

SHMG MFM

Non-Invasive Prenatal Screening (NIPS)

*Provider Guide*

* NIPS is a screening test that involves the collection of a maternal blood sample during pregnancy to assess the risk for the fetus to have specific chromosome abnormalities, including:
  + Trisomy 13 (Patau syndrome), trisomy 18 (Edward’s syndrome) and trisomy 21 (Down syndrome)
  + Sex chromosome abnormalities (X0, XXX, XXY, XYY) - OPTIONAL
  + Gender – OPTIONAL
  + Triploidy, vanishing twin, microdeletions/microduplications (depending on the lab)
  + Twins: patient will only get one result, gender is reported as presence/absence of a Y chromosome – will tell them if both are girls or if at least one is a boy
* The test is looking at the amount of cell-free “fetal” DNA (cffDNA) to determine the pregnancy risks. cffDNA is fragmented DNA from the placenta - not the fetus. Placental DNA typically reflects fetal DNA but sometimes it does not. This can lead to false positive and false negative results.

**What is NIPS?**

**Who is this test for?**

* **All patients should receive appropriate pre and post-test counseling with regards to the limitations and benefits of this testing**
* Any woman desiring screening for aneuploidy
* Any woman who is high-risk:
  + Maternal age 35 years or older at delivery
  + Sonographic findings indicating an increased risk of aneuploidy
  + History of a prior pregnancy with one of the following: trisomies 13, 18, or 21, a sex-chromosome abnormality, or triploidy
  + Positive screening results for aneuploidy (first trimester, sequential, integrated, or quad screen)
  + Parental balanced Robertsonian translocation (involving chromosomes 13, 18, or 21)
  + Family history of a sex-linked disorder (ex. Duchenne muscular dystrophy)
* Testing is available from 10w0d gestation
* Turn around time 7-10 days

**What are the benefits?**

* Testing is non-invasive: minimal risks to the pregnancy
* Increased accuracy: lower false positive and false negative rates than traditional maternal serum screening
* Able to perform testing at a wider range of gestational ages
* Typically, only one blood draw is required
* Provides risk estimate for the most common aneuplodies in pregnancy

**What are the limitations?**

* This is a screening test – abnormal results should be confirmed with diagnostic testing such as CVS or amniocentesis
* Risk assessment is limited to specific fetal aneuplodies - approximately 50% of cytogenetic abnormalities routinely identified by amniocentesis will not be detected when trisomy 21, 18, and 13 are the only aneuploidies being screened (unbalanced translocations, deletions, duplications, triploidy (depending on the lab), or if Down syndrome is due to a translocation vs real trisomy)
* Uninformative test results due to insufficient isolation of cell-free fetal DNA could lead to a delay in diagnosis or eliminate the availability of information for risk assessment. Biologic factors associated with reduced available cell-free fetal DNA include a high body mass index and early gestational age (<10 weeks gestation) Accuracy of the results depends on several factors including the “fetal fraction” (FF), or the % of cffDNA in mom’s blood. For most labs this cutoff is 4%. FF increases from 10-22 weeks and then remains fairly stable for the remainder of pregnancy.
* Does not screen for open neural tube defects. Maternal serum α-fetoprotein testing can still be offered at 15–20 weeks gestation to screen for open neural tube defects

**What do the results mean?**

* Diagnostic testing is always recommended following a high-risk result
* HIGH-RISK results can represent the following:
  + Fetal aneuploidy
  + Confined placental mosaicism
  + Residual cffDNA from a vanishing twin
  + Maternal aneuploidy (in the case of sex chromosome abnormalities- this depends on the specific testing technology)
  + Limitations of the technology
  + Maternal medical conditions (in rare cases, maternal malignancy has been detected through NIPS)
  + Other unknown biological factors
* LOW-RISK results do not eliminate the chance for the fetus to have one of the conditions. In general, the false positive rate is <0.1%.
* NO-CALL results occur in approximately 3-5% of cases. The majority will be resolved with a 2nd blood draw, but some individuals will not be able to receive results even with a 2nd blood draw. This is more likely to occur at early gestational ages and with higher maternal BMIs. In rarer cases this can indicate the fetus has an aneuploidy



Non-Invasive Prenatal Screening (NIPS)

*Panorama*

**\*\*Preferred NIPS\*\***

* Timing: from 10w0d gestation
* Complete requisition form (see attached example) and attach a copy of insurance card(s)
* **OPT OUT** of 22q11.2 and microdeletion/duplication panel unless ultrasound findings are suspicious or there’s a family history
* Place order in Epic: enter “Panorama” under order entry
* Send patient to the lab with the requisition form
* Collection kits are stocked at Spectrum Health laboratory locations

**DO NOT ORDER FOR THESE INDICATIONS:**

* IVF with egg donor or surrogate (can use Harmony instead)
* Multiples (coming soon) (can use Harmony instead)
* If there’s been a twin demise (can order sequential/integrated/quad instead)

**Ordering**

**Billing**

|  |  |
| --- | --- |
| Commercial Insurance | **In-Network Insurance**  Coverage depends on coinsurance, copays, and deductibles.  If patient’s OOP is higher than $349 for Panorama ($449 with 22q), the patient will receive a phone call and be given an option to pay $349 as a cash price (won’t go towards deductible) or the insurance price (this amount would be put towards deductible).  Compassionate care pricing: patients may qualify for $145 if they make less than 4x the poverty limit (household income, # of people). Patient needs to fill out an application and send it in for approval.  **Out-of-Network Insurance & Anyone Whose Plan Denies Coverage**  Patient will receive a discounted price of less than $200. ***The patient may see an EOB listing their responsibility of $3000. Please let the patients know they are not responsible for that amount.*** If they receive a bill from Natera for that amount, they need to call the customer service number listed on the invoice and tell them they’re supposed to pay less than $200 and the lab will adjust that bill for them. |
| Medicaid | Anyone with Medicaid or a Medicaid secondary will not be balance-billed. |
| Self-Pay | $349 |
| No-call Results | Will still be billed to insurance (if a patient has 2 draws, only 1 draw will be billed). No-call results can indicate an increased risk for aneuploidy so the lab deems this to be an “informative result”. |
| Billing Questions | **Chris Kirby:** ckirby@natera.com; 231-740-9642 |

**Test Performance**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Condition | Sensitivity | Specificity | Positive Predictive Value | Negative Predictive Value |
| Trisomy 21 | >99% | >99% | 91% | >99.99% |
| Trisomy 18 | 98.2% | >99% | 93% | >99.99% |
| Trisomy 13 | >99% | >99% | 38% | >99.99% |
| Monosomy X | 94.7% | >99% | 50% | >99.99% |
| Triploidy | >99% | >99% | 5.3% | >99.99% |
| XXX, XXY, XYY | n/a | n/a | 89% | n/a |
| Female | >99.9% | >99.9% | n/a | n/a |
| Male | >99.9% | >99.9% | n/a | n/a |



Non-Invasive Prenatal Screening (NIPS)

*Harmony*

* Timing: from 10w0d gestation
* Complete requisition form (see attached example) and attach a copy of insurance card(s)
* Place order in Epic: enter “Genetic send out” under order entry and enter details including test being ordered, name of lab, collection information
* Send patient to the lab with the requisition form
* The patient must be sent to the lab with a Harmony collection kit (attempting to get these stocked at SH lab sites)

**DO NOT ORDER FOR THESE INDICATIONS:**

* Multiples greater than twins
* If there’s been a twin demise (can order sequential/integrated/quad instead)

**Ordering**

**Billing**

|  |  |
| --- | --- |
| Commercial Insurance | **In-Network Insurance**  Coverage depends on coinsurance, copays, and deductibles.  In-network pricing varies from $400-$750. The patient could be responsible for the entire amount if they haven’t met their deductible. If patients pay their bill within 30 days, they will qualify for a 10% discount.  Roche has financial assistance programs for those with lower incomes. Contact the rep for more information.  **Out-of-Network Insurance & Anyone Whose Plan Denies Coverage**  Max price of $199. ***The patient may see an EOB listing their responsibility of $2900. Please let the patients know they are not responsible for that amount.*** The final bill should be adjusted to $199 before it is sent to the patient. |
| Medicaid | Anyone with Medicaid or a Medicaid secondary will not be balance-billed. |
| Self-Pay | $349 |
| No-call Results | The lab will not bill for a no-call result. They can reimburse the patient’s blood draw fee, if applicable, for these results. |
| Billing Questions | **Marcea Mones:**  marcea.mones@roche.com ; 269-330-2511 |

**Test Performance**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Condition | Sensitivity | Specificity | Positive Predictive Value | Negative Predictive Value |
| Trisomy 21 | >99% | >99.9% | n/a | >99.99% |
| Trisomy 18 | 97.4% | >99.9% | n/a | >99.99% |
| Trisomy 13 | 93.8% | >99.9% | n/a | >99.99% |
| Monosomy X | 92.6% | >99% | n/a | >99.99% |
| Female | >99% | >99% | n/a | n/a |
| Male | >99% | >99% | n/a | n/a |

Limitations

* Does not offer microdeletions/duplications
* Cannot determine risk for triploidy or vanishing twin
* Cannot distinguish between maternal and fetal DNA (ie. in the case of sex chromosome abnormalities)