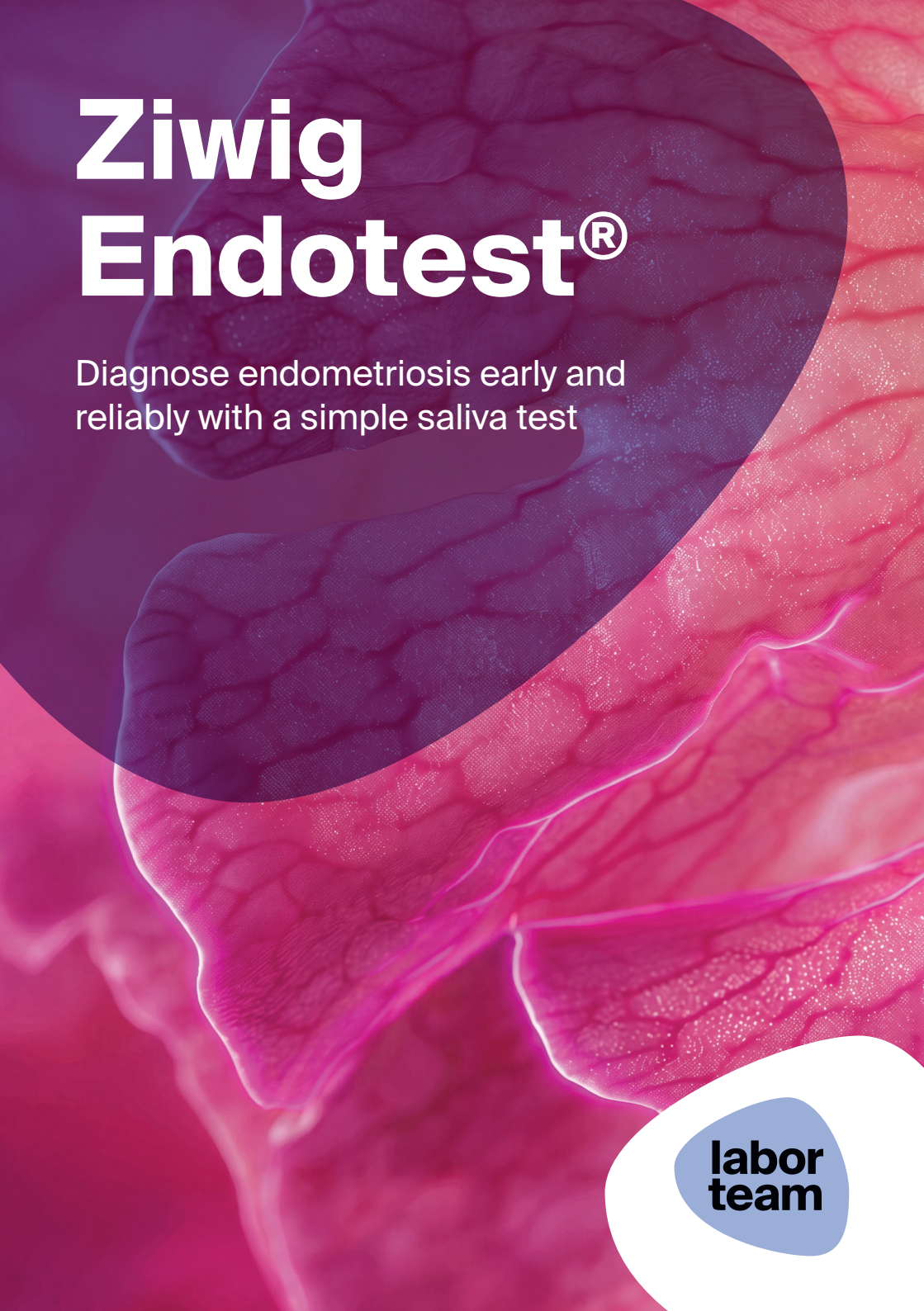
Ziwig Endotest®

Diagnose endometriosis early and reliably with a simple saliva test



labor team



The majority of women with endometriosis experience many years of pain before getting a diagnosis. For some, getting to that stage may even require surgery.

But now a new innovation, the first of its kind in the world, can help patients avoid this suffering. A team of endometriosis doctors, artificial intelligence experts, molecular biologists and laboratory doctors have joined forces to develop a diagnostic test based on the sequencing of microRNAs found in saliva.

This non-invasive saliva test, known as Ziwig Endotest®, was validated in the largest clinical trial ever carried out in this field[4]. It facilitates the early diagnostics of all forms of endometriosis[4-8] with almost 100% accuracy[1, 6].

The distribution of Ziwig Endotest® by labor team enables doctors to diagnose and treat endometriosis at an early stage.

Ziwig is an innovative French biotech specializing in salivary RNA analysis and AI.

It operates as an ecosystem at the crossroads of several medical, scientific and digital disciplines.

It is strongly committed to disruptive innovations that accompany the transformation of healthcare systems towards more effective, more humane and more accessible precision medicine.

ZIWIG®'s work has given rise to several publications in international peer-reviewed scientific journals.

www.ziwig.com

Endometriosis: pain and infertility

Endometriosis occurs when areas of endometrium-like tissue (the mucous membrane that covers the inside of the uterus) are found in various organs outside of the uterine cavity, such as the ovaries, vagina, rectum, bladder, bowel. During menstruation, these areas of tissue react to hormonal changes and cause inflammation, which in turn leads to significant pain and a variety of other symptoms.[9]

The illness can also be completely asymptomatic. In this case, it is most often diagnosed by chance when the woman visits a doctor due to struggling to conceive. A large proportion of endometriosis patients suffer from infertility.



It is estimated that endometriosis affects 10% of women of childbearing age in Switzerland. It can affect all women who experience periods and its symptoms can be felt as early as adolescence.

Symptoms of endometriosis and approximate proportion of women affected[12]

75-90 %
Painful periods

30-40 %
Infertility

40 %
Pelvic pain

30-70 %
Pain during sexual intercourse

15 %
Extreme fatigue

3 %
Urinary tract disorders

30 %
Digestive disorders

Pain chronification and hypersensitivity

Persistent pain can lead to the phenomenon of hypersensitivity. The threshold for pain perception falls, which in turn favours pain chronification.

This chronic pain can occur in endometriosis at any stage and persist even once the endometriosis lesions are gone.

Far-reaching effects

The pain can cause sleep disturbances that lead to chronic fatigue and psychological impacts (irritability, depression, etc.). This can then impact the woman's familial and social relationships. Their sexuality is affected. The impacts of endometriosis on the woman's career are dramatic, resulting in repeated absences from school or work.



In around a third of cases, endometriosis may stabilise, or even get better, with treatment or on its own. Mostly, however, the symptoms – particularly the pain – worsen over time.

The necessity of a non-invasive diagnostic test

The development of a non-invasive diagnostic test to confirm endometriosis has been an important focus of medical research for many years. More than 100 potential biomarkers have been evaluated in recent decades.

One of these, microRNAs – a class of molecules first described in 1993 – has proven to be a particularly promising option, gaining traction from a growing volume of results from studies involving tumours and neurodegenerative disorders.

Early diagnosis allows treatment to be targeted, thereby slowing or even ceasing the deterioration of pain and other symptoms. It also optimises infertility treatment and improves patients' quality of life.



High throughput sequencing and artificial intelligence

Developed by the French biotech firm ZIWIG®, the innovative Ziwig Endotest® takes advantage of two cutting-edge technologies: high throughput sequencing and artificial intelligence. Using just a saliva sample, it checks 109 different microRNAs for endometriosis.

This technique can identify all varieties of endometriosis[4-8] with almost 100% accuracy[1, 6] and was validated in the largest clinical trial ever carried out in this field[4].

MicroRNAs are small, non-coding RNAs that play a role in gene expression. When a microRNA bonds with its target, a specific messenger RNA, it blocks its translation into proteins and/or induces its degradation.

MicroRNAs are also secreted into the extracellular medium inside various transport structures, which protect them from the RNase enzymes in circulation and give them significant stability.

These circulating microRNAs are found in varying quantities in most biological fluids (blood, urine, breast milk, tears, saliva, etc.).

Over recent years, evidence indicating that microRNAs are involved in the pathophysiological mechanisms of endometriosis has been growing. A direct link between the dysregulation of certain microRNAs and the development of endometriosis lesions has been proven.[10]

Ziwig Endotest® and its benefits

The Ziwig Endotest® saliva test can bring down the average time to diagnosis from several years to just a few days.

- Clear result
- Fast diagnosis
- All forms of endometriosis can be diagnosed.[4-8]
- High reliability (sensitivity > 95%, specificity > 95%, diagnostic accuracy (AUC) > 95%)[1, 6]
- Simple, non-invasive sampling



Intended use of Ziwig Endotest®

Ziwig Endotest® has been validated for patients aged from 18 to 43 who exhibit symptoms that indicate endometriosis[11]:

chronic pelvic pain
+/- dysmenorrhea
+/- deep dyspareunia
+/- painful dysuria/miction
+/- painful dyschezia/defecation
+/- painful rectal bleeding or haematuria during menstruation
+/- pain in the shoulder tip
+/- infertility

Ziwig Endotest® may be useful in the following situations:

- Patients with suspected endometriosis following normal or inconclusive results of diagnostic imaging.
- Patients with persistent endometriosis symptoms despite medical treatment and normal or inconclusive results of diagnostic imaging.

Exclusions

Endometrioma and endometriosis of the rectosigmoid, identified using ultrasound or an MRI scan.

Ziwig Endotest® requires a medical prescription. The saliva sample must be collected under the supervision of a medical specialist.

- The patient must be at least 18 years old and no older than 43 years old at the time the test is performed.
- The patient must not have any prior history of cancer or infection with the human immunodeficiency virus (HIV).
- The patient must not be pregnant at the time the test is performed.
- Ziwig Endotest® can be performed during hormone treatment.
- Ziwig Endotest® can be performed at any point in the cycle.

Profile number	20'000
Price	CHF 867.90
Material & quantity	Saliva in tube (test set M275), fluid 1 cm above the fill line
Time to perform test	max. 14 days

Instructions saliva sample

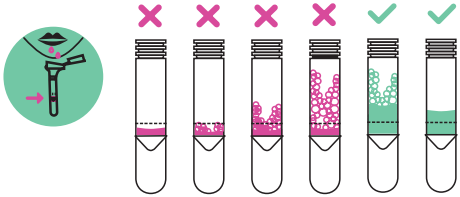
Prerequisites

- Wait for at least 30 minutes after eating, drinking, brushing teeth, chewing gum or smoking before providing a sample.
- Do not wear lipstick or lip balm when providing a sample.
- The best time to provide a sample is in the morning with an empty stomach and when in good health (no acute infection).



Please note

The amount of FLUID provided must be sufficient and exceed the fill line by at least 1 cm (air bubbles not included).



Instructions



1. Spit into the tube until the volume of saliva (no bubbles) exceeds the fill line by 1 cm.
2. Close the lid tightly by pressing the funnel lid down firmly until you hear a loud click.
3. Unscrew the funnel from the tube.
4. Use the small cap to seal the tube tightly.
5. Shake the tube for 5 seconds. Keep the tube at 4° C until sent to the laboratory. It can remain at room temperature during shipping.

Checking the sample

A medical specialist must perform three visual checks:

- Check that the sampling set components do not have any defects.
- Check the volume of saliva:
  The volume of saliva must reach 1 cm above the fill line on the tube.
- The appearance of the saliva once mixed with the stabilising fluid must be clear and transparent with no discolouration, and contain no food or other residues.
- Check that the expiry date of the kit (indicated next to the tube identification information) has not passed.

If any of these three checks results in an anomaly, take a new sample from the patient.

How Ziwig Endotest® fits in with existing diagnostic tests

Compared to existing methods, Ziwig Endotest® represents a huge step forward in the diagnosis of endometriosis[13] as it can diagnose all forms of the condition[4-8].

However, Ziwig Endotest® is not intended to replace diagnostic pelvic imaging (MRI, ultrasound). Diagnostic imaging remains essential even after diagnosis, e.g. for describing the lesions, mapping them, classifying them and establishing a prognosis for the illness.



The most commonly used pelvic imaging processes are ultrasound and magnetic resonance imaging. Their diagnostic capabilities are satisfactory for some forms of endometriosis (ovarian cysts, deep endometriosis), but insufficient for others (peritoneal endometriosis).

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M14823/1026