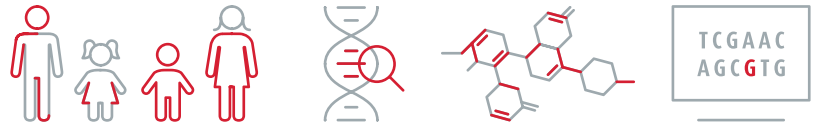


CentoMetabolic[®]



CentoMetabolic[®] – A one-test solution for all clinically relevant metabolic disorders

CENTOGENE is committed to developing innovative solutions to help end the diagnostic odyssey of patients suffering from rare genetic diseases. Our CentoMetabolic[®] panel has been designed to test a wide range of metabolic disorders. It integrates genetic and biochemical testing, including enzyme assays as well as a selection of proprietary biomarkers. When genetic variants relevant to your patient are detected in CentoMetabolic[®], we will automatically complement with biomarker and/or enzyme testing (if available) and include the results in your medical report.

CentoMetabolic[®] gives the confidence of a thorough evaluation for a potential metabolic diagnosis while simultaneously providing an opportunity to prove the consequences of the identified genetic variant.

Who should consider CentoMetabolic[®]?

Physicians providing treatment for patients matching any of the following criteria:

- Suspected metabolic disorder
- Metabolic crisis
- Babies with hypotonia
- Abnormal newborn screening results
- Admission to a neonatal intensive care unit (NICU), especially due to epilepsy of unclear origin and disturbed consciousness
- Symptoms related to neurological conditions of unknown etiology

What genes and disorders are targeted by CentoMetabolic[®]?

CentoMetabolic[®] targets more than 150 metabolic disorders. The content and design of the panel is based on our continuously enhanced medical expertise and knowledge in rare metabolic diseases.

The following table shows the distribution of genes and targeted metabolic disorders depending on 11 different disease categories.

TYPES OF METABOLIC DISORDERS COVERED	TARGETED DISORDERS	NUMBER OF GENES*
Disorders of Carbohydrate Metabolism	31	33
Disorders of Cholesterol and Lipoprotein Metabolism	29	31
Disorders of Amino and Organic Acid Metabolism	19	24
Disorders of Glycolipid and Glycoprotein Metabolism	18	17
Transmembrane Protein Defects	17	17
Peroxisomal Disorders	17	16
Porphyrias and Bilirubinemia	12	13
Disorders of Hormone Biogenesis or Function	6	6
Disorders of Nucleotide Metabolism	4	4
Disorders of Metal Metabolism and Transport	3	6
Disorders of Phosphate Metabolism	3	3

*Due to overlapping phenotypes, particular genes are listed in more than one category as they are associated with more than one disorder

CONTACT AND CUSTOMER SERVICE

Phone: +49 (0)381 80 113-416 Email: customer.support@centogene.com
 Fax: +49 (0)381 80 113-401 www.centogene.com

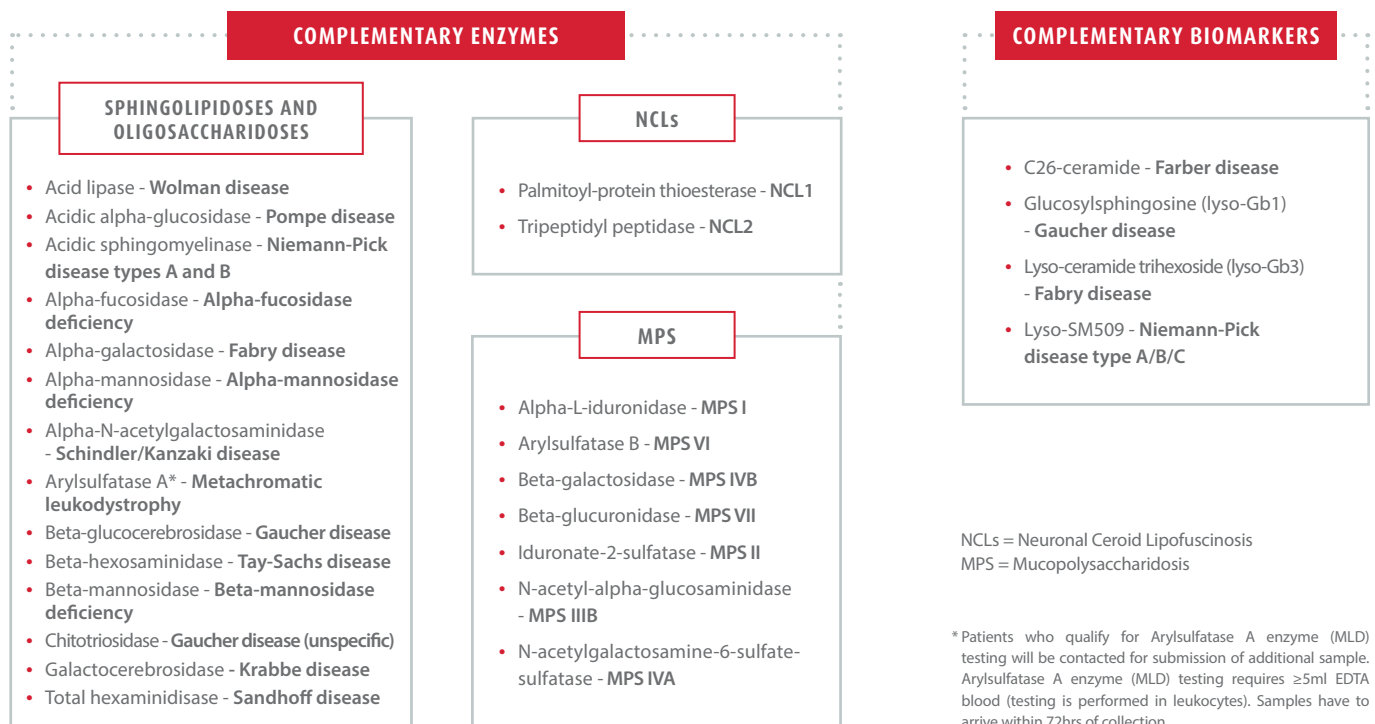
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Following GLP and
GMP guidelines.



CENTOGENE's biomarkers and enzyme testing

Biomarkers serve as measurable indicators of pathological processes. They are typically directly linked to genetic variants in specific genes and can predict, diagnose, monitor, and assess the severity of a disease. Measuring the cellular activity of an enzyme can also be used as a tool for the diagnosis and monitoring of a disease. Our multiomic- and big data-based approaches allow us to continuously discover new highly specific biomarkers. Any new biomarker will be included in this panel and represents an opportunity to advance our understanding of metabolic diseases as well as develop better tailored therapies for patients.



CentoMetabolic® - Key features

- Bidirectional next-generation sequencing of target regions of all genes in the panel, including coding regions and +/- 10 bp exon/intron boundaries
- All relevant deep intronic variants described in CentoMD® and HGMD® are included
- Coverage: ≥99.5% of targeted regions covered at ≥ 20x
- Low quality single nucleotide variants (SNVs) and all relevant deletion/insertion variants are confirmed by Sanger sequencing prior to reporting
- Fast and precise diagnostic with a TAT of 15 business days
- Specificity of >99.9% for all reported variants
- Our test combines genetic and biochemical testing for the widest range of rare metabolic diseases
- Complementary biochemical testing by proprietary biomarkers and enzyme-activity assays when applicable
- Required Material: 1 filter card

GENES INCLUDED

ABCA1, ABCC2, ABCD1, ABCD4, ADA, AGA, AGL, AGPS, ALAD, ALAS2, ALDOA, ALDOB, ALPL, APOA2, APOA5, APOB, APOC2, APOE, ARG1, ARSA, ARSB, ASAH1, ASL, ASS1, ATP7A, ATP7B, BCKDHA, BCKDHB, CBS, CETP, CLN3, CLN5, CLN6, CLN8, CPOX, CPS1, CTNS, CTS, CTSB, CTSK, CYP11B1, CYP17A1, CYP19A1, CYP21A2, DBT, DHCR7, ENO3, ENPP1, EPHX2, FECH, FGF23, FUCA1, G6PC, G6PD, GAA, GALC, GALE, GALK1, GALNS, GALT, GBA, GBE1, GHR, GK, GLA, GLB1, GM2A, GNPAT, GNPTAB, GNPTG, GNS, GUSB, GYG1, GYS2, HCFC1, HEXA, HEXB, HFE, HFE2, HGD, HGSNAT, HMBS, HPRT1, HSD3B2, HYAL1, IDS, IDUA, ITIH4, KHK, LAMP2, LCAT, LDHA, LDLR, LIPA, LIPI, LMBRD1, LPA, LPL, MAN2B1, MANBA, MCOLN1, MFSD8, MMACHC, MMADHC, NAGA, NAGLU, NAGS, NEU1, NPC1, NPC2, OTC, PAH, PEX1, PEX10, PEX12, PEX13, PEX14, PEX16, PEX19, PEX2, PEX26, PEX3, PEX5, PEX6, PEX7, PFKM, PGAM2, PGK1, PGM1, PHKA1, PHKA2, PHKB, PHKG2, PKLR, POR, PPOX, PPP1R17, PPT1, PRKAG2, PYGL, PYGM, RBCK1, SGSH, SLC17A5, SLC25A13, SLC25A15, SLC25A36, SLC2A1, SLC2A2, SLC2A3, SLC3A1, SLC3A2, SLC40A1, SLC6A19, SLC7A7, SLC7A9, SLC01B1, SLC01B3, SMPD1, SUMF1, TFR2, TPP1, UGT1A1, UMPS, UROD, UROS