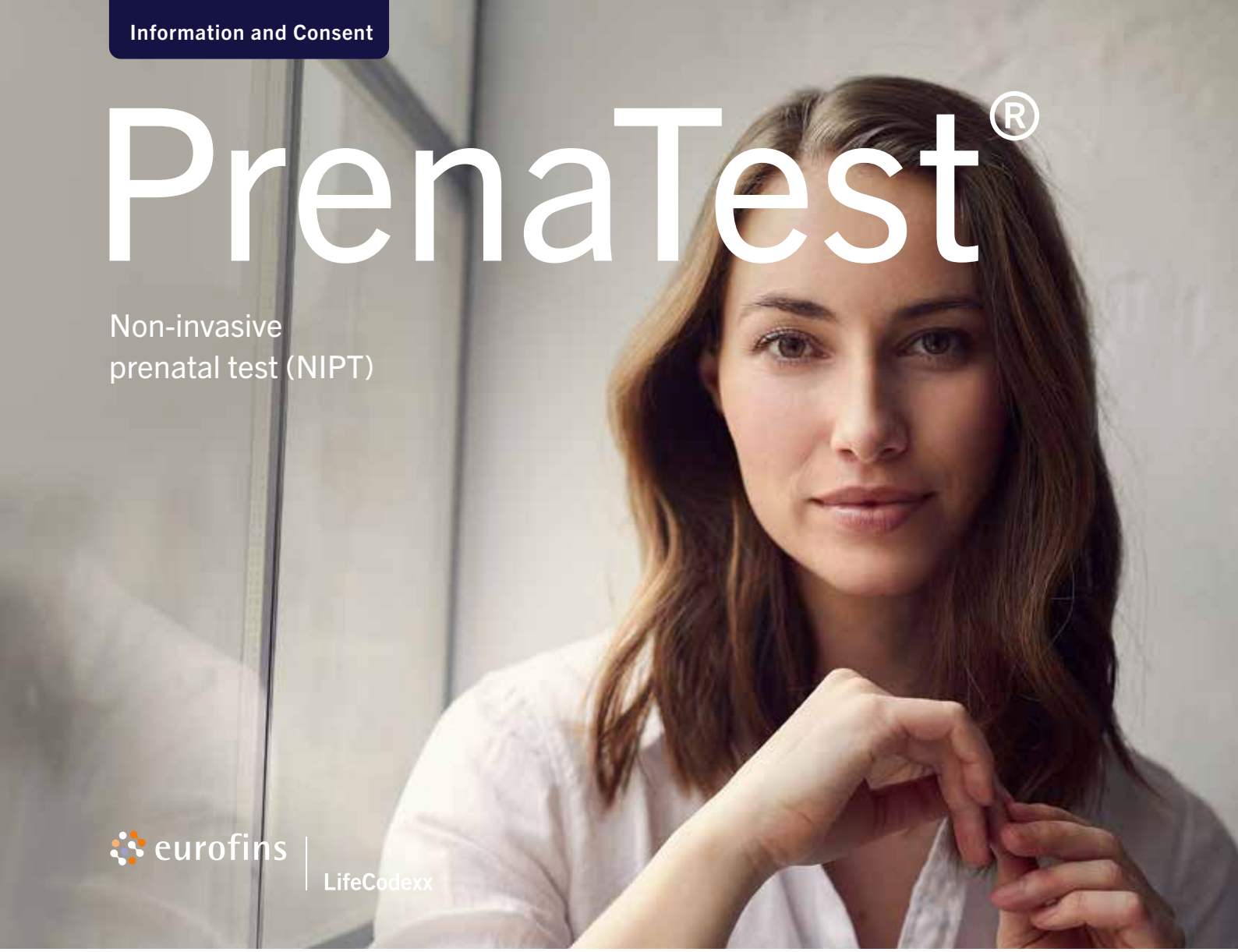
Information and Consent

PrenaTest®

Non-invasive
prenatal test (NIPT)



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To be kept at the medical practice

Information and consent to perform PrenaTest®

Non-invasive prenatal test to determine chromosomal disorders in an unborn child

Dear patient,

The non-invasive PrenaTest®, along with other test methods, offers the possibility of detecting the presence of chromosomal disorders in your child starting in the ninth week of pregnancy.

Before the test and the blood sampling are performed, it is important for you to understand the possibilities, limitations and risks of this test method in order to make an informed decision.

What can PrenaTest® detect in my child?

PrenaTest® can determine the following numerical chromosomal disorders in your unborn child:

Trisomies 21, 18 and 13
If a certain chromosome is present in the cells of the child three times instead of two times as usual, this is referred to as „trisomy." The most frequent chromosomal disorder compatible with life is trisomy 21, in which chromosome 21 is present three times in the child instead of twice. It causes Down syndrome and occurs approximately once in every 500 to 800 births. The risk of maldistribution of chromosome 21 increases with increasing age of the woman and also of the man. Trisomy 18, also known as Edwards syndrome, occurs much more rarely. It occurs in approximately one out of 5,000 newborns. Trisomy 13, known as Patau syndrome, is even rarer. Estimates indicate that it occurs once in every 16,000 births.

Monosomy X (X0) / Ullrich-Turner syndrome
If one chromosome is missing from a pair of chromosomes and is thus present only once instead of twice as usual, this is known as „monosomy". In monosomy X (also known as Turner syndrome or Ullrich-Turner syndrome), the second sex chromosome is missing. It is the only viable monosomy in humans, affects only girls, and occurs approximately once in every 2,500 female infants.

Triple X syndrome (XXX)
In so-called triple X syndrome, three copies of the X chromosome are present. This disorder also affects only girls and occurs approximately once in 1,000 female newborns.

Klinefelter syndrome (XXY)
In Klinefelter syndrome, which affects only boys, an additional X chromosome is present in the cells of the body. This occurs in approximately one out of 500 male newborns.

XYY syndrome/Jacobs syndrome (XYY)
In XYY syndrome, which also affects only boys, there is an additional Y chromosome in the cells. This occurs in approximately one out of 1,000 male newborns.

Rare autosomal aneuploidies (RAAs)
These are trisomies or monosomies of all other chromosomes, that is, chromosomes nos. 1 – 12, 14 – 17 and 19 – 22 as well as monosomies of chromosomes nos. 13, 18 and 21. For example, in the case of trisomy 16, chromosome 16 is present three times instead of twice; in monosomy 16, it is present only once instead of twice. The clinical manifestation depends on the affected chromosome and may vary. In some cases, the clinical manifestation is also normal. Contact your doctor for detailed information and advice regarding the possible effects of a rare autosomal aneuploidy.

Copy Number Variations (CNVs):
(Micro-)deletions/-duplications ≥7 Mb size
Copy number variations are structural chromosomal changes. CNVs include partial deletions - the loss of chromosome parts – and partial duplications – the gain of chromosome parts. PrenaTest® can detect CNVs of autosomes (chromosomes 1 – 22) at a size of ≥7 megabase pairs. However with a frequency of 1-2 per 10,000 births they are very rare. CNVs are often associated with severe clinical manifestations and lead to malformations of internal organs and/or to disturbances in the physical and mental development of the unborn child. The clinical pictures described in connection with CNVs include e. g. Prader-Willi syndrome, Angelman syndrome and trisomy 9q. The degree of clinical impact depends on the size of the chromosomal region affected or on the genes located in this region. CNVs may also be clinically inconspicuous. Contact your doctor for detailed information and advice regarding possible implications of partial (micro-)deletions and -duplications (CNVs).

Microdeletion syndrome 22q11
This syndrome involves a chromosomal change on chromosome 22 which can affect the development of the unborn child. It occurs in approximately one out of 6,000 newborns. This test can be optionally performed. Your doctor will request the testing for this chromosomal disorder, also known as "DiGeorge syndrome," only if it is specifically medically suspected.

More information about PrenaTest®

Can PrenaTest® also be used in the case of a twin pregnancy?
PrenaTest® can also be performed in the case of a twin pregnancy and following fertility treatment (including after egg donation).

How is PrenaTest® performed?
After you have received comprehensive information and genetic counseling from your doctor and after you have signed the informed consent form, your doctor will take a blood sample from you. This blood is sent to the designated laboratory. Depending on PrenaTest® option selected, your doctor receives the test result within a few working days after your blood sample is received in the laboratory and after successful quality control. He/she will inform you of the result. Current test run times can be found at www.lifecodexx.com.

If the test result is negative – does that mean that my child is healthy?
An unremarkable, negative test result means that the presence of the chromosomal disorders tested in your child can be ruled out with a high degree of accuracy. Chromosomal disorders other than those listed are not detected by PrenaTest® and thus no statements can be made about them. If your child is affected by another illness, PrenaTest® cannot provide any information about this. PrenaTest® is also unable to determine certain special forms of chromosomal disorders. For more information, see the section entitled „Limits of the test“ and talk to your doctor.

If the test result is positive – what‘s the next step?
An abnormal, positive test result means that your unborn child is highly likely to have the chromosomal disorder in question. According to medical recommendations, the test result should then be further clarified diagnostically by an invasive examination, generally amniotic fluid testing. This is also necessary because in very rare cases, the chromosomal disorder demonstrated may be present in the placenta, however the unborn child itself is not affected by it.

How accurate is PrenaTest®?
The high accuracy of PrenaTest® has been proven in clinical studies. Test accuracies of more than 99% were achieved, depending on the chromosomal disorder tested. This number means that out of 100 pregnant women whose unborn child is affected by a chromosomal disorder, more than 99 will be determined correctly. The test accuracy for trisomy 21 is higher than for trisomies 13 and 18 or for the other chromosomal changes investigated. In addition, the probability that an abnormal (that is,
positive) test result is not correct is very low. This is indicated by the so-called false-positive rate of 0.1%. This value implies that in a group of 1,000 unaffected pregnant women, one pregnant woman will receive an abnormal (that is, positive) test result, although her unborn child is in fact not affected by a chromosome disorder.

Limits of the test
With PrenaTest® structural chromosomal changes as partial deletions/duplications below a size of 7 Mb cannot be detected (except 22q11.2 microdeletion). In the case of structural chromosomal changes (disorders) either a piece of a chromosome is missing (deletion) or added (duplication) or a piece was incorporated incorrectly in the chromosome. Also mosaics cannot be detected with certainty. In mosaics either certain tissue cells or cells of the entire organism of the embryo have different genetic information.

It is important for you to know that 100% test accuracy should not be expected when noninvasive prenatal tests are used. In rare cases, there may be no or an unclear test result. However, this does not indicate anything about the health of your child. You may then repeat the test at no additional charge. The waiting time for the test result will be accordingly prolonged. Please contact your doctor for detailed information and advice.

Alternatives to PrenaTest®
Non-invasive prenatal tests available to you as an alternative to PrenaTest® in the first and second trimester of pregnancy include, above all, ultrasound examinations, if necessary in combination with testing for certain maternal blood values. A definitive diagnosis of the presence or the exclusion of one of the trisomies listed, other chromosomal disorders or certain other diseases can be made only using an invasive method, such as amniotic fluid testing or a chorionic villus biopsy. The risk of a miscarriage due to such an invasive procedure is 0.2-1%.

Please keep in mind: Most prenatal tests do not reveal any abnormalities, which helps alleviate concerns and contributes to an untroubled course of pregnancy. However, if a test reveals abnormalities, this may frequently to some extent cause significant uncertainty and conflicts. Your doctor will provide you with comprehensive information and support. In addition, psychosocial counseling is recommended, particularly in these situations. Your doctor will provide you with information about this..

Genetic counseling

In addition to this information, you are to receive genetic counseling in accordance with the German Genetic Diagnostics Act (GenDG) prior to further testing as well as after test results are available. Counseling prior to genetic testing in accordance with the GenDG comprises:

- clarification of your personal medical issue
- evaluation of any available medical findings or reports
- the test-related documentation of abnormalities in your personal and family health history (past medical history)
- information on the need for genetic counseling arising from your medical issue or your past medical history
- information on the possibilities, limits and the material extraction-related risks of the test methods that can be used for clarification.
- an assessment of the genetic risks, including a discussion of the implications of all information for your life and family planning and, where applicable, for your health
- options for support in the case of physical and psychological stress as a result of the testing and its result
- an estimation of the need for comprehensive genetic counseling by a doctor specializing in human genetics

The genetic counseling by your doctor is provided after you have received information and given your consent for the genetic testing – prior to the testing being performed and again during communication of results.

Informed consent to undergo PrenaTest® in accordance with the German Genetic Diagnostics Act (GenDG), section 9

I have received, read and understood general written information (and, where applicable, additional special written information) about genetic analyses in accordance with the GenDG.
With my signature, I give my consent to perform PrenaTest® as well as to perform the necessary blood sampling. I had enough opportunity to discuss unanswered questions. I have been advised that I may withdraw my consent, in whole or in part, at any time and without stating any reasons, without this resulting in any disadvantages for me, and that I have the right not to be informed of test results (right to not know).

I am aware that I may stop any test methods which have been initiated up to the time at which results are communicated and that I may request the destruction of the test material, including the components obtained from it, as well as all results recorded up to that point in time.

The withdrawal must take place in writing. I am aware that I am obligated to pay for the services provided so far to Eurofins LifeCodexx, in accordance with the General Terms and Conditions.

Additional comments on the information and counseling (to be filled out by the doctor)

Place / date

Last name and first name of patient (please print)

Signature of patient or legal representative

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