

## Natera **Core**

Support every step of the way



#### We hear your concerns...

Time with my patients is precious and limited

I need an easier way

I'm a clinician, not a billing expert

This needs to fit into my practice workflow

I don't have time on my day as it is

I spend too much time talking about insurance

Guidelines and coverage policies are complex and rapidly changing



Your integrated support resource



Your integrated support resource

### Services for providers and patients at every step











#### **Education**

Patient-friendly
materials and
information sessions,
covering basic genetics
to specific tests

#### Access

Programs and price transparency – rooted in our commitment to provide affordable testing for all who can benefit

#### **Ordering**

Flexible options based around your needs, including intuitive remote ordering and EMR solutions

#### Results

Clear, actionable reports, served with time-saving tools and access to expert guidance

#### **Next Steps**

Value-add services that go beyond the test to address what's next

Supporting both in-office and remote workflows





#### **Education**

Patient-friendly materials and information sessions, covering basic genetics to specific tests

## Patient brochures, videos, and online content







**Brochures** 

Videos

Online content

## Genetic information sessions and family history intake



Pre-test genetic information sessions



Pre-test family history and education with NEVA

#### **Texting program**



Office posters



Patient cards





#### Access

Programs and price transparency — rooted in our commitment to provide affordable testing for all who can benefit

## Broad in-network coverage







View a list of in-network plans

### Personalized cost estimates





Pre-test cost estimates

Price Transparency Program (PTP)

## Financial access programs



\$



Compassionate
Care Program

Self-pay cash option

Interest-free payment plans





#### **Ordering**

Flexible options based around your needs, including intuitive remote ordering

## A range of ordering options







NateraSync EMR Solutions



Online via
NateraConnect

## Flexible phlebotomy options



Patient Service Centers (PSC)



Nationwide mobile phlebotomy service

## End-to-end remote testing



Online education and cost estimates



Virtual Testing (Simple Ordering)



Post-test Sessions scheduled by phone or online





#### Results

Clear, actionable reports, served with time-saving tools and a side of expert guidance

### Online results management



Results tracking



Patient resultsrelease settings

## Flexible results delivery options



Positive results delivery via Genetic Information Session



E-Results Sync: Results delivery to the EMR

#### Patient Call-Out Program (PCOP) with NEVA



Interactive results delivery with NEVA



Proactive GIS scheduling for positive results





#### **Next Steps**

Value-add services that go beyond the test to address what's next

Post-test genetic info sessions and provider consultations



#### Schedule by:



Calling Natera Customer Care



Visiting the online patient portal



Texting SESSION to 484848 (patients only)

**Family testing** program



Empower testing for first-degree relatives of patients with a positive result is available at no additional charge.



Visit natera.com/empower for more details.

**Spectrum Advantage Program** 



**Empower and Horizon patients** can access Spectrum preimplantation genetic testing at discounted rates



# Education



#### **Education**

Patient-friendly materials and information sessions, covering basic genetics to specific tests

## Educational resources for patients







**Brochures** 

Videos

Online content

## Genetic information sessions and family history intake



Pre-test genetic information sessions



Streamlined family history collection with NEVA

#### **Texting program**



Office posters



Patient cards



#### Educational resources for patients







**Brochures** 

**Videos** 

**Texting Program** 

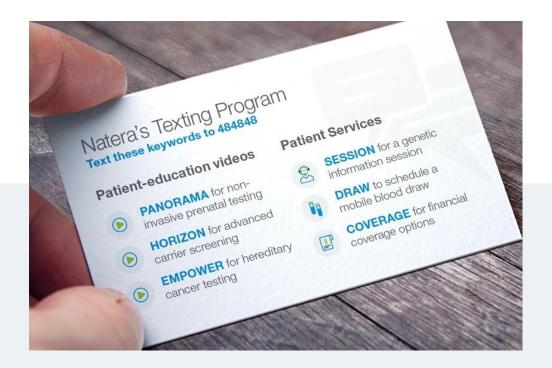
Available in multiple languages including Spanish, Chinese, Vietnamese, Russian, and Arabic

#### Texting program

#### Convenient access to education and other key services







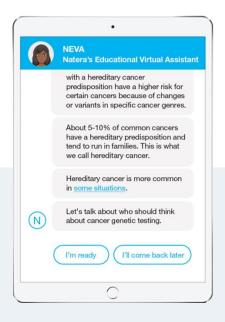
**Office posters** 

**Patient cards** 



#### On Demand Education and Counseling

#### Natera provides genetic education throughout the testing process



NEVA, Natera's
Educational Virtual
Assistant



**Educational videos** 



Genetic information sessions



#### Pre-test genetic information sessions

#### **Pre-test genetic information sessions**



#### Schedule by:



Calling Natera Customer Care at (844) 778-4700



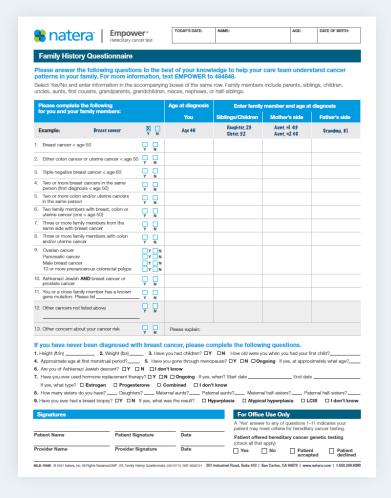
Visiting the online patient portal <a href="my.natera.com/services/genetic\_information">my.natera.com/services/genetic\_information</a>



Texting **SESSION** to **484848** 

#### Hereditary Cancer Risk Assessment Tools

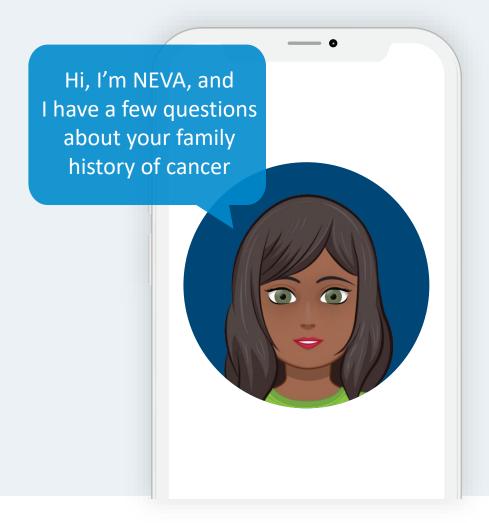
#### Efficiently identify patients meeting criteria for testing



Please check all that a	pply	anatera Empower Hereditary cancer test				
,	parents, siblings, children, u news, or half-siblings) had ar	ncles, aunts, first cousins, grandparents, ny of the following:				
1 breast, colo	n, or uterine cancer diagnosed	under age 50				
Ovarian cancer, pancreatic cancer, or male breast cancer diagnosed at any age						
3 breast canc	3 breast cancers on the same side of family diagnosed at any age					
Ashkenazi Je	Ashkenazi Jewish ancestry with breast cancer or prostate cancer diagnosed at any age					
3 or more cold	3 or more colon and/or uterine cancers on the same side of family diagnosed at any age					
Hereditary cancer testing help to discuss this with my pro		increased risk for developing cancer. I want				
Patient name:						
Provider you are seeing today						

#### **NEVA for Risk Assessment**

#### **NEVA** makes it easier to collect family cancer history



- AI-enabled family history collection based on the latest NCCN guidelines
- Trained by Natera's expert genetic counselors and has provided interactive education to thousands of patients
- NEVA is EMR-connected to simplify the education and risk assessment workflow
- NEVA is available to patients 24/7/365
- Rated as friendly, knowledgeable, and helpful for your patients

#### NEVA EMR Sync automates the pre-test workflow

Automate invites through integration with the EMR-based patient schedule

An invite is automatically sent 7 days prior to appointment To: daisydavis@gmail.com Hi Daisy, Your provider has requested that you share some information about your health and family history before your upcoming appointment.

Once a patient completes NEVA, the summary is sent to the patient record in the EMR atera's Educational Virtual Assistar (+) Previous question Question 2 Do you know if any member in your family had cancer? Yes No I don't know

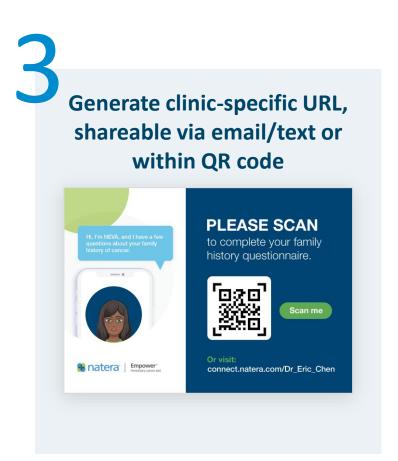


#### Invite Your Patients to Chat with NEVA

Send invitations from your NateraConnect ordering platform in three ways

**Invite individual patients** from Connect **New Patient** First Name Last Name Date Of Birth mm/dd/yyyy Appointment Date mm/dd/yyyy

**Upload patient list in Connect for batch invites** First Name Last Name Date of Birth Email address 12/1/2020 Jane Doe 1/1/1990 jane@ 12/1/2020 Smith 5/20/1975 Jeremy Jeremy@ 12/1/2020 Jamie 6/3/1982 Jamie@ Jones



#### Patient completes education and risk assessment in NEVA

**NEVA** guides patients through family cancer history questions

An email and/or text message is sent to the patient to complete NEVA To: daisydavis@gmail.com Hi Daisy, Your provider has requested that you share some information about your health and family history before your upcoming appointment.

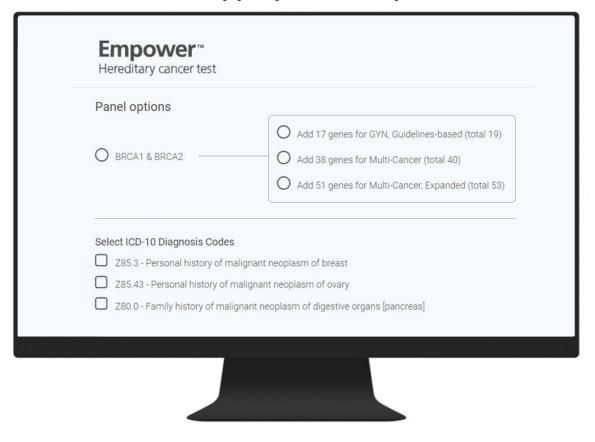
Patients are guided through questions about their personal and family history of cancer. atera's Educational Virtual Assistar (+) Previous question Question 2 Do you know if any member in your family had cancer? Yes No I don't know

You are ready to discuss testing with appropriate patients at their appointment. **Risk Assessment Results** This patient appears to meet medical guidelines (NCCN or USPSTF) for hereditary cancer testing. Mary Doe 11/23/1970 888-888-888 marydoe@gmail.com Caucasian Family history 01/12/2020 01/01/2021 Cancer Type Age at diagnosis

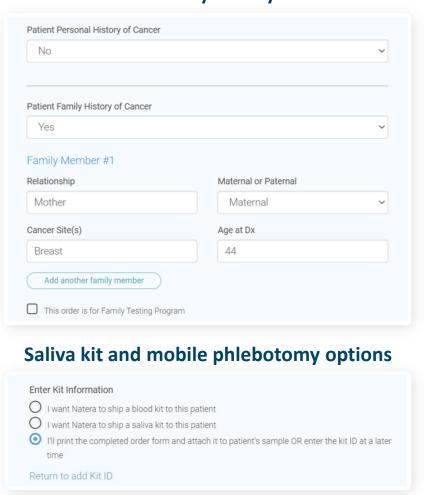
#### Access and Complete Prefilled Test Orders

#### **Submit orders in NateraConnect**

#### Select appropriate test panel



#### **Prefilled family history details**



# Access



#### Access

Programs and price transparency — rooted in our commitment to provide affordable testing for all who can benefit

## Broad in-network coverage







View a list of in-network plans

### Personalized cost estimates





Pre-test cost estimates

Price Transparency Program (PTP)

## Financial access programs







Compassionate
Care Program

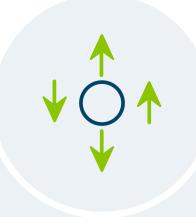
Self-pay cash option

Interest-free payment plans



#### High-Quality Testing, Made Affordable

We work from all angles to give patients access to testing, and help providers stay focused on care.







Broad in-network coverage

Personalized cost estimates

Financial access programs

#### In-Network Provider with Most Insurance Plans

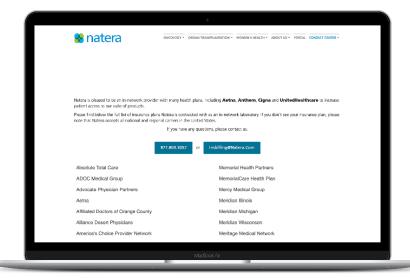
Natera is proud to accept most national and regional healthcare plans.











#### Pre-test cost estimates

#### **Obtain via:**

Email: <a href="mailto:estimate@natera.com">estimate@natera.com</a>



Text: 650.210.7046

#### Welcome to Natera!

If you are considering one of our Panorama or Horizon tests and would like an estimate of your out-of-pocket cost when paying with insurance, there are two ways to contact us:

Email: estimate@natera.com

We will email you back

Text: 650.210.7046

We will text you back



#### In your email or text, please provide the following:

Tests you're considering (consult your doctor): Panorama with 22q.11.2

- Panorama without 22q.11.2
- ☐ Panorama Extended Panel
- ☐ Horizon 4
- ☐ Horizon 14
- ☐ Horizon 27
- ☐ Horizon 106
- ☐ Horizon 274

#### Personal information:

- Physician name
- Clinic name and city
- Patient name
- · Patient date of birth
- Picture of insurance card (front and back) OR insurance info (please include plan name; policy holder name; member ID; group number)

#### www.natera.com

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Personalized cost estimates and \$249 self-pay cash option

1

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2

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3

4



Your medical provider orders a test. We start processing your sample.

We generate an insurance estimate.

If we estimate your cost to exceed \$249,2 we'll contact you via text or email and you choose how you pay: insurance or cash.

If you choose insurance, we'll send you a bill once your health plan confirms exactly how much you owe.

#### If you choose insurance

If you've not met your deductible, what you pay will go towards that amount, after which insurance begins to contribute to your care.

If your insurance plan denies the claim, you will be eligible for our discounted cash price.

<sup>1</sup> Estimates are based on previously processed claims from 2017-2018.

<sup>2 \$349</sup> if ordering microdeletions or Horizon extended panels.

Personalized cost estimates and self-pay cash option

1

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2

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3

4



Your medical provider orders a test. We start processing your sample.

We generate an insurance estimate.

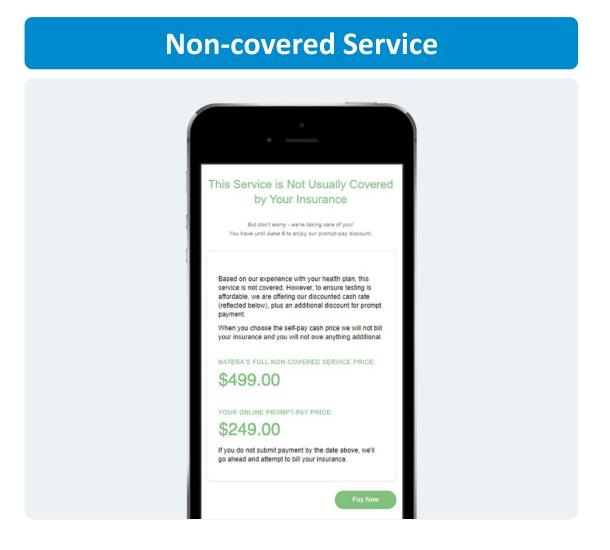
If we estimate your cost to exceed self-pay cash option, we'll contact you via text or email and you choose how you pay: insurance or cash.

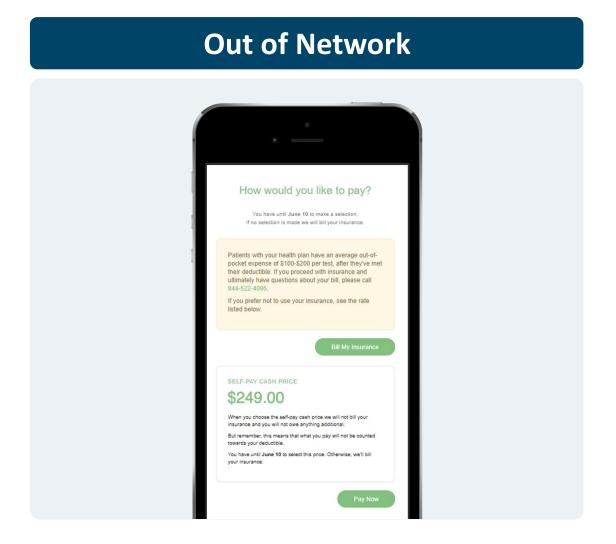
If you choose insurance, we'll send you a bill once your health plan confirms exactly how much you owe.

If you choose insurance

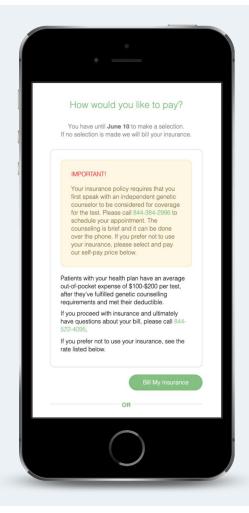
If you've not met your deductible, what you pay will go towards that amount, after which insurance begins to contribute to your care.

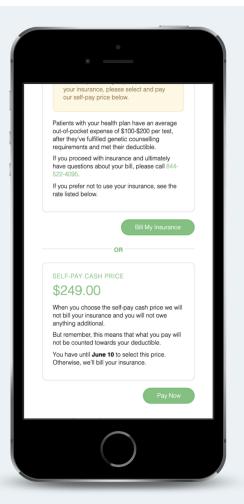
If your insurance plan denies the claim, you will be eligible for our discounted cash price.





#### **Example PTP Patient Messages when Pre-Test Counseling by 3rd Party GC is Required**





#### Compassionate Care Program

## Testing from \$0 to \$149 for patients experiencing financial hardship

Annual Household Income Equal to or Less Than					
Total Household Size (Including unborn child)	1	\$49,960	\$37,470	\$24,980	
	2	\$67,740	\$50,730	\$33,820	
	3	\$85,320	\$63,990	\$42,660	
	4	\$103,000	\$77,250	\$51,500	
	5	\$120,680	\$90,510	\$60,340	
	6	\$138,360	\$103,770	\$69,180	
	7	\$156,040	\$117,030	\$78,020	
	8	\$173,720	\$130,290	\$86,860	
		\$149/test	\$99/test	\$0/test	

#### Apply by:



Visiting the online patient portal

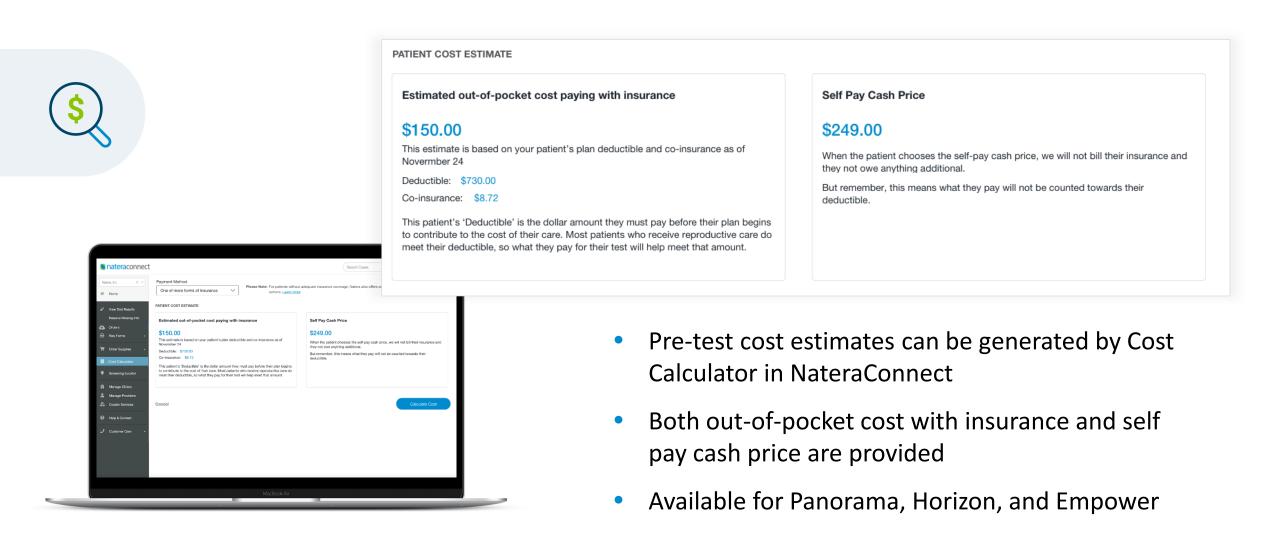


Submitting a paper application



#### **Connect Cost Calculator**

#### Real-time cost estimates via online portal



# +=

## Ordering



#### **Ordering**

Flexible options based around your needs, including intuitive remote ordering

A range of ordering options







NateraSync EMR Solutions



Online via
NateraConnect

## Flexible phlebotomy options



Patient Service Centers (PSC)



Nationwide mobile phlebotomy service

## End-to-end remote testing



Online education and cost estimates



Virtual Testing (Simple Ordering)

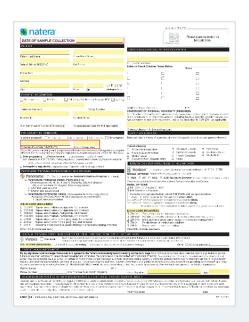


Post-test Sessions scheduled by phone or online



#### Flexible ordering options to suit your needs

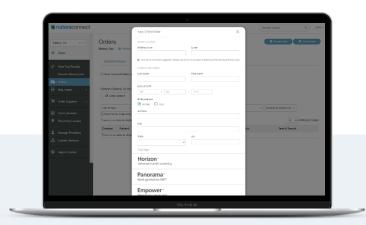
#### Ranging from paper reqs to entirely digital solutions



**Paper requisitions** 



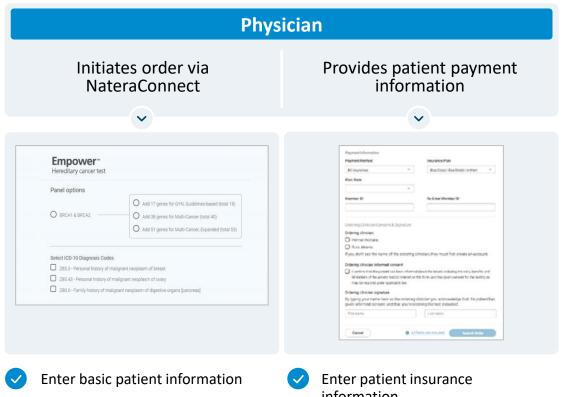
NateraSync EMR Solutions

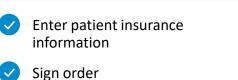


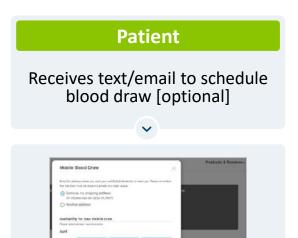
**Online via NateraConnect** 

## Online ordering

## Streamlined step-by-step guided workflow









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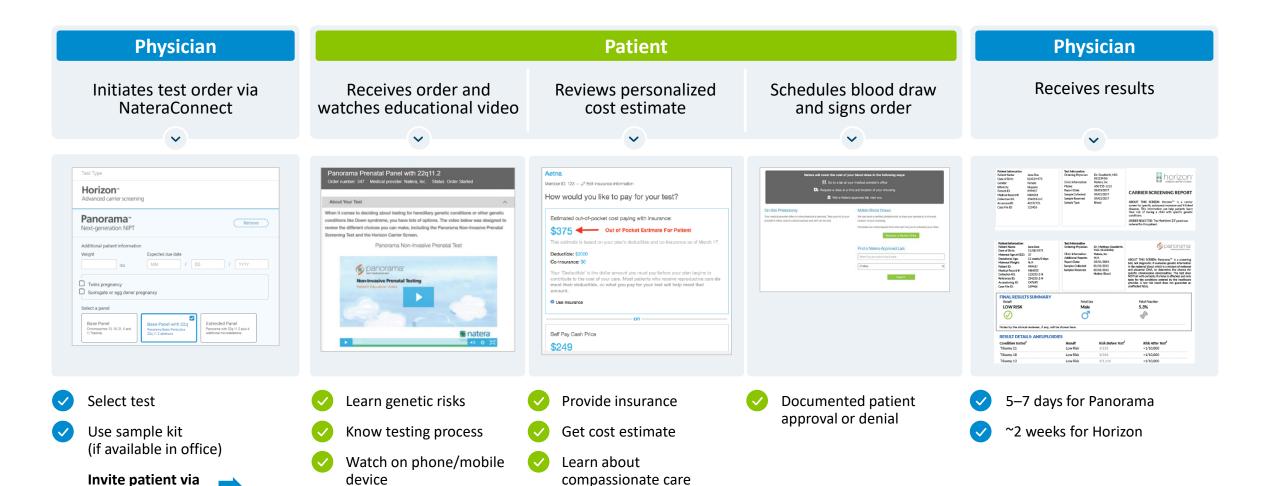


Select desired test panel

Use in-office kit or invite patient for remote blood draw options

## Virtual testing (aka Simple Ordering)

## Streamlined step-by-step guided workflow



email or text

## Online Ordering and Virtual Testing Workflows

Which workflow is right for you?

	Virtual Testing	Online Ordering	
	(Simple Ordering)		
Provider initiates online order via NateraConnect	eraConnect		
Patient receives email/text to complete order	<b>⊘</b>	×	
Patient watches test-education video		×	
Patient enters insurance information	<b>⊘</b>	✓ (Provider)	
Patient receives pre-test cost estimate	<b>⊘</b>	×	
INPUT submits partner information (for PAE, joint reports)	<b>⊘</b>	×	
Patient receives flexible phlebotomy options			
	Fully virtual/remote testing	Online ordering	
Potentially appropriate use cases	Minimal provider workload desired	Control over workflow desired	
	Compliant patient population	Less-compliant patient populati	
	<ul> <li>Integrated pre-test education and cost estimate desired</li> </ul>	Existing patient-education process	

## NateraSync EMR Solutions

## Modular services configurable to your EMR system and business requirements



#### **Epic EMR Solutions**

Streamlined ordering and results solution developed by Epic



#### e-Results Sync

Patient lab results delivered directly to your EMR and can be routed to patient record



#### **Total EMR Sync**

Full bi-directional data and workflow interoperability with HL7 interface development

#### Secure

Direct HIPAA compliant data exchange



#### **Flexible**

>100 EMR vendors supported



#### Proven

>1,500 accounts successfully integrated





## **Epic Orders and Results Anywhere Network**

Order tests and receive results directly in your Epic EMR with new Epic solution

#### **How it Works**

- Epic's Order and Results Anywhere network allows Epic customers to easily enable ordering and results delivery in the EMR
- Delivers the benefits of a traditional HL7 bi-directional integration without the long timelines and costly implementation.

#### **Get Started**

- Connect to the Orders and Results Anywhere network with less than 24 hours of total work time.
- Epic Sherlock Checklist available to understand implementation process
- Natera EMR Support Team available to assist with implementation

#### **Available with**

Panorama™ Next-generation NIPT

Horizon™ Advanced carrier screening

**Empower**™
Hereditary cancer test

Prospera™ Transplant assessment **Spectrum**™
Preimplantation genetics

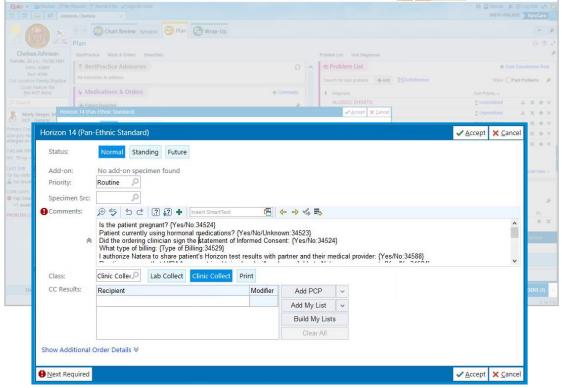
Renasight Kidney gene panel

**Anora**™ Miscarriage test (POC) **Signatera**™ Residual disease test (MRI **Altera**™ Tumor genomic profile

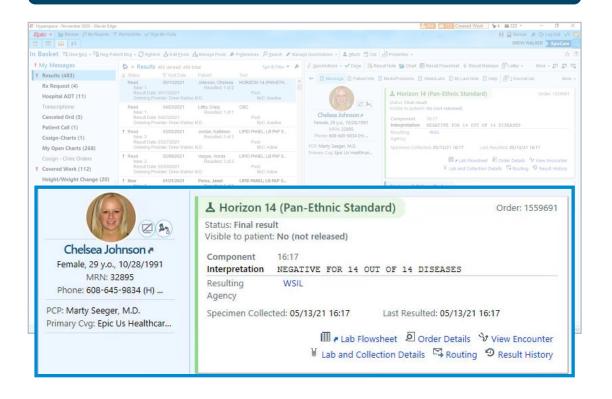


## Epic Orders and Results Anywhere Network

# Ordering | Compact - Howenbur 200 - Gazer Eagle | Compac



#### **Results**



## Mobile phlebotomy services

- Available in all 50 states
- No cost to patient
- Patient can schedule by:

Visiting the online patient portal



Texting **DRAW** to **484848** 



## NateraConnect

## **Accessing online ordering**



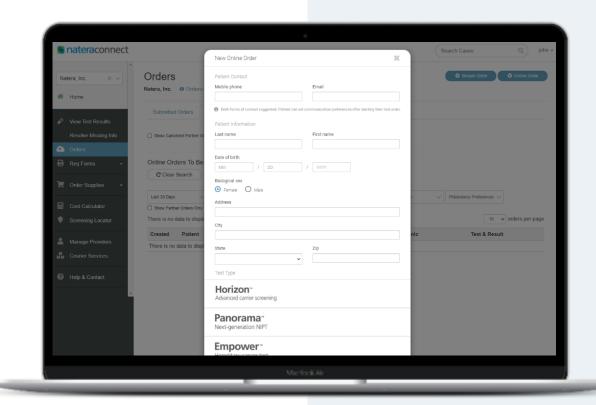
#### **Benefits:**

- Initiation of test orders
- Step-by-step guided workflow with no missing information
- Paperless process
- Real-time order status



## Offers fully virtual testing when combined with:

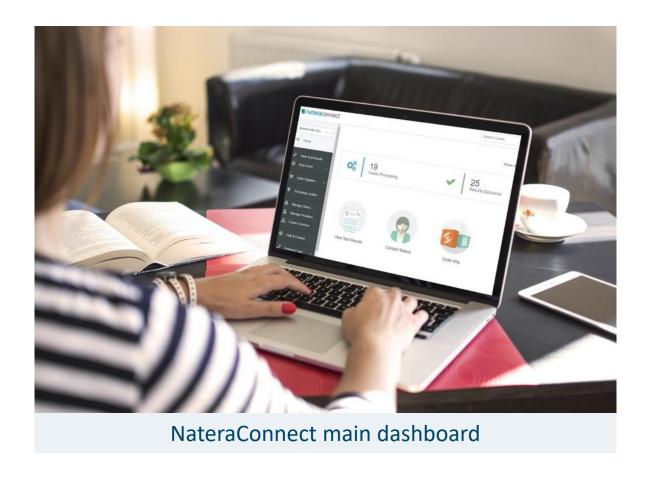
- Mobile phlebotomy
- Patient pre-test education
- Pre-test cost estimate



## **NateraConnect**

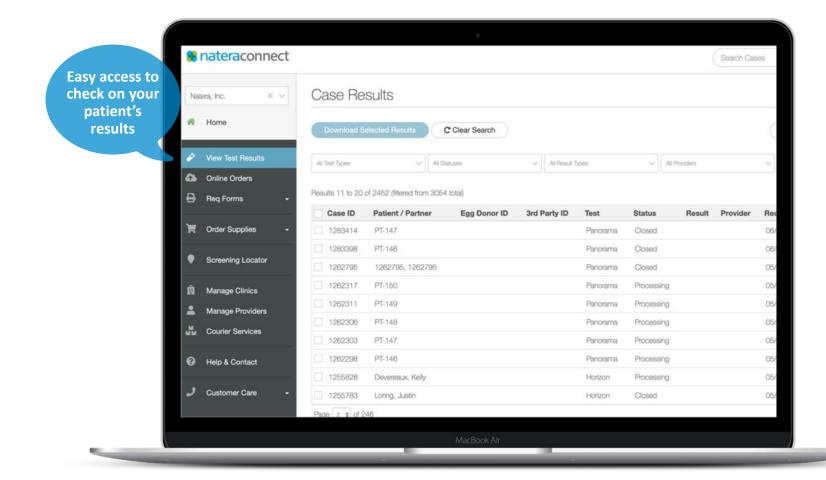
## Online provider portal for integrated testing management

- Track order status, view results, and correct missing information
- Order kits, requisitions, and patient brochures.
- Locate blood-draw resources.
- Manage preferences for releasing results to patients.



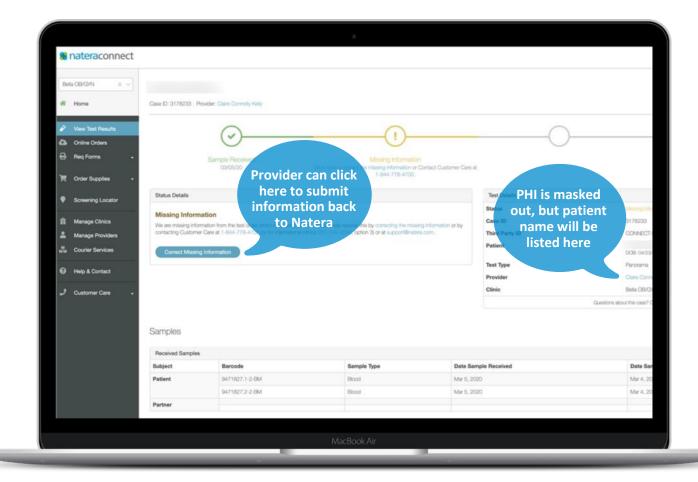
## **Locating patient results**





## Viewing and correcting missing information

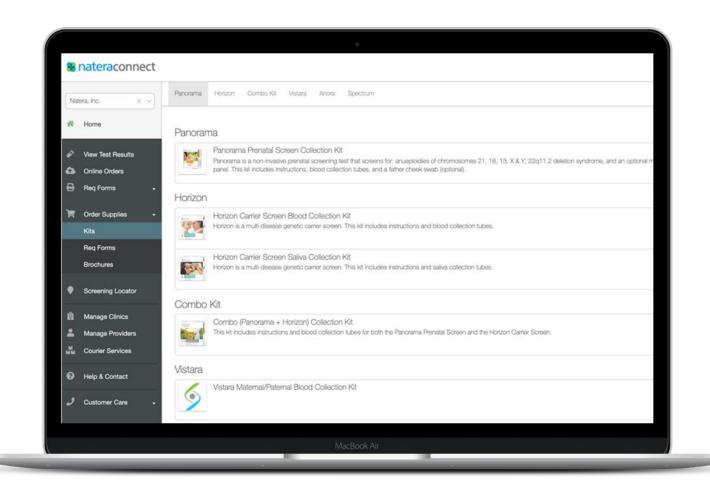




## **Ordering test kits**



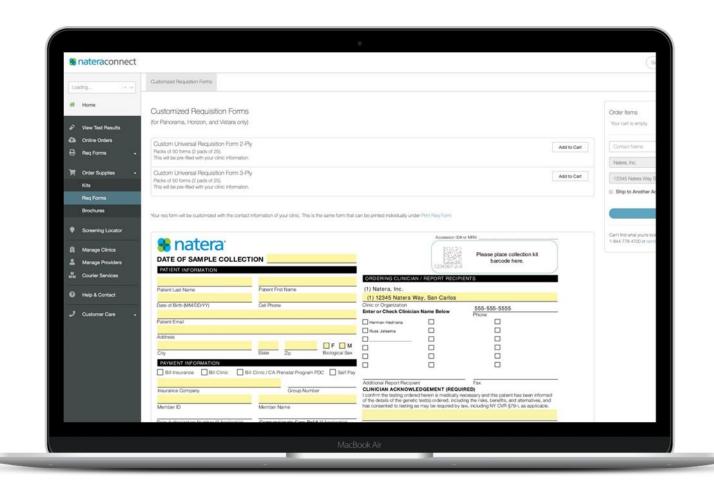
Visit NateraConnect to order kits and have them sent directly to your clinic.



## **Ordering requisition forms**



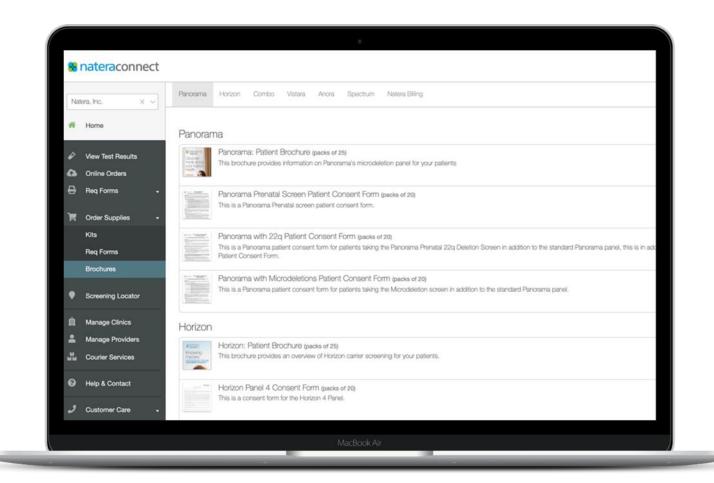
Visit NateraConnect to order two- and three-ply custom requisition forms.



## **Ordering patient brochures**



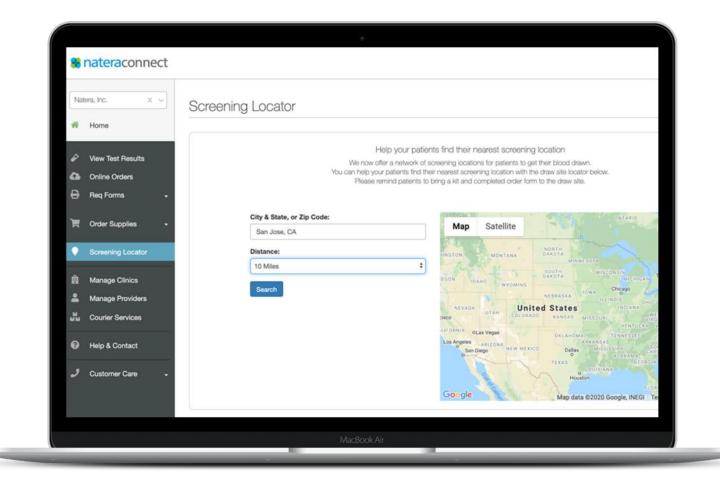
Visit NateraConnect to order patient brochures for your office.



## **Locating blood-draw resources**



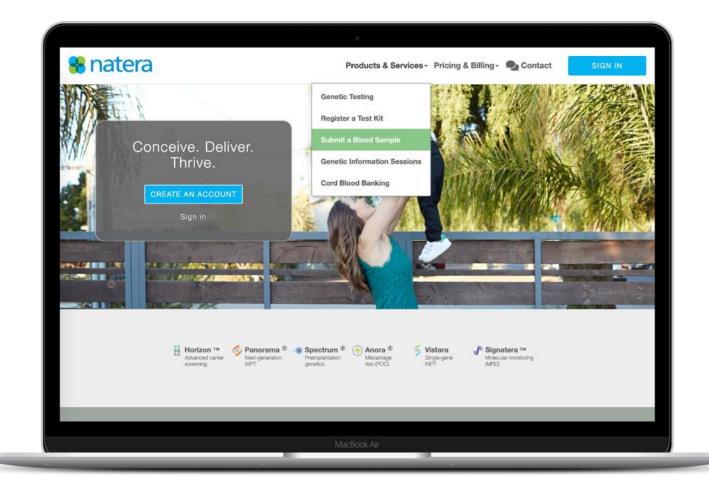
Visit NateraConnect to locate the nearest Patient Service Center (patient blood-draw location).



## Flexible phlebotomy options

## Patient access via my.natera.com





## A range of patient-selected draw locations

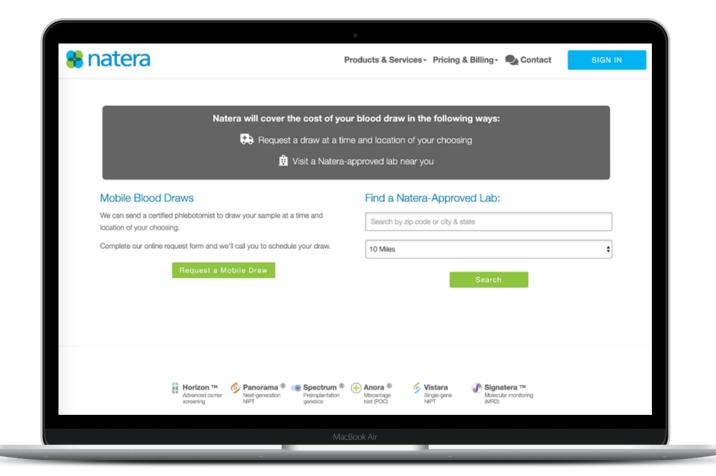
**Including Patient Service Centers (PSC) or mobile blood draw (at-work or at-home)** 





Patients can also text

DRAW to 484848 to access
blood-draw options.



# Results



## Results

Clear, actionable reports, served with time-saving tools and a side of expert guidance

## Online results management



Results tracking



Patient resultsrelease settings

## Flexible results delivery options



Positive results delivery via Genetic Information Session



E-Results Sync: Results delivery to the EMR

#### Patient Call-Out Program (PCOP) with NEVA



Interactive results delivery with NEVA



Proactive call out to clinicians for positive results



## e-Results Sync

## Receive patient lab results directly in your EMR

#### **How it Works**

- Patient lab results are sent directly to your EMR inbox through DIRECT messaging, available in nearly every EMR.
- Once received, simply attach the PDF result to the patient record, eliminating the need to scan paper test results.

#### **Get Started**

- Once your DIRECT EMR address is confirmed, Natera will enable results delivery in less than a day.
- If you do not have a DIRECT address, one can be created by your hospital's IT team.

## **Compatible Tests**

Panorama™ Next-generation NIPT Horizon™ Advanced carrier screening **Anora**™ Miscarriage test (POC) **Spectrum**™ Preimplantation genetics

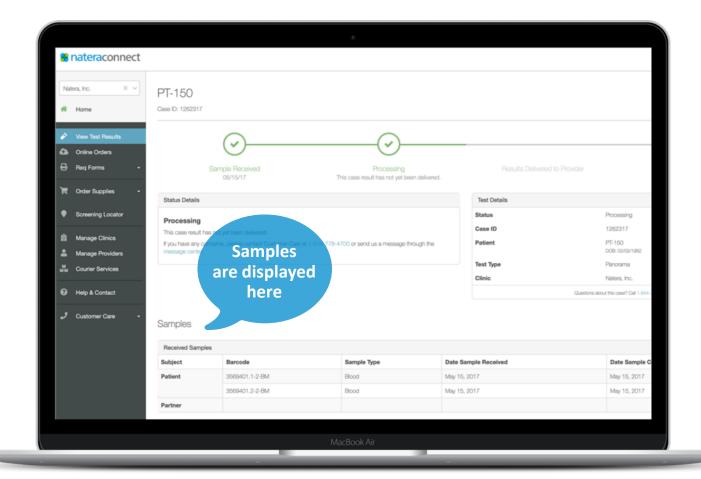
**Empower**™ Hereditary cancer test Prospera™ Transplant assessment



## Online results management

## Results tracking (checking sample status and case details)



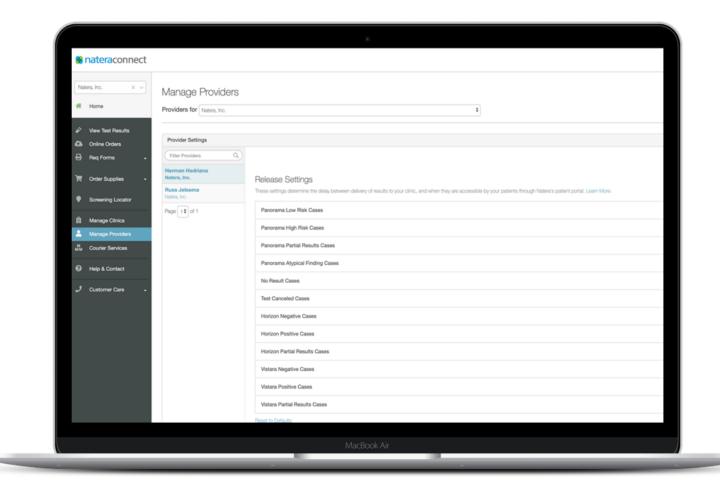


## Online results management

## Selecting patient results-release timing



NateraConnect enables you to select when results are released to patients. Results will automatically release to patients after the specified number of days. Release timing can be customized for negative vs. positive results, and a range of between  $1-10^*$  days can be set.



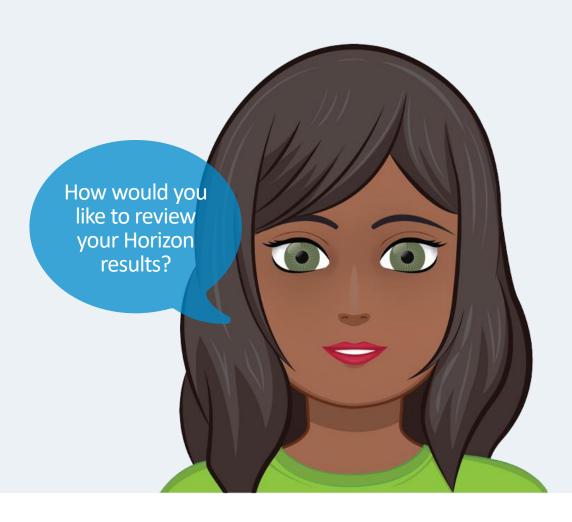


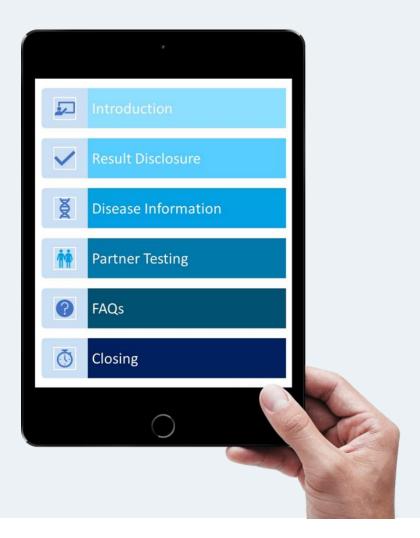


## Interactive results delivery via NEVA

#### Horizon™ Advanced carrier screening

### **Natera's Educational Virtual Assistant**





## **NEVA**



## **NEVA** makes genetic information sessions more accessible

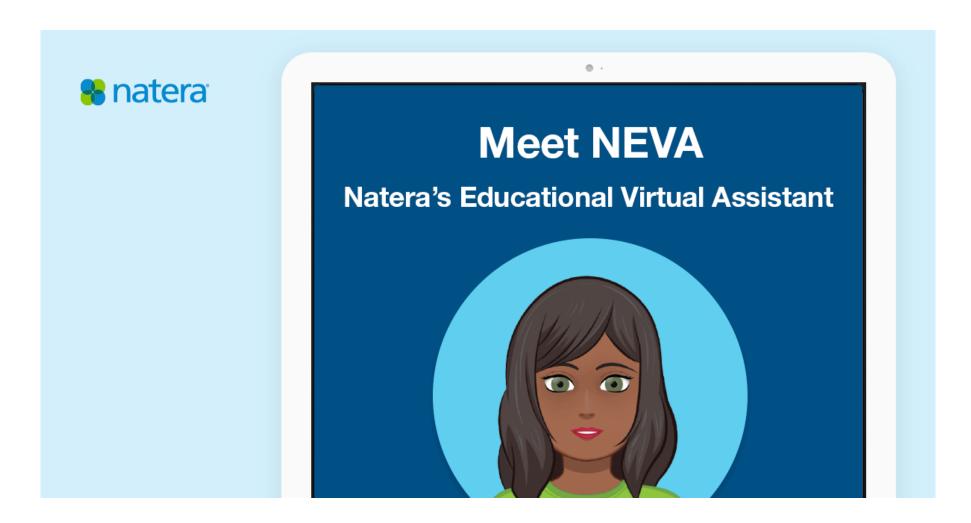


- Rapid, convenient patient access to results and counseling for patients, 24 x 7 x 365
- Complements genetic information sessions for patients
- Accurate information written by genetic counselors
- Al-enabled technology
- Patient-rated as friendly, knowledgeable, and helpful

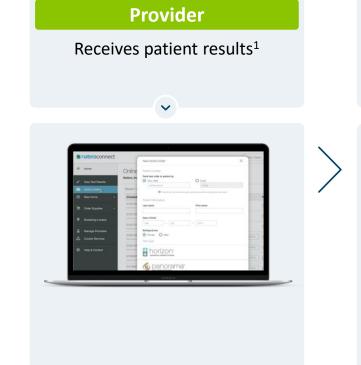
## **NEVA**



## **NEVA** uses an interactive interface to communicate with patients



## Patient Call-Out Program (PCOP) with NEVA



#### **Patient**

Receives email/text to log onto Patient Portal and NEVA greets patient

Natera's Educational Virtual Assistant

Yes, go on

If only one parent is a carrier of a

never have that genetic disease.

Does this make sense?

genetic disease, their children almost

OK, Great. Would you like some more information about cystic fibrosis?

Terrific. Let's dive a little deeper into the genetics of cystic fibrosis.

Completes NEVA or schedules genetic information session<sup>2</sup>







#### Provider

Receives email/fax documenting NEVA session completed



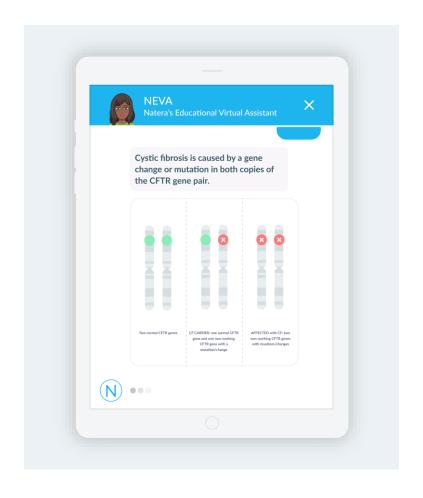


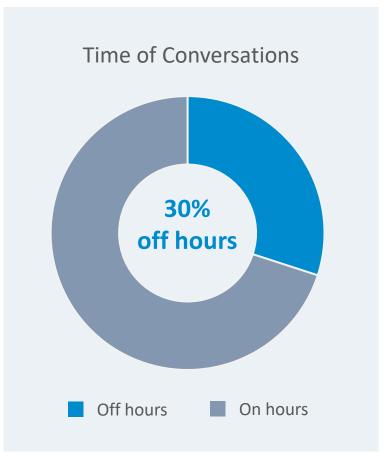
- NEVA session transcript can be downloaded by patient and provider
- Patient receives Horizon results report

- 1. ~1 business day between when provider receives patient's results and patient receives email/text to log onto Patient Portal
- 2. If patient is positive and does not complete NEVA interaction, Natera customer care will contact patient



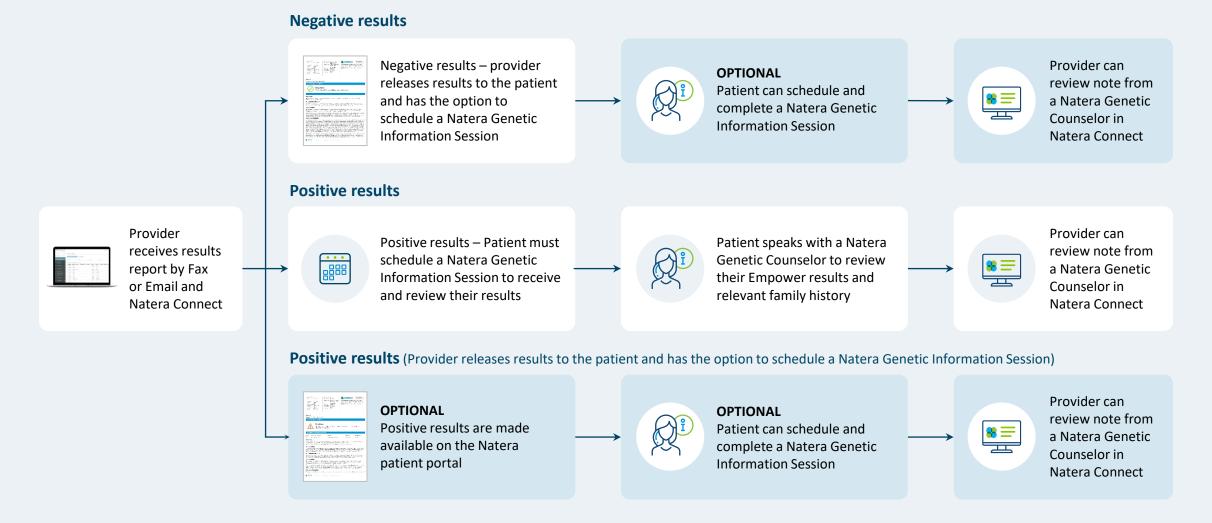
## NEVA supports scalable and convenient post-test counseling







## **Empower: Post-test Workflow**



## NIPT Gender Sender



## Simplifying fetal-sex reporting for patients and providers

#### Physician → NateraConnect

Release report to patient as usual

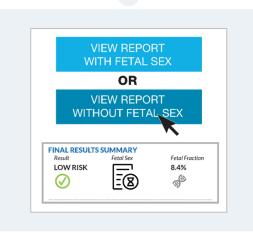


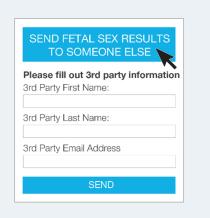
- Release manually or NateraConnect can release automatically
- You're done!

#### Patient → My Natera portal

Option to view report with or without fetal sex

Option to send fetal sex to friends and family





- Chooses not to see fetal sex
- Reviews results before sending fetal sex information
- Always has option to see fetal sex if desired

#### Friend → Email

3<sup>rd</sup> party receives fetal sex reults

Congratulations! Your friend Jane is having



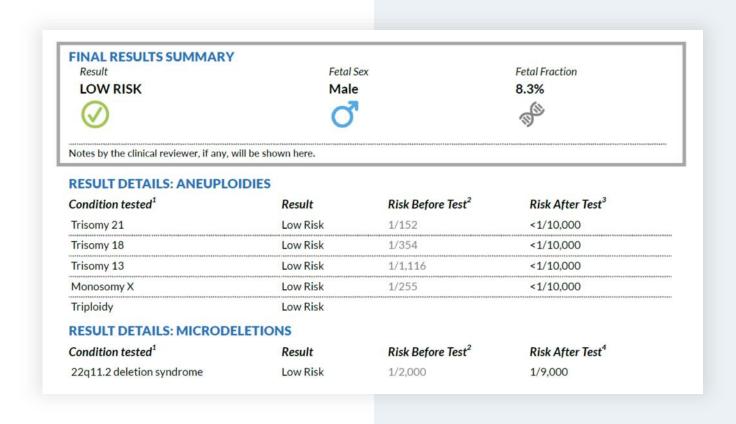
Surprise reveal can be planned





#### **Panorama NIPT**

Low-risk, Singleton report





#### **Panorama NIPT**

High-risk Trisomy 21, Singleton report

#### **FINAL RESULTS SUMMARY**

Result

HIGH RISK for Trisomy 21

Fetal Sex

**Fetal Fraction** 

Male





8.3%

This is a screening test only. Genetic counseling and diagnostic testing should be offered to further evaluate these findings.

Panorama analyzes DNA from the placenta. In some cases placental DNA can differ from that of the fetus; therefore, no irreversible decisions should be made based upon results of this screening test alone.

#### **RESULT DETAILS: ANEUPLOIDIES**

Condition tested <sup>1</sup>	Result	Risk Before Test <sup>2</sup>	Risk After Test <sup>3</sup>
Trisomy 21	High Risk	1/152	9/10
Trisomy 18	Low Risk	1/354	<1/10,000
Trisomy 13	Low Risk	1/1,116	<1/10,000
Monosomy X	Low Risk	1/255	<1/10,000
Triploidy	Low Risk	***************************************	***************************************





#### **Horizon**

Negative report

**Patient Information** 

Patient Name: Jane Doe Date of Birth: 02/02/1975 Gender: Female Ethnicity: Hispanic Patient ID: P99457 Medical Record #: M84555 Collection Kit: 254233-2-N 40192731 Accession ID: Case File ID: 123456

Test Information

Ordering Physician: Dr. Goodbirth, M.D. (G123456)

Clinic Information: Natera, Inc.
Phone: 650 555-1212
Report Date: 02/01/2013

Sample Collected: 01/31/2013 Sample Received: 02/01/2013 Sample Type: Blood



#### CARRIER SCREENING REPORT

ABOUT THIS SCREEN: Horizon™ is a carrier screen for specific autosomal recessive and X-linked diseases. This information can help patients learn their risk of having a child with specific genetic conditions.

**ORDER SELECTED:** The **Horizon 27** panel was ordered for this patient.

#### FINAL RESULTS SUMMARY:



#### **NEGATIVE FOR 27 OUT OF 27 DISEASES**

No pathogenic variants were detected in the genes that were screened. The patient's remaining carrier risk after negative screening results is listed for each disease/gene on the Horizon website at <a href="http://www.natera.com/hrzn27s">http://www.natera.com/hrzn27s</a>. Please see the following pages of this report for a comprehensive list of all conditions included on this individual's screen.

Carrier screening is not diagnostic and may not detect all possible pathogenic variants in a given gene.



**Horizon** 

Joint report

UXMSNGA HUGNEYD Date of Birth:

Gender:

Ethnicity:

Collection Kit:

Case File ID:

Report Date:

Ordering Physician:

01/01/1990 Female

3899350

03/15/2021

African American 925301715-2-C

Ethnicity: Collection Kit: Case File ID:

BJYSMGY

OAZCPHS

Gender:

Date of Birth:

3899351 Report Date: 03/15/2021

01/01/1990

African American

925309034-2-C

Male

Ordering Physician:



#### FINAL RESULTS SUMMARY:

Risk Details	UXMSNGA HUGNEYD	BJYSMGY OAZCPHS	Reproductive Risk
Panel Information Horizon 274 Carrier Screening Panel Horizon 274 Carrier Screening Panel		Horizon 274 Carrier Screening Panel	
Spinal Muscular Atrophy Gene: SMN1	CARRIER SMN1: 1 copy	CARRIER SMN1: 1 copy	1 in 4

Carrier screening is not diagnostic and may not detect all possible pathogenic variants in a given gene.

#### RECOMMENDATIONS

Individuals who would like to review their Horizon report with a Natera Laboratory Genetic Counselor may schedule a telephone genetic information session by calling 650-249-9090 or visiting naterasession.com. Clinicians with questions may contact Natera at 650-249-9090, 855-866-6478 (toll free) or email support@natera.com. Individuals with positive results may wish to discuss these results with family members to allow them the option to be screened. Comprehensive genetic counseling to discuss the implications of these test results and possible associated reproductive risk is recommended.



#### **Horizon**

Positive report

**Patient Information** 

Patient Name: John Doe Date of Birth: 02/02/1975 Gender: Male Ethnicity: Hispanic Patient ID: P99457 Medical Record #: M84555 Collection Kit: 254233-2-N Accession ID: 40192731 Case File ID: 123456

**Test Information** 

Ordering Physician: Dr. Goodbirth, M.D. (G123456)

 Clinic Information:
 Natera, Inc.

 Phone:
 650 555-1212

 Report Date:
 02/01/2013

 Sample Collected:
 01/31/2013

 Sample Received:
 02/01/2013

Sample Type: Blood



#### CARRIER SCREENING REPORT

ABOUT THIS SCREEN: Horizon™ is a carrier screen for specific autosomal recessive and X-linked diseases. This information can help patients learn their risk of having a child with specific genetic conditions

ORDER SELECTED: Cystic Fibrosis was ordered for this patient.

#### FINAL RESULTS SUMMARY:



#### **CARRIER for Cystic Fibrosis**

Positive for the pathogenic variant [name of mutation] in the CFTR gene. If the patient's partner is a carrier for Cystic Fibrosis, their chance to have a child with this condition is 1 in 4 (25%).

Carrier screening is not diagnostic and may not detect all possible pathogenic variants in a given gene.



## **Empower**

Negative report

#### **FINAL RESULTS SUMMARY**



#### Negative

No known pathogenic or likely pathogenic variants were detected.

#### Interpretation

No known or potential disease-causing pathogenic variants or variants of uncertain significance were detected by the methods described in the Methodology & Limitations section below.

#### Genes analyzed on this panel

APC, ATM, BARD1, BMPR1A, BRCA1, BRCA2, BRIP1, CDH1, CDK4, CDKN2A, CHEK2, DICER1, EPCAM, HOXB13, KIT, MEN1, MIFF, MLH1, MRE11A, MSH2, MSH6, MUTYH, NBN, NF1, PALB2, PDGFRA, PMS2, PTEN, RAD50, RAD51C, RAD51D, SDHA, SDHB, SDHC, SDHD, SMAD4, SMARCA4, STK11, TP53, TSC1, TSC2, VHL, MSH3, POLE, RPS20, POLD1, NTHL1, AXIN2, BAP1, CTNNA1, GALNT12, GREM1, RNF43

#### Recommendations

Clinical correlation and genetic counseling are recommended for this individual to discuss associated cancer risks as well as cancer screening and prevention/risk reduction options. Test results should be interpreted in the context of the patient's clinical presentation and family history. Medical management should be based on the patient's clinical risk factors such as family history, lifestyle and age.

Individuals who would like to review their Empower test report with a Natera Laboratory Genetic Counselor may schedule a telephone genetic information session by calling 650-249-9090 or visiting naterasession.com. Clinicians with questions may contact Natera at 650-249-9090 or email support@natera.com. Individuals with positive results may wish to discuss these results with family members to allow them the option to be screened. Comprehensive genetic counseling to discuss the implications of these test results and possible associated reproductive risk is recommended.



## **Empower**

Positive report

#### FINAL RESULTS SUMMARY



#### **Positive**

A pathogenic variant in the BRCA1 gene was detected. This variant is associated with an INCREASED CANCER RISK.

Next-generation sequencing-based copy number analysis was inconclusive (see below). Redraw for blood sample will be accepted.

#### FINDINGS: POSITIVE VARIANT(S)

Gene	Associated Disease(s)	Variant	Zygosity	Classification
BRCA1	Hereditary Breast and Ovarian Cancer Syndrome	c.68_69delAG (p.E23Vfs*17)	heterozygous	pathogenic

#### Interpretation

A heterozygous pathogenic variant, c.68\_69delAG (p.E23Vfs\*17) in the BRCA1 gene, was detected. This change creates a premature termination codon in the BRCA1 gene and is expected to result in an absent or disrupted protein product. Loss-of-function variants in BRCA1 are considered to be pathogenic (PMID: 20104584). This pathogenic variant is a known common cause of breast and ovarian cancer in the Ashkenazi Jewish population (PMID: 9042909, 22430266) and has been observed in individuals from other ethnicities (PMID: 8651293, 8571953, 9921907). This variant has also been reported in individuals affected with pancreatic cancer (PMID: 15994883, 22430266, 23658460, 24737347). This variant has been classified as pathogenic by multiple submitters and reviewed by an expert panel in the ClinVar database (Variation ID: 17662).

Please note, due to compromised sample quality of this specimen, next-generation sequencing-based copy number variation (CNV) analysis was uninformative. CNV analysis did not pass our internal quality control metrics, and the presence of large deletions and/or duplications cannot be excluded. Natera will repeat the next-generation sequencing-based CNV analysis at no additional charge if a new sample from the patient is submitted (blood sample is required). The blood sample must be submitted with a new requisition and a copy of this report.

# Patient-friendly reports



### **Empower**

Negative with VUS report

VUS is always included as an additional finding

#### **FINAL RESULTS SUMMARY**



### Negative

No known pathogenic or likely pathogenic variants were detected.

#### Genes analyzed on this panel

APC, ATM, BARD1, BMPR1A, BRCA1, BRCA2, BRIP1, CDH1, CDK4, CDKN2A, CHEK2, DICER1, EPCAM, HOXB13, KIT, MEN1, MIFF, MLH1, MRE11A, MSH2, MSH6, MUTYH, NBN, NF1, PALB2, PDGFRA, PMS2, PTEN, RAD50, RAD51C, RAD51D, SDHA, SDHB, SDHC, SDHD, SMAD4, SMARCA4, STK11, TP53, TSC1, TSC2, VHL, MSH3, POLE, RPS20, POLD1, NTHL1, AXIN2, BAP1, CTNNA1, GALNT12, GREM1, RNF43

#### ADDITIONAL FINDINGS: VARIANTS OF UNCERTAIN SIGNIFICANCE (VUS)

Variants of uncertain significance (VUS) are common and the American College of Medical Genetics and Genomics (ACMG) states that a VUS should NOT be used in clinical decision making. A VUS means that a change in the DNA was detected, but there is not enough information to determine whether or not the change increases the risk of cancer. Many VUS represent normal human variation. Medical management should be based on the patient's personal and/or family history.

Gen	ne	Variant	Zygosity	Classification
ATM	N	c.6736_6755del20insCA (p.C2246_T2252delinsH)	heterozygous	vus

#### Interpretation

A heterozygous variant of uncertain significance (VUS) was detected in the ATM gene as tabulated above. This variant has been reported by one submitter in the ClinVar database (Variant ID: 420013, also known as c.641-16421\_641-16402delinsTG) and was classified as likely pathogenic. This variant has also been previously reported in a homozygous state in one patient with ataxia-telangiectasia (PMID: 10425038). This variant has not been previously reported in the gnomAD population database. Due to the limited information currently available in public databases and in the medical literature, we have classified this change as a variant of uncertain significance.



# Report supplements

### Clarifying positive results and next steps



### **Panorama NIPT**

Trisomy 21 supplement

Panorama™ Report Supplement: Trisomy 21 (Down syndrome)



#### Your screening test result shows a high risk for Trisomy 21 (Down syndrome).

You are receiving this fact sheet because you had a Panorama screening result that showed a 'high risk' for this specific chromosome condition. This screening result DOES NOT mean your baby has this condition. The blood test you took is a screening test that looks to see if your baby is at a higher than average chance to have certain chromosome conditions. It does not diagnose or confirm the condition. To know for sure whether or not your baby has this condition, you need to have a diagnostic test such as an amniocentesis or CVS during pregnancy or a blood test after your baby is born. More information on follow-up diagnostic testing is listed below. Decisions about your pregnancy SHOULD NOT be made based on the screening results alone as your baby may not have this condition.

#### What is Down syndrome?

Trisomy 21, also called Down syndrome, is a chromosome condition caused by an extra 21st chromosome. Usually, humans have 46 chromosomes that come in 23 pairs. Children who have Down syndrome have three copies of chromosome 21 Instead of two.

#### What are the common features of Down syndrome?

Children with Down syndrome have intellectual disabilities and specific physical features. They may have heart defects, weak muscle tone, and can be smaller than average. Other health and learning problems can also occur in children with Down syndrome but these problems will vary from child to child. Every child with Down syndrome is unique.

#### How common is Down syndrome?

About 1 in 600 babies is born with Down syndrome<sup>s</sup>.

#### Do children with Down syndrome need extra medical care?

Yes, children with Down syndrome will need extra medical care depending on the child's specific health problems.

#### Do babies with Down syndrome have a normal lifespan?

Most people with Down syndrome five into their 60s and mary like even longer. The presence of medical conditions, like heart defects, can affect the lifespan in these children and adults. Miscarriage occurs in about 30% of pregnancies with Down syndrome.

#### Do bables with Down syndrome have normal IQs?

Most children with Down syndrome have intellectual disabilities that range from mild to moderate. Early intervention has been shown to benefit children born with Down syndrome. Many children with Down syndrome learn to read and write and participate in normal activities.

#### How does Down syndrome happen?

In most cases, Down syndrome happens by chance. There is nothing you can do before or during pregnancy to cause or prevent Down syndrome.

#### What is the next step?

Natera's Pancrama Test screens the mother's blood to find the baby's DNA and looks for specific obvorceone problems. This form of screening is new?. It is recommended that you talk to a doctor or genetic counselor about more testing to find out if the baby has Down syndrome. Two tests are available in pregnancy to check the baby's chromosomes. One test is chorionic villus sampling (CVS), which can be done at 10 to 12 weeks of pregnancy. Another test is amnicoentesis, which can be done as early as 15 weeks of pregnancy, if you do not want more prenatal testing, chromosome testing can be done for the baby after he or she is born.

#### Panorama™ Report Supplement: Trisomy 21 (Down syndrome)



#### Where can I learn more about Down syndrome?

Your healthcare provider can refer you to a genetics professional in your area. Genetics professionals such as medical geneticists and genetic counselors can discuss conditions like Down syndrome in more detail and answer any questions you may have about your results.

Additional information on Down syndrome can be found online:

- March of Dimes http://www.marchofdimes.com/baby/birthdefects\_ chromosomal.html
- National Down Syndrome Society http://www.ndss.org
- National Down Syndrome Society Local Support
   Group Listings
- http://www.ndss.org/Resources/Local-Support
- Genetics Home Reference
   http://ghr.nlm.nih.gov/condition/down-syndrome

#### Where can I find a genetic counselor?

You may find a local genetic counselor through the National Society of Genetic Counselors at www.nsgc.org.

- Nussibisum et al. 2007 Thompson and Thompson Genetics in Medicine (7th Ed.) Cadord Saunders, Philadelphia, PA.
- The Pancrams pranalal covering test was developed by Nations, Inc., a laboratory certified under the Christal Laboratory improvement Amendments (CLIA). This test has not been cleaned or approved by the U.S. Food and Drug Administration (FDA).



# Report supplements

## Clarifying positive results and next steps



# Horizon Carrier Screen SMA supplement



#### SPINAL MUSCULAR ATROPHY

#### Understanding Your Horizon™ Carrier Screen Results

#### What is Spinal Muscular Atrophy?

Spinal Muscular Atrophy (SMA) is a serious inherited disorder that typically begins in infancy or childhood and causes worsening muscle weakness, decreased ability to breathe, and loss of motor skills. Most children with SMA have one of the early-onset forms with symptoms that begin in infancy. Without treatment, death often occurs before the age of two. Some children have juvenile onset SMA and develop muscle weakness and other symptoms later in childhood and typically have a normal lifespan. In rare cases symptoms do not begin until early adulthood, are less severe, and do not affect lifespan. Currently there is no cure for SMA, although new medications may be available to lessen or stop the progression of symptoms of SMA, especially when treatment is started early. Clinical trials involving potential new treatments for this condition may be available (see <a href="https://www.clinicaltrials.gov">www.clinicaltrials.gov</a>.

#### What causes Spinal Muscular Atrophy?

SMA is caused by a change, or mutation, in both copies the SMNI gene pair. These mutations, which often delete part or all of these genes, cause the genes to work improperly or not work at all. When both copies of the SMNI gene are missing or do not work correctly, it leads to the symptoms described above.

SMA is inherited in an autosomal recessive manner. This means that, in most cases, both parents must be carriers of a mutation in one copy of SMN2 to have a child with SMA. People who are SMA carriers are usually healthy and do not have symptoms nor do they have SMA themselves. Usually a child inherits two copies of each gene, one copy from the mother and one copy from the father. If the mother and father are both carriers for SMA, there is a 1 in 4, or 25%, chance in each pregnancy for both partners to pass on their SMM2 gene mutations to the child, who would then have SMA. With further testing (not offered through Natera), it is sometimes, but not always, possible to determine whether a given carrier couple is at risk to have a child with a severe, early-onset form of SMA, the juvenile form, or the later-onset form.

Individuals found to carry more than one mutation for SMA should discuss their risk for having an affected child, and any potential risks to their own health, with their health care provider.

#### What can I do next?

You may wish to speak with a local genetic counselor about your carrier test results. A genetic counselor in your arrea can be located on the National Society of Genetic Counselors website (www.nsg.org).

1



Your siblings and other relatives are at increased risk to also have this mutation. You are encouraged to inform your family members of your test results as they may wish to consider being tested themselves.

If you are pregnant, your partner can have carrier screening for SMA ordered by a health care professional. Partner screening may include SMNI testing and possibly Enhanced SMA testing. Enhanced SMA testing can provide information on the chance to still be a carrier even after a normal (negative) SMA carrier screen. Your doctor or a local genetic counselor can help decide which carrier test is best for your partner. If your partner is not found to be a carrier of SMA, your risk of having a child with SMA is sereatly reduced.

Couples at risk of having a baby with SMA can opt to have prenatal diagnosis done through chorionic villus sampling or amniocentesis during pregnancy or can choose to have the baby tested after birth for SMA.

If you are not yet pregnant, your partner can have carrier testing for SMA ordered by a health care professional. Partner testing may include SMVII testing and possibly Enhanced SMA testing. Enhanced SMA testing can provide information on the chance to still be a carrier even after a normal (negative) SMA carrier screen. Your doctor or a local genetic counselor can help decide which carrier test is best for your partner. If your partner is found to be a carrier for SMA, you have several reproductive options to consider.

- Natural pregnancy with or without prenatal diagnostic testing of the fetus or testing the baby after birth for SMA.
- · Preimplantation genetic diagnosis (PGD) with in vitro fertilization (IVF) to test embryos for SMA
- . Adoption or use of a sperm or egg donor who is not a carrier for SMA

#### What resources are available?

- Families of SMA: <a href="http://curesma.org/FSMACommunity/understandingsma">http://curesma.org/FSMACommunity/understandingsma</a>
- GeneReviews: https://www.ncbi.n/m.nih.gov/books/NBK1352/
- Prenatal diagnosis done through CVS: <a href="http://www.marchofdimes.org/chorionic-villus-sampling.aspx">http://www.marchofdimes.org/chorionic-villus-sampling.aspx</a>
- Prenatal diagnosis done through amniocentesis: <a href="http://www.marchofdimes.org/amniocentesis.aspx">http://www.marchofdimes.org/amniocentesis.aspx</a>
- PGD with IVF: <a href="http://www.natera.com/spectrum">http://www.natera.com/spectrum</a>

2

# Report supplements

**Evidence-based cancer risks and guidelines-based patient management recommendations** 



# **Empower Hereditary Cancer Test**

**BRCA2** supplement

#### Cancer Risk Estimates for BRCA2

Cancer risk estimates for a positive result are typically based on individuals with a family or personal history of cancer. Your risk may be different if you do not have a personal or family history of cancer.

	Female	Cancer type	General Population - Estimated Lifetime Cancer Risk*	Positive Result - Estimated Lifetime Cancer Risk**
		Breast	12.80%	Up to 84% risk
	$\bigcirc$	Ovarian	1.3%	Up to 27% risk
	¥	Pancreatic	1.60%	2-7%
	-	Melanoma	1.80%	Increased

#### Risk Management and Screening Guidelines for Hereditary Breast and Ovarian Cancer Syndrome \*

The following information is a summary of current US guidelines. Please discuss with your healthcare provider as screening recommendations may vary by country and can change often.

Cancer type	Mode of Screening or Risk Reduction	Typical Age to Begin	How often
Female Breast	Breast self-exam	18	Monthly
	Breast exam with clinician	25	Every 6-12 months
	Breast MRI with contrast	25-29 or individualized if family history of breast cancer below age 30	Annually
	Mammogram with consideration of tomosynthesis (3-D Mammogram)	30	Annually
	Risk-reducing medication	Individualized	Discuss with your healthcare provider
	Risk-reducing breast surgery (mastectomy); discuss with your healthcare provider	Individualized; a consideration for those with a personal and/or family history of breast cancer	N/A
Male Breast	Breast self-exam	35	Monthly
	Breast exam with clinician	35	Annually

Report supplements include detailed patient management recommendations based on medical guidelines



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MLB-10123\_NAT\_BRGA 2 Supplement\_20200128



# Next Steps



# **Next Steps**

Value-add services that go beyond the test to address what's next

Post-test genetic info sessions and provider consultations



#### Schedule by:



Calling Natera Customer Care



Visiting the online patient portal



Texting SESSION to 484848 (patients only)

**Family testing** program



Empower testing for first-degree relatives of patients with a positive result is available at no additional charge.



Visit natera.com/empower for more details.

**Spectrum Advantage Program** 



**Empower and Horizon patients** can access Spectrum preimplantation genetic testing at discounted rates



# Post-test genetic info sessions and provider consultations

Patient and provider access to board-certified genetic experts



### Schedule by:



Calling Natera
Customer Care



Visiting the online patient portal



Texting **SESSION** to **484848** (patient only)

- Appointments available Mon–Fri 6am to 5pm Pacific
- Scheduled online or via phone
- Note summarizing session is sent to health care provider within
   48 hours and available on Natera Connect for easy reference

## On-Demand Genetic Information Sessions

Same day genetic information sessions available for Horizon and Panorama



### **Schedule by:**



Calling Natera Customer Care

- Patients can choose between two options:
  - On-Demand: Request same day callback
  - Appointment: Schedule an appointment on a specific day/time
- On-Demand service available Mon–Fri 6am to 5pm Pacific, until capacity met

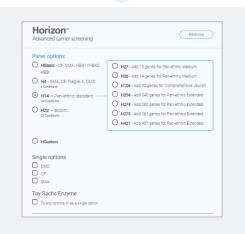
## Horizon Partner Auto-Enroll



### Automated workflow for carrier screen partner testing

Physician

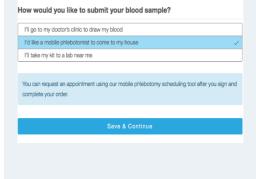
Approves partner order in NateraConnect\*



- Order automatically generated
- Select test panel and sign





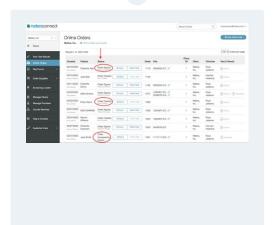


- Receives order by text/email
- Watches educational video and gets personalized cost
- Schedules blood draw
- Signs order

Phlebotomy Services



Accesses real time update on order status



Stay informed on Order Status

Patient tests positive

<sup>\*</sup> Partner information and consent must be provided to complete partner testing

# **Empower Family Testing Program**



Testing for first-degree relatives of patients with a positive result is available at no additional charge



Order must be received within 90 days of original report date



Panel must be the same size or smaller compared to previous relative's test order.



Not available to family members covered by government insurance plans.

# Spectrum Advantage Program

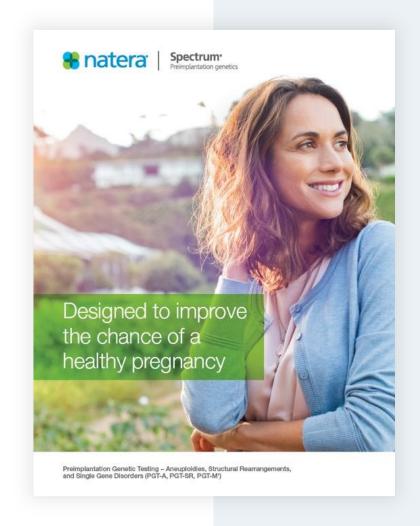
### **Increased access to PGT**



Spectrum<sup>®</sup> Preimplantation genetics

For couples screened positive with Horizon, Natera offers Spectrum Advantage \$99 pre-implantation genetic testing\*





<sup>\*</sup> Spectrum PGT-M and PGT-A must be performed within one year of Horizon screening results. Promotional price good for one test run. Shipping and batching fees apply. Restrictions apply. Both male and female must have completed a Horizon panel (Horizon 4, 14, 27, 106, 137, or 274). Prior carrier screening identifying positive risk for a disorder voids special pricing.



# Spectrum Advantage Program

### **Increased access to PGT**



**Empower**™ Hereditary cancer test

For patients who test positive with Empower hereditary cancer testing, Natera offers Spectrum Advantage pre-implantation genetic testing at a significant discount\*



<sup>\*</sup>Spectrum PGT-M and PGT-A must be performed within one year of Empower test results. Does not apply for patients with a VUS result. Shipping and batching fees apply. Promotional price good for one test run and not valid if patient chooses to file insurance. Restrictions apply. Prior carrier screening/genetic testing identifying positive risk for a disorder voids special pricing. Patients that have participated in the Empower family testing program are not eligible for Spectrum Advantage.





The tests described have been developed and their performance characteristics determined by the CLIA-certified laboratory performing the test. The tests have not been cleared or approved by the US Food and Drug Administration (FDA). Although FDA is exercising enforcement discretion of premarket review and other regulations for laboratory-developed tests in the US, certification of the laboratory is required under CLIA to ensure the quality and validity of the tests. CAP accredited, ISO 13485 certified, and CLIA certified. © 2021 Natera, Inc. All Rights Reserved.