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LABORATORY



HTS Labs

Ziwig Endotest[®]

A saliva test for the early and reliable
diagnosis of endometriosis



Ziwig





The average time for diagnosis in women is approximately 8 years¹. During this time they might see any number of physicians and undergo numerous tests and examinations before a diagnosis, which sometimes requires surgery, is made.

New technology now allows women suffering from endometriosis to benefit from an early diagnosis. A French team of experts specialising in endometriosis has recently developed a saliva based diagnostic test that uses Next Generation Sequencing of microRNA's with AI.

This non-invasive test, called Ziwig Endotest®, allows for the early detection of all types of endometriosis with a performance that exceeds that of conventional diagnostic tests²⁻⁶ (sensitivity >95%, specificity >95%, diagnostic accuracy AUC >95%⁴).

The Ziwig Endotest® is indicated for the diagnosis of endometriosis based on a miRNA signature, for female patients between the age of 18 and 43 years clinically suspected of endometriosis. It is a prescriptive-use only device, and saliva collection must be done under the supervision of a healthcare professional.

The Ziwig Endotest® has not been validated for use outside of the indicated population and it is not valid for, among others, use by: 1) Pregnant patients, 2) Patients with a history of Cancer and/or with Human Immunodeficiency Virus (HIV), 3) Patients with an acute infectious disease status and/or a disease that can be transmitted via saliva, 4) Patients with a gynaecological infection requiring surgical management.

The Ziwig Endotest® can only be used in accordance with the guidelines detailed in the instructions provided with the collection kit. Further studies are expected.

Ziwig Endotest® has been validated by one of the largest clinical trials⁶ for endometriosis in collaboration with 18 French specialist endometriosis centres. The diagnostic performance was initially tested from blood⁶, which later progressed to saliva samples⁴, providing clinicians with a reliable and rapid diagnostic test. Ziwig Endotest® has obtained the CE label.

Endometriosis affects about 10% of women in the UK. It potentially affects all women and can present from adolescence.

Endometriosis is characterised by the presence of endometrial-like epithelium and/or stroma outside 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 with conceiving. The prevalence of endometriosis in women with infertility is 30–50%.

Main symptoms of endometriosis:

- Severe menstrual pain
- Pain during sexual intercourse
- Pelvic pain
- Pain in the right shoulder
- Digestive issues
- Intense fatigue
- Urinary disorders
- Infertility
- Pain during defaecation
- Alternating diarrhoea/constipation
- Impacted well being

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When to request the Ziwig Endotest®

Ziwig Endotest® is validated for women between 18 and 43 years of age, presenting with one or more conditions associated with endometriosis.^{4,9}

Suggestive conditions include⁹:

- Chronic pelvic pain
- Dysmenorrhoea
- Dyspareunia
- Pelvic pain outside menstruation
- Pain suggestive of sciatica
- Pain in the right shoulder during menstruation
- Blood in stool or urine during menstruation
- Infertility
- Pain during defaecation or urination
- Alternating diarrhoea/constipation

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

A saliva test, why and when?

Compared to current methods Ziwig Endotest® represents a major innovation in the detection of endometriosis.⁸

Patient care will benefit greatly from the reduction in time to diagnose endometriosis, and this represents a major paradigm shift in clinical practice.²

The advantages of Ziwig Endotest®:

- Clear Positive/Negative results
- Early diagnosis
- All forms of endometriosis can be diagnosed²⁻⁶
- The Endotest Diagnostic has a sensitivity > 95%, a specificity > 95% and diagnostic accuracy (AUC) > 95%.⁴
- Non-invasive saliva sample



About Ziwig

Ziwig Endotest® has been developed by Ziwig®, a French company whose ambition is to improve women's health through a holistic approach and the development of products, services and a care ecosystem guided by science and the unique biology of each individual. This approach is supported by ongoing research excellence and is based on the close collaboration of medical experts and engineers specialized in cutting-edge technologies such as artificial intelligence and Next Generation human RNA Sequencing.

Its functioning is based on an ecosystem, driven by the quest for excellence and patient centered, that uses disruptive technologies. This contributes to the emergence of precision medicine that is individualised, predictive and participatory, serving women's well-being and quality of life.

www.ziwig.com

For information on how to access this service please discuss with your healthcare provider.



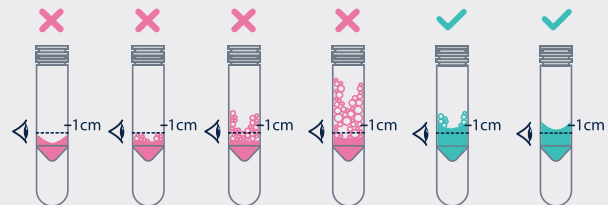
Instructions for collecting saliva samples

30 minutes before sampling

- Wash your hands
- Do not use if you are sick (infection)
- Do not eat or drink
- Do not smoke
- 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 1cm (not including bubbles).



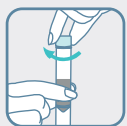
1 Spit in the funnel until the amount of liquid in the tube reaches about 1 cm above the fill line. Do not include the bubbles in the measurement.



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 small cap.



5 Shake the capped tube for 5 seconds and then place the tube into the long, self seal, sample bag.



6 There are two barcode stickers on the underside of the clear plastic box containing the saliva collection device. Affix one of the stickers to your request form, other barcode is not required. There are two name labels with the request form. Complete the labels with the patient's name, DOB and sex and affix one label to the white section on the tube (taking care not to cover the fill line) and affix the other name label on the long clear sample bag. Place the labelled sample tube into the labelled clear bag and place back into the plastic box. Return the saliva sample using the outer cardboard box.



7 Ensure your request form is enclosed with your saliva sample and sent to the laboratory in the outer coloured Royal Mail Tracked 24 plastic envelope provided.

Important checklist

- Before you return the saliva sample, please place the completed request form into the returning postal pack.
- Make sure one barcode sticker is applied to the request form. Affix a label with the patient's name, DOB and sex to the sample tube and another to the long sample bag.
- Place the labelled saliva tube into the labelled long sample bag then into the collection kit and close the box and place it into the return postal envelope.
- Please post your sample to The Doctors Laboratory as soon as possible from any Royal Mail post box in the UK. No stamp is required within the UK.

If you need assistance please contact
The Doctors Laboratory on 020 7307 7373
or email endotest@tdlpathology.com

Treatment and care

Currently endometriosis remains without a complete cure and chronic pain can persist even after treatment.

However, early diagnosis allows for targeted care that can slow or even stop the worsening of pain and other symptoms. Furthermore, an optimised 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 pain.⁸ 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.

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

The science

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 tumours 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 present in the circulation and give 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 lesions.¹⁰

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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!



**Unit H9
Maynooth Business Campus
Straffan Rd, Maynooth
Co. Kildare W23 NY98
Ireland**

**T 01-9012000
E info@htslabs.ie
W www.htslabs.ie**

