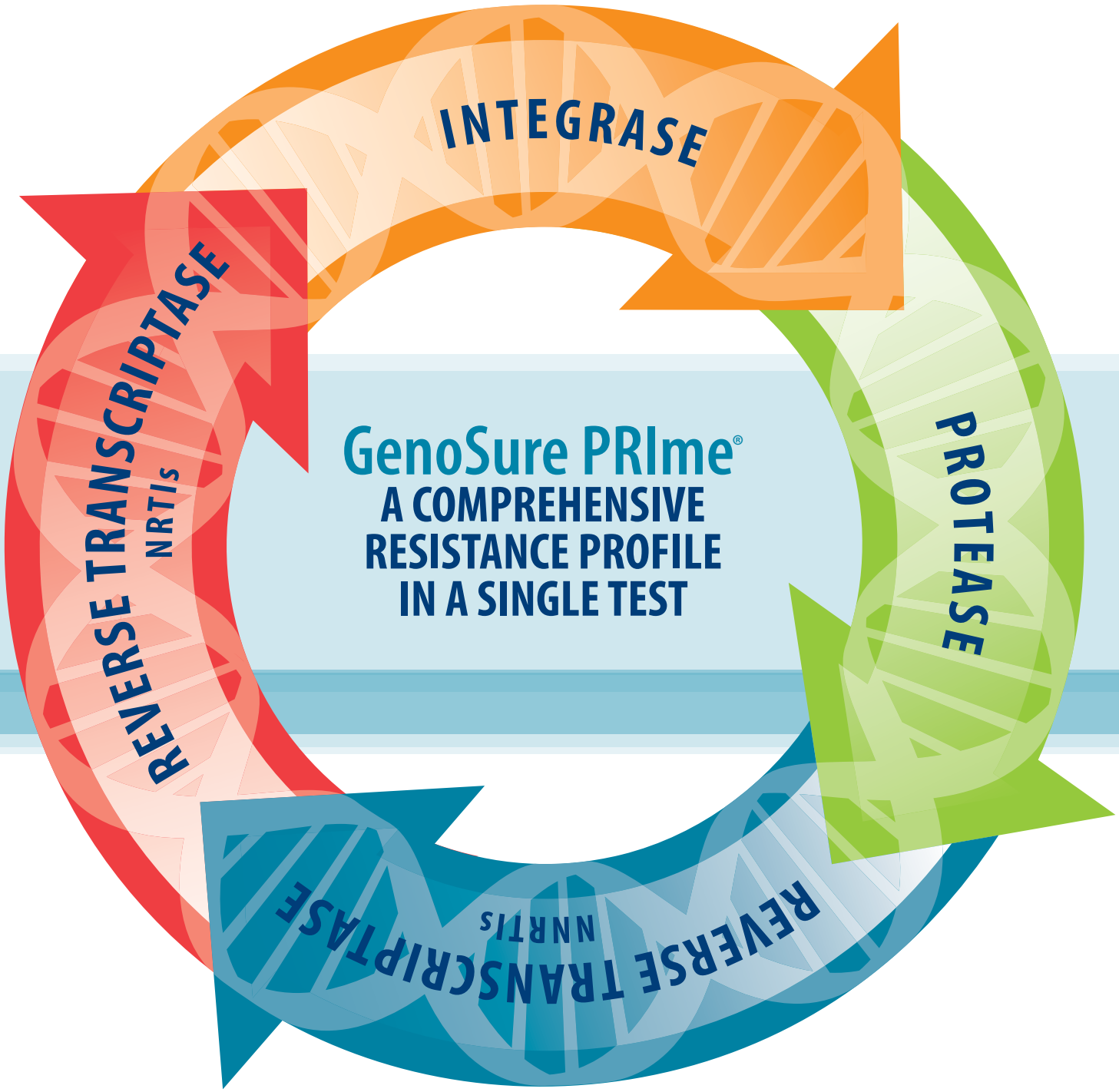

GenoSure PRIme®

A COMPREHENSIVE RESISTANCE PROFILE IN A SINGLE TEST

Monogram BIOSCIENCES
LabCorp Specialty Testing Group

LabCorp
Laboratory Corporation of America

GenoSure PRIme®

HIV DRUG RESISTANCE ASSAY PR RT IN

To Aid in First-line Therapy Decisions

- The Department of Health and Human Services guidelines for antiretroviral use in patients with HIV-1 recommend genotypic testing as the preferred resistance testing in treatment-naïve patients.[1]
- GenoSure PRIme is the first assay to provide genotypic resistance information on all DHHS-preferred first-line treatment options, including those containing integrase inhibitors.
- Recent studies have demonstrated the transmission of drug-resistant viruses in up to 16% of treatment-naïve patients.[1]
- Testing for integrase strand transfer inhibitors (INI) may be warranted[2] and should be obtained if there is a concern for resistance to this class of drugs.[1]

Consider GenoSure PRIme for baseline resistance testing and detection of transmitted drug resistance.

To Aid in Therapy Decisions for Treatment-experienced Patients

- The DHHS guidelines recommend genotypic testing as the preferred resistance test for patients experiencing virologic failure while on first- or second-line antiretroviral therapy.[1]
- In patients failing integrase inhibitor-based regimens, genotypic testing for integrase inhibitor resistance should be considered.[1]
- Genotypic testing using GenoSure PRIme provides an assessment of viral susceptibility to every commercially available PI, NRTI, NNRTI, and INI in a single assay.

Consider GenoSure PRIme when contemplating changes to your patient's course of therapy.

Features of GenoSure PRIme

- GenoSure PRIme is the first HIV-1 genotype to provide susceptibility information for four drug classes in a single report: NRTIs, NNRTIs, PIs, and INIs.
- GenoSure PRIme evaluates the HIV-1 polymerase (pol) region including the complete protease and integrase coding regions and amino acids 1-400 of reverse transcriptase.
- GenoSure PRIme uses Monogram's proprietary database of more than 100,000 matched HIV-1 genotype-phenotype results.

A single assay providing a comprehensive picture of resistance to PIs, NRTIs, NNRTIs, and INIs.

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Lists key resistance-associated mutations.

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Patient Name	DOB	Patient ID/Medical Record #	Gender	Monogram Accession #
Date Collected	Date Received	Date Reported	Mode	Report Status
Referring Physician			Reference Lab ID/Order #	
Comments			**HIV-1 Subtype:** B	

	Drug		GenoSure PRIme	Assessment*		Comments
	Generic Name	Brand Name	Drug Resistance Associated Mutations Detected	Drug		
NRTI	**Abacavir**	Ziagen	L74V, Y115F, M184V	**ABC**	Resistant	
	Didanosine	Videx	L74V, Y115F, M184V	**ddI**	Resistant	
	Emtricitabine	Emtriva	M184V	**FTC**	Resistant	
	Lamivudine	Epivir	M184V	**3TC**	Resistant	
	Stavudine	Zerit	None	**d4T**	Sensitive	1
	Tenofovir	Viread	Y115F	**TFV**	Sensitive	2
	Zidovudine	Retrovir	None	**ZDV**	Sensitive	2
NNRTI	**Efavirenz**	Sustiva	None	**EFV**	Sensitive	
	Etravirine	Intelence	None	**ETR**	Sensitive	
	Nevirapine	Viramune	None			
	Rilpivirine	Edurant	None			
INI	**Dolutegravir**	Tivicay	T97A, Y143R			
	Elvitegravir	Elvitegravir	T97A, Y143R			
	Raltegravir	Isentress	T97A, Y143R			
PI	**Atazanavir**	Reyataz	K20T, E35D, M46I, I84V			
		Reyataz / r	K20T, E35D, M46I, I84V			
	Darunavir	Prezista / r	K20T, M46I, I84V			
	Fosamprenavir	Lexiva / r	E35D, M46I, I84V			
	Indinavir	Crixivan / r	K20T, M46I, A71T, I84V			
	Lopinavir	Kaletra	K20T, M46I, A71T, I84V			
	Nelfinavir	Viracept	K20T, E35D, M46I, A71T, I84V			
	Ritonavir	Norvir	K20T, E35D, A71T, I84V			
	Saquinavir	Invirase / r	K20T, E35D, A71T, I84V			
	Tipranavir	Aptivus / r	K20T, E35D, I84V			

Provides an assessment of susceptibility: *sensitive, resistant,* or *resistance possible.*

A comprehensive summary of all mutations observed in each region is provided. This may be useful for tracking longitudinal changes and development of novel resistance mutations.

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Patient Name	DOB	Patient ID/Medical Record #	Gender	Monogram Accession #
Date Collected	Date Received	Date Reported	Mode	Report Status

* Assessment of drug susceptibility is based upon detected mutations and interpreted using an advanced proprietary algorithm (version 15).
‖ Interpretation algorithms for ritonavir-boosted protease inhibitors appropriate for the following dosages: AMP/r 600mg/100mg BID; ATV/r 300mg/100mg QD; IDV/r 800mg/200mg BID; LPV/r 400mg/100mg BID; SQV/r 1000mg/100mg BID; TPV/r 500mg/200mg BID; and DRV/r 600mg/100mg BID.
* **Mixtures** are indicated by amino acids separated by a slash. Deletions in the amino acid sequence are indicated by a ^ symbol.

Summary of Mutations Observed

RT	L74V, Q102K, Y115F, K122A, K166K/R, E169E/G, D177E, I178L, M184V, T200R, E203E/G, V245E, A272P, V293I, P294Q, E297K, Q334L, M357T, K358R, T377M, A400T
IN	L45Q, V72I, T97A, V113I, T124A, Y143R, V234L
PR	G16A, K20T, E35D, N37D, M46I, L63P, A71T, I72R, V77I, I84V, I93L

Genotype Comments (clinical significance may vary)

1	Assessment for this drug was derived considering the sensitizing effect of mutation M184V.
2	Assessment for this drug was derived considering the sensitizing effect of mutations L74V and M184V.

Assay Performance Characteristics

- Assay is highly reproducible and sufficiently sensitive enough to allow testing of patient samples with viral loads as low as ***500 copies/mL***.
- Detects ***mixtures*** of wild-type and drug-resistant viruses when present at levels as low as ***10% of the total population***.
- Provides sequence information for all of ***protease and integrase and through amino acids 400 of reverse transcriptase***.
- Uses Monogram's HIV genotyping algorithm, which is based on a large database of ***over 100,000 matched HIV genotype-phenotype results*** and is reviewed and updated on a regular basis.
- ***Includes HIV-1 subtype*** which provides information that can be important for long-term drug treatment strategy and genotype interpretation.

For more information on interpreting this report, please visit www.MonogramHIV.com or call Customer Service at 800-777-0177 between the hours of 6:30am to 5:00pm PT Monday through Friday.

GenoSure PRIme is a DNA sequence assay based on primer extension and chain termination that analyzes the protease (amino acids 1-99), reverse transcriptase (amino acids 1-400) and integrase (amino acids 1-288) coding regions in HIV-1. Subtype is determined using the protease and reverse transcriptase sequence information. This assay meets the standards for performance characteristics and all other quality control and assurance requirements established by the Clinical Laboratory Improvement Amendments. This test is validated for testing specimens with HIV-1 viral loads equal to or above 500 copies/mL and should be interpreted only on such specimens. The results should not be used as the sole criteria for patient management. The results have been disclosed to you from confidential records protected by law and are not to be disclosed to unauthorized persons. Further disclosure of these results is prohibited without specific consent of the persons to whom it pertains, or as permitted by law.

Summary

For Treatment-naïve Patients

DHHS panel recommendations include more than 20 drug combinations as initial treatment options for treatment-naïve patients.[1] These include members of the PI, NRTI, NNRTI, and INI classes of antiretrovirals.

For Treatment-experienced Patients

The management of patients on antiretroviral therapy is complex. As many as 20% of patients on antiretroviral therapy experience treatment failure due to drug resistance.[3]

GenoSure PRIme provides a complete picture of resistance to PIs, NRTIs, NNRTIs, and INIs to aid in selecting the optimal therapy for each patient.

Test Name	HIV-1 GenoSure PRIme
LabCorp Test Number	551700
Specimen Collection	5 mL plasma in a an EDTA or PPT tube, shipped frozen
Limitation	This procedure may not be successful when the HIV viral load is <500 copies/mL. If there is insufficient virus to produce results, HIV-1 RNA Quantitation will be performed to confirm viral load, resulting in a separate CPT code.

For full test information, visit LabCorp's online test menu at www.LabCorp.com/testmenu.

GenoSure PRIme is also available as a reflex from a quantitative viral load.

HIV-1, quantitative, real-time PCR (Graphical) With reflex to HIV-1 GenoSure PRIme 550630

HIV-1, quantitative, real-time PCR (Nongraphical) With reflex to HIV-1 GenoSure PRIme 550655

References

1. Panel on Antiretroviral Guidelines for Adults an Adolescents. Guidelines for the use of antiretroviral agents in HIV-1-infected adults and adolescents. Department of Health and Human Services. March 27, 2012;1-239. Available at: http://www.aidsinfo.nih.gov/ContentFiles/AdultandAdolescentGL.pdf. Accessed March 29, 2012.
2. Hurt CB. Transmitted resistance to HIV integrase strand-transfer inhibitors: right on schedule. *Antiviral Therapy.* 2011;16: 137-140.
3. World Health Organization. HIV drug resistance fact sheet. April 2011. Available at http://www.who.int/hiv/facts/drug_resistance/en/index.html. Accessed March 29, 2012.

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