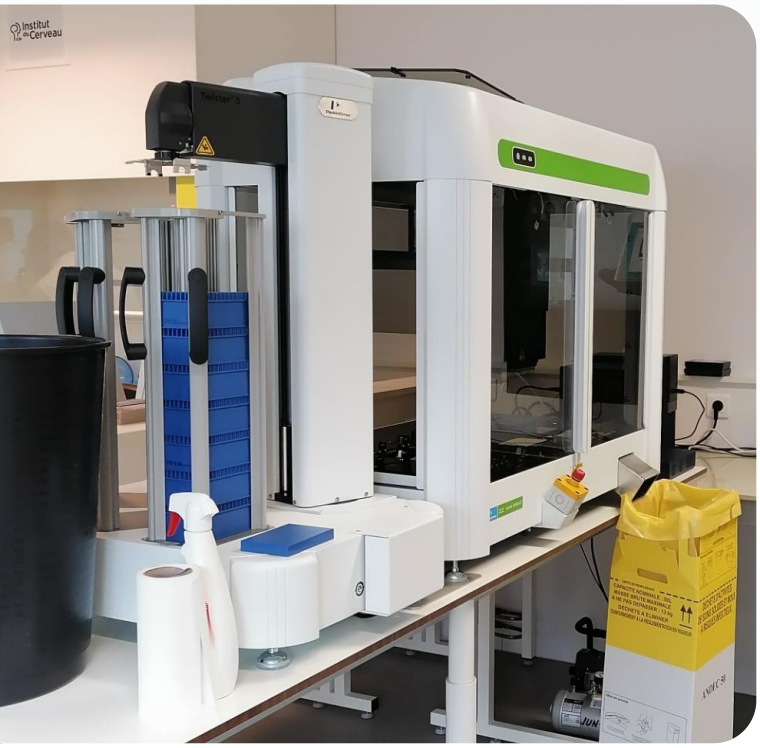
For healthcare professionals, Ziwig Endotest makes it possible to identify the presence of endometriosis and the associated risk of infertility, and to put in place a personalised care plan tailored to the desire for pregnancy. A negative saliva test result eliminates the possibility of endometriosis, which is otherwise difficult to diagnose (ultrasound, MRI, etc.), allowing healthcare professionals to explore other possible causes of symptoms and infertility.

For patients

Ziwig Endotest® makes it possible to rule out or confirm the presence of the disease by shortening the period of diagnostic uncertainty and medical wandering. Improving quality of life rather than diagnosis can thereby become the focus of attention. Among patients with difficulties conceiving, in many cases endometriosis is the underlying cause. Thanks to the saliva test, valuable months or years can be saved, during an assisted reproductive process which is often a source of uncertainty and stress for women.

Ziwig

Science



Since 2022, Ziwig's scientific work has continued to open new perspectives, by **quantifying more than 2,600 miRNAs in saliva**, by **linking known miRNAs to pathophysiological mechanisms**, and by **combining 109 miRNA** to create a robust diagnostic signature for endometriosis.

Ziwig Endotest® wins the Prix Galien 2022

The development of a non-invasive test for the diagnosis of endometriosis has been the subject of active medical research for many years.

Before 2022, only a handful of biomarkers had been evaluated in prospective trials. Among them, a new class of molecules first described in 1993, microRNAs, emerged as a promising option, supported by a growing number of studies in diverse fields such as tumors and neurodegenerative disorders.

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

MicroRNAs are also released into the extracellular environment via various transport structures that protect them from ribonucleases present in different body fluids, giving them remarkable stability. Circulating microRNAs are found in varying quantities in body fluids (blood, urine, breast milk, tears, saliva, sperm, etc.).

In recent years, there has been increasing evidence of the contribution of microRNAs to the pathophysiological mechanisms of endometriosis. A direct link has been proven between the deregulation of certain microRNAs and the development of endometriosis lesions[14]. A link has also been established between the risk of infertility and endometriosis[6]. MicroRNAs were the subject of two Nobel Prizes in Medicine and Physiology in 2006 and 2013.

Some of Ziwig Endotest®'s scientific work has been published in international peer-reviewed scientific journals.

NEJM Evidence

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About Ziwig

Ziwig® is an innovative French biotech specializing in salivary RNA analysis and artificial intelligence (AI). Ziwig® operates as an ecosystem at the crossroads of several medical, scientific and digital disciplines, and is strongly committed to disruptive innovations that support the transformation of healthcare systems towards more efficient, more personalized and more human-friendly precision medicine.

In December 2023, Ziwig launched GYN-ARN, a highly promising new study for women's health. This is a pioneer study into the development of a multi-pathology diagnostic saliva-based test in gynaecology. GYN-ARN aims to identify the RNA signatures specific to gynaecological pathologies, symptomatic, benign or malignant, for which surgical management may be indicated. The pathologies studied include endometriosis, adenomyosis, ovarian cysts, fibroids, early cervical dysplasia, as well as uterine and cervical cancers.

www.ziwig.com

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