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NON-INVASIVE PRENATAL TESTING: AN UPDATE

INTRODUCTION

Non-invasive prenatal testing (NIPT) is a prenatal screening test that is performed using a maternal peripheral whole blood sample. The test calculates the risk of a foetus being affected with certain chromosomal abnormalities using next-generation sequencing technology. Cell-free DNA (cfDNA) fragments in maternal blood are sequenced and analysed in order to report over-representations (trisomies) of chromosomes 21, 18 and 13. Foetal gender and sex chromosome aneuploidies (monosomy X, trisomy X, XXY and XYY) can also be detected. An additional option of analysing all chromosomes (including segmental deletions and duplications >7Mb) is now available. This option will require up-front payment, irrespective of medical aid approval, and should be accompanied by appropriate pre-test genetic counselling. The VeriSeq™ NIPT Solution v2 from Illumina (CE-IVD approved) is the platform used for all the test options listed below.

ELIGIBILITY

- Both singleton and twin pregnancies, including pregnancies conceived using IVF and self/donor eggs, are eligible from 10 weeks of gestation onwards. Twin pregnancies are only eligible for the NIPT1 option.
- NIPT is not recommended in cases of recent maternal blood transfusion, maternal malignancy or previous organ transplant or stem cell therapy, as this could lead to false negative or false positive results.

TEST OPTIONS

NIPT test	Mnemonic	Standard Price (2024)	Specimen type and TAT
Chromosomes 21, 18, 13 with or without foetal gender	NIPT1	R5 658.21	1 x full streck tube *TAT: 7 working days
Chromosomes 21, 18, 13 AND sex chromosome aneuploidies with or without foetal gender	NIPT2	R6 344.01	
All chromosomes with or without foetal gender	NIPT3	R9 425.00	

* TAT: Turnaround time from receipt in the NRL NGS Laboratory.

Please note: Testing for microdeletions will only be performed on specific request and by arrangement.

PERFORMANCE METRICS

(Data from Veriseq NIPT Solution V2 package insert)

Chromosome	N	Sensitivity	95% CI	Specificity	95% CI
Trisomy 21	2236	>99.9% (130/130)	97.1–100	99.9% (1982/1984)	99.63–99.97
Trisomy 18	2236	>99.9% (41/41)	91.4–100	99.9% (1995/1997)	99.64–99.97
Trisomy 13	2236	>99.9% (26/26)	87.1–100	99.9% (2000/2002)	99.64–99.97
Any anomaly*	2300	95.5% (318/333)	92.7–97.3	99.34% (1954/1967)	98.87–99.61
RAA**	2300	96.4% (27/28)	82.3–99.4	99.8% (2001/2005)	99.49–99.92
CNV >7Mb**	2300	74.1% (20/27)	55.3–86.8	99.8% (2000/2004)	99.49–99.92

* Includes sex chromosome anomalies from genome wide screen.

** RAA (rare autosomal aneuploidies) excludes chromosomes 21, 18 and 13. RAA and CNV (copy number variants) >7Mb are only reported with the NIPT3 option.

INTERPRETATION OF RESULTS

Results are reported as **ANOMALY DETECTED** or **NO ANOMALY DETECTED**:

No anomaly detected There is a low risk that the foetus has the conditions tested for.	**Limitations** • This result does not eliminate the possibility of chromosomal abnormalities of the tested chromosomes (false negative). • It does not eliminate the possibility that the pregnancy has other chromosomal abnormalities (for example, microdeletions), genetic conditions or other birth defects.
Anomaly detected There is a high risk that the foetus has the condition tested for.	**Limitations** • NIPT is a screening test. A high-risk test result must be confirmed by performing a diagnostic test on a foetal sample (such as a chorionic villus sample (CVS) or amniocentesis sample). • False positive: The results might not reflect the chromosomes of the foetus, but instead reflect chromosomal changes to the placenta (confined placental mosaicism) or in the mother (chromosomal mosaicism). • Chromosomal aneuploidies are detectable in twin pregnancies, but cannot differentiate between the individual foetuses. Sensitivity and specificity are limited in twin gestations.
Foetal gender Result reported: male/female	**Limitations** • In twin gestations, the presence of a Y chromosome indicates that at least one twin is male. The absence of a Y chromosome indicates that both twins are female. • In case of organ transplantation from a male donor to the mother, sex chromosome status for the foetus cannot be determined.

For more information or assistance, contact the NGS Laboratory at **012 678 0645** or email **nipt@ampath.co.za**.