

Policy

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Purpose

This policy outlines the coverage criteria for pharmacogenetic testing. Pharmacogenetic testing is a type of genetic analysis that examines how an individual's genes may influence their response to medications. It aims to identify genetic variations that can affect how a person metabolizes, absorbs, or reacts to specific drugs. This policy outlines the medical necessity criteria for these services.

Definitions, Abbreviations, and Acronyms

Acronym	Meaning
LCD	Local Coverage Determination
NCD	National Coverage Determination
CPIC	Clinical Pharmacogenetics Implementation Consortium

Policy

Longevity Health requires prior authorization for all pharmacogenetic testing. This serves as accompanying guidance to the existing NCDs and LCDs.

Clinical Indications

In order to be considered for this pharmacogenetic testing, the member must have a diagnosis and an accompanying proposed or existing medication regimen on which this testing is focused. The clinical records must include the member's diagnosis as well as the drug for which testing is being requested.

Coverage Criteria

Section 1862(a) (1) (A) of the Social Security Act directs the following:

“No payment may be made under Part A or Part B for any expenses incurred for items or services not reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member.”

Also, it is required that the service meets, but does not exceed, the beneficiary's medical need.

As such, one of the following must be demonstrated in the clinical record accompanying the prior authorization request to be considered medically necessary:

- Demonstrated therapeutic failure of existing/prior pharmacological treatment that was prescribed in alignment with normal standards of care.
- Documented side effects with possible association to an existing treatment plan. Side effects must be reasonably associated with the medication for this condition to apply.

If a member is currently being treated with a medication for a condition, the existence of the diagnosis and provision of medication alone is insufficient to justify medical necessity. If the above criteria is not met, the pharmacogenetic testing would be exceeding the beneficiary's medical need and therefore not covered based on the language in Section 1862(a) (1) (A) of the Social Security Act.

To demonstrate the medical necessity as outlined above, clinical records with dates of service within 90 days prior to authorization request must be provided. This should include a clinical encounter from the ordering provider with information surrounding the history of the chronic condition, medication therapy attempted and response, and note of any therapeutic failure or side effects that may be relevant to the test ordered.

Covered Services

Longevity Health, in alignment with Section 1862(a) (1) (A) of the Social Security Act, does not consider investigational or experimental tests to be medically necessary. Longevity Health relies on the guidance from the Clinical Pharmacogenetics Implementation Consortium (CPIC) who, based on available research, provides recommendations for utilization of pharmacogenetic lab testing. The CPIC assigns levels to available tests. Level A and B gene/drug pairs have sufficient evidence for at least one prescribing action to be recommended. CPIC level C and D gene/drug pairs are not considered to have adequate evidence or actionability to have prescribing recommendations. Based on this, Longevity Health will only consider tests assigned a level A or B by the CPIC to be appropriate for use.

Gene	Drug	CPIC Level
HLA-B	abacavir	A
HLA-B	allopurinol	A
MT-RNR1	amikacin	A
CYP2C19	amitriptyline	A
CYP2D6	amitriptyline	A

UGT1A1	atazanavir	A
CYP2D6	atomoxetine	A
SLCO1B1	atorvastatin	A
NUDT15	azathioprine	A
TPMT	azathioprine	A
DPYD	capecitabine	A
HLA-A	carbamazepine	A
HLA-B	carbamazepine	A
CYP2C9	celecoxib	A
CYP2C19	citalopram	A
CYP2C19	clopidogrel	A
CYP2D6	codeine	A
G6PD	dapsone	A
CACNA1S	desflurane	A
RYR1	desflurane	A
MT-RNR1	dibekacine	A
CYP2B6	efavirenz	A
CACNA1S	enflurane	A
RYR1	enflurane	A
CYP2C19	escitalopram	A
DPYD	fluorouracil	A
CYP2C9	flurbiprofen	A
CYP2C9	fluvastatin	A
SLCO1B1	fluvastatin	A
CYP2C9	fosphenytoin	A
HLA-B	fosphenytoin	A
MT-RNR1	gentamicin	A
CACNA1S	halothane	A
RYR1	halothane	A
CYP2C9	ibuprofen	A
UGT1A1	irinotecan	A
CACNA1S	isoflurane	A
RYR1	isoflurane	A
CFTR	ivacaftor	A
MT-RNR1	kanamycin	A
CYP2C19	lansoprazole	A

CYP2C9	lornoxicam	A
SLCO1B1	lovastatin	A
CYP2C9	meloxicam	A
NUDT15	mercaptopurine	A
TPMT	mercaptopurine	A
CACNA1S	methoxyflurane	A
RYR1	methoxyflurane	A
G6PD	methylene blue	A
MT-RNR1	neomycin	A
MT-RNR1	netilmicin	A
G6PD	nitrofurantoin	A
CYP2D6	nortriptyline	A
CYP2C19	omeprazole	A
CYP2D6	ondansetron	A
HLA-B	oxcarbazepine	A
CYP2C19	pantoprazole	A
MT-RNR1	paromomycin	A
CYP2D6	paroxetine	A
IFNL3	peginterferon alfa-2a	A
IFNL4	peginterferon alfa-2a	A
IFNL3	peginterferon alfa-2b	A
IFNL4	peginterferon alfa-2b	A
G6PD	pegloticase	A
CYP2C9	phenytoin	A
HLA-B	phenytoin	A
CYP2C9	piroxicam	A
SLCO1B1	pitavastatin	A
CYP2D6	pitolisant	A
MT-RNR1	plazomicin	A
SLCO1B1	pravastatin	A
G6PD	primaquine	A
G6PD	rasburicase	A
MT-RNR1	ribostamycin	A
ABCG2	rosuvastatin	A
SLCO1B1	rosuvastatin	A
CYP2C19	sertraline	A

CACNA1S	sevoflurane	A
RYR1	sevoflurane	A
SLCO1B1	simvastatin	A
CYP2C9	siponimod	A
MT-RNR1	streptomycin	A
CACNA1S	succinylcholine	A
RYR1	succinylcholine	A
CYP3A5	tacrolimus	A
G6PD	tafenoquine	A
CYP2D6	tamoxifen	A
CYP2C9	tenoxicam	A
NUDT15	thioguanine	A
TPMT	thioguanine	A
MT-RNR1	tobramycin	A
G6PD	toluidine blue	A
CYP2D6	tramadol	A
CYP2D6	tropisetron	A
CYP2C19	voriconazole	A
CYP2D6	vortioxetine	A
CYP2C9	warfarin	A
CYP4F2	warfarin	A
VKORC1	warfarin	A
POLG	divalproex sodium	A/B
CYP2D6	eliglustat	A/B
NAT2	hydralazine	A/B
CYP2D6	oliceridine	A/B
CYP2D6	pimozide	A/B
CYP2D6	tetrabenazine	A/B
POLG	valproic acid	A/B
GBA	velaglucerase alfa	A/B
CYP2C9	acenocoumarol	B
CYP4F2	acenocoumarol	B
CYP2D6	aripiprazole	B
UGT1A1	belinostat	B
CYP2C19	brivaracetam	B
SCN1A	carbamazepine	B

NAGS	carglumic acid	B
CYP2C19	clomipramine	B
CYP2D6	clomipramine	B
CYP2D6	desipramine	B
CYP2C19	dexlansoprazole	B
CYP2C19	doxepin	B
CYP2D6	doxepin	B
CYP2D6	fluvoxamine	B
CYP2D6	hydrocodone	B
CYP2C19	imipramine	B
CYP2D6	imipramine	B
CYP2D6	metoprolol	B
HPRT1	mycophenolic acid	B
CYP4F2	phenprocoumon	B
SCN1A	phenytoin	B
CYP2D6	risperidone	B
CYP2B6	sertraline	B
CYP2C19	trimipramine	B
CYP2D6	trimipramine	B
ABL2	valproic acid	B
ASL	valproic acid	B
ASS1	valproic acid	B
CPS1	valproic acid	B
NAGS	valproic acid	B
OTC	valproic acid	B
CYP2D6	venlafaxine	B
HLA-A	allopurinol	B/C
NAT2	amifampridine	B/C
NAT2	amifampridine phosphate	B/C
CYP2D6	amoxapine	B/C
CYP2D6	amphetamine	B/C
CYP2D6	aripiprazole lauroxil	B/C
CYP2C9	avatrombopag	B/C
CYP2D6	brexpiprazole	B/C
ADRB1	bucindolol	B/C
CYP2B6	bupropion	B/C

CYP2C19	carisoprodol	B/C
CYP2D6	cevimeline	B/C
CYP2C19	clobazam	B/C
CYP2D6	clozapine	B/C
SLC28A3	daunorubicin	B/C
CYP2D6	deutetabenazine	B/C
CYP2D6	dextromethorphan	B/C
CYP2C19	diazepam	B/C
UGT1A1	dolutegravir	B/C
CYP2D6	donepezil	B/C
SLC28A3	doxorubicin	B/C
CYP2C9	dronabinol	B/C
SLCO1B1	elagolix	B/C
CYP2C9	erdafitinib	B/C
CYP2D6	flecainide	B/C
CYP2D6	gefitinib	B/C
CYP2D6	haloperidol	B/C
CYP2D6	iloperidone	B/C
CYP2D6	labetalol	B/C
HLA-DRB1	lapatinib	B/C
CYP2C9	lesinurad	B/C
G6PD	lidocaine	B/C
MTHFR	l-methylfolate	B/C
CYP2D6	lofexidine	B/C
CYP2D6	meclizine	B/C
CYP2D6	metoclopramide	B/C
CYP2D6	mirabegron	B/C
CYP2D6	mirtazapine	B/C
BCHE	mivacurium	B/C
CYP2B6	nevirapine	B/C
UGT1A1	nilotinib	B/C
HLA-B	pazopanib	B/C
UGT1A1	pazopanib	B/C
CYP2D6	perphenazine	B/C
NAT2	procainamide	B/C
CYP2D6	propafenone	B/C

CYP2D6	protriptyline	B/C
UGT1A1	raltegravir	B/C
BCHE	succinylcholine	B/C
NAT2	sulfamethoxazole / trimethoprim	B/C
NAT2	sulfasalazine	B/C
CYP2D6	tamsulosin	B/C
CYP2D6	thioridazine	B/C
CYP2D6	timolol	B/C
CYP2D6	valbenazine	B/C
CYP2D6	zuclopentixol	B/C
ADRA2C	acebutolol	C
ADRB1	acebutolol	C
CYP2D6	acebutolol	C
GRK4	acebutolol	C
GRK5	acebutolol	C
CYP2C9	aceclofenac	C
TNF	adalimumab	C
COMT	alfentanil	C
OPRM1	alfentanil	C
HLA-C	allopurinol	C
G6PD	aminosalicylic acid	C
MC4R	amisulpride	C
MC4R	aripiprazole	C
CYP2C9	aspirin	C
G6PD	aspirin	C
HLA-DPB1	aspirin	C
CFTR	ataluren	C
ADRA2C	atenolol	C
ADRB1	atenolol	C
GRK4	atenolol	C
GRK5	atenolol	C
CYP3A4	atorvastatin	C
CYP3A5	atorvastatin	C
HMGCR	atorvastatin	C
ADRA2C	betaxolol	C
ADRB1	betaxolol	C

CYP2D6	betaxolol	C
GRK4	betaxolol	C
GRK5	betaxolol	C
ADRA2C	bisoprolol	C
ADRB1	bisoprolol	C
CYP2D6	bisoprolol	C
GRK4	bisoprolol	C
GRK5	bisoprolol	C
COMT	buprenorphine	C
OPRM1	buprenorphine	C
HLA-B	carbimazole	C
MTHFR	carboplatin	C
ADRA2C	carvedilol	C
ADRB1	carvedilol	C
ADRB2	carvedilol	C
CYP2D6	carvedilol	C
GRK4	carvedilol	C
GRK5	carvedilol	C
G6PD	chloramphenicol	C
G6PD	chloroquine	C
G6PD	chlorpropamide	C
G6PD	ciprofloxacin	C
COMT	citalopram	C
CYP2D6	citalopram	C
GRIK4	citalopram	C
HTR2A	citalopram	C
SLC6A4	citalopram	C
CES1	clopidogrel	C
HTR2C	clozapine	C
MC4R	clozapine	C
COMT	codeine	C
OPRM1	codeine	C
CYP3A5	cyclosporine	C
G6PD	dabrafenib	C
HLA-B	dapsone	C
CYP2D6	darifenacin	C

HTR2A	desvenlafaxine	C
SLC6A4	desvenlafaxine	C
CYP2C8	diclofenac	C
CYP2C9	diclofenac	C
ABCB1	digoxin	C
G6PD	dimercaprol	C
CYP2D6	dolasetron	C
G6PD	doxorubicin	C
CYP2C19	duloxetine	C
CYP2D6	duloxetine	C
HTR2A	duloxetine	C
SLC6A4	duloxetine	C
F5	eltrombopag	C
COMT	escitalopram	C
CYP2D6	escitalopram	C
GRIK4	escitalopram	C
HTR2A	escitalopram	C
SLC6A4	escitalopram	C
ADRA2C	esmolol	C
ADRB1	esmolol	C
GRK4	esmolol	C
GRK5	esmolol	C
CYP2C19	esomeprazole	C
TNF	etanercept	C
ABCB1	fentanyl	C
COMT	fentanyl	C
OPRM1	fentanyl	C
CYP2D6	fesoterodine	C
CYP2C19	flibanserin	C
CYP2C9	flibanserin	C
CYP2D6	flibanserin	C
CYP2C19	fluoxetine	C
CYP2D6	fluoxetine	C
GRIK4	fluoxetine	C
HTR2A	fluoxetine	C
SLC6A4	fluoxetine	C

CYP3A4	fluvastatin	C
CYP3A5	fluvastatin	C
HMGCR	fluvastatin	C
CYP2C19	fluvoxamine	C
HTR2A	fluvoxamine	C
SLC6A4	fluvoxamine	C
G6PD	furazolidone	C
CYP2D6	galantamine	C
G6PD	gliclazide	C
G6PD	glimepiride	C
G6PD	glipizide	C
G6PD	glyburide	C
MC4R	haloperidol	C
F5	hormonal contraceptives for systemic use	C
COMT	hydrocodone	C
OPRM1	hydrocodone	C
COMT	hydromorphone	C
OPRM1	hydromorphone	C
G6PD	hydroxychloroquine	C
CYP2C8	ibuprofen	C
CYP2C9	indomethacin	C
TNF	infliximab	C
NAT2	isoniazid	C
ADRA2C	labetalol	C
ADRB1	labetalol	C
ADRB2	labetalol	C
GRK4	labetalol	C
GRK5	labetalol	C
HLA-DQA1	lapatinib	C
COMT	levomethadone	C
OPRM1	levomethadone	C
HTR2A	levomilnacipran	C
SLC6A4	levomilnacipran	C
CYP3A4	lovastatin	C
CYP3A5	lovastatin	C
HMGCR	lovastatin	C

CYP2C9	lumiracoxib	C
G6PD	mafenide	C
G6PD	mepacrine	C
G6PD	mesalazine	C
COMT	methadone	C
CYP2B6	methadone	C
CYP2D6	methadone	C
OPRM1	methadone	C
HLA-B	methazolamide	C
HLA-C	methazolamide	C
HLA-B	methimazole	C
ABCB1	methotrexate	C
MTHFR	methotrexate	C
SLCO1B1	methotrexate	C
CYP2D6	methylphenidate	C
ADRA2C	metoprolol	C
ADRB1	metoprolol	C
GRK4	metoprolol	C
GRK5	metoprolol	C
HTR2A	milnacipran	C
SLC6A4	milnacipran	C
CYP2D6	modafinil	C
COMT	morphine	C
OPRM1	morphine	C
G6PD	moxifloxacin	C
CYP2C9	nabumetone	C
ADRA2C	nadolol	C
ADRB1	nadolol	C
ADRB2	nadolol	C
GRK4	nadolol	C
GRK5	nadolol	C
G6PD	nalidixic acid	C
OPRM1	naloxone	C
COMT	naltrexone	C
OPRM1	naltrexone	C
CYP2C9	naproxen	C

ADRA2C	nebivolol	C
ADRB1	nebivolol	C
CYP2D6	nebivolol	C
GRK4	nebivolol	C
GRK5	nebivolol	C
ABCB1	nevirapine	C
HLA-B	nevirapine	C
HLA-DRB1	nevirapine	C
G6PD	nicorandil	C
G6PD	nitrofural	C
G6PD	norfloxacin	C
G6PD	ofloxacin	C
HTR2C	olanzapine	C
MC4R	olanzapine	C
HLA-A	oxcarbazepine	C
COMT	oxycodone	C
CYP2D6	oxycodone	C
OPRM1	oxycodone	C
MC4R	paliperidone	C
CYP2D6	palonosetron	C
CYP2C19	paroxetine	C
GRIK4	paroxetine	C
HTR2A	paroxetine	C
SLC6A4	paroxetine	C
G6PD	phenazopyridine	C
ADRA2C	pindolol	C
ADRB1	pindolol	C
ADRB2	pindolol	C
GRK4	pindolol	C
GRK5	pindolol	C
CYP3A4	pitavastatin	C
CYP3A5	pitavastatin	C
HMGCR	pitavastatin	C
CYP3A4	pravastatin	C
CYP3A5	pravastatin	C
G6PD	probenecid	C

ADRA2C	propranolol	C
ADRB1	propranolol	C
ADRB2	propranolol	C
CYP2D6	propranolol	C
GRK4	propranolol	C
GRK5	propranolol	C
HLA-B	propylthiouracil	C
MC4R	quetiapine	C
CYP2D6	quinidine	C
CYP2D6	quinine	C
G6PD	quinine	C
CYP2C19	rabeprazole	C
COMT	remifentanil	C
OPRM1	remifentanil	C
DRD2	risperidone	C
HTR2C	risperidone	C
MC4R	risperidone	C
CYP2C8	rosiglitazone	C
CYP3A4	rosuvastatin	C
CYP3A5	rosuvastatin	C
HMGCR	rosuvastatin	C
CYP2D6	sertraline	C
GRIK4	sertraline	C
HTR2A	sertraline	C
SLC6A4	sertraline	C
ABCB1	simvastatin	C
CYP3A4	simvastatin	C
CYP3A5	simvastatin	C
CYP3A5	sirolimus	C
G6PD	sodium nitrite	C
ADRA2C	sotalol	C
ADRB1	sotalol	C
ADRB2	sotalol	C
GRK4	sotalol	C
GRK5	sotalol	C
COMT	sufentanil	C

OPRM1	sufentanil	C
G6PD	sulfacetamide	C
G6PD	sulfadiazine	C
G6PD	sulfadimidine	C
G6PD	sulfamethoxazole / trimethoprim	C
G6PD	sulfanilamide	C
G6PD	sulfasalazine	C
G6PD	sulfisoxazole	C
CYP3A4	tacrolimus	C
DYPD	tegafur	C
CYP2D6	terbinafine	C
G6PD	tolazamide	C
G6PD	tolbutamide	C
CYP2D6	tolterodine	C
COMT	tramadol	C
OPRM1	tramadol	C
G6PD	trametinib	C
CYP2C19	venlafaxine	C
GRIK4	venlafaxine	C
HTR2A	venlafaxine	C
SLC6A4	venlafaxine	C
HTR2A	vilazodone	C
SLC6A4	vilazodone	C
G6PD	vitamin c	C
G6PD	vitamin k	C
CYP2C19	vortioxetine	C
HTR2A	vortioxetine	C
SLC6A4	vortioxetine	C
MC4R	ziprasidone	C
ITPA	interferon alfa-2b, recombinant	C/D
CYP3A5	midazolam	C/D
COMT	nicotine	C/D
ABCB1	ondansetron	C/D
UGT2B15	oxazepam	C/D
FDPS	alendronate	D
GP1BA	aspirin	D

LTC4S	aspirin	D
PTGS1	aspirin	D
APOE	atorvastatin	D
CETP	atorvastatin	D
COQ2	atorvastatin	D
KIF6	atorvastatin	D
LDLR	atorvastatin	D
LPA	atorvastatin	D
CRHR1	budesonide	D
ADORA2A	caffeine	D
TYMS	capecitabine	D
ACE	captopril	D
EPHX1	carbamazepine	D
CETP	cerivastatin	D
LPA	cerivastatin	D
EGF	cetuximab	D
ACYP2	cisplatin	D
ERCC1	cisplatin	D
GSTM1	cisplatin	D
NQO1	cisplatin	D
XPC	cisplatin	D
FKBP5	citalopram	D
ANKK1	clozapine	D
GSTP1	cyclophosphamide	D
NQO1	cyclophosphamide	D
SOD2	cyclophosphamide	D
CBR3	daunorubicin	D
HAS3	daunorubicin	D
CBR3	doxorubicin	D
HAS3	doxorubicin	D
NQO1	doxorubicin	D
SERPINC1	eltrombopag	D
CBR3	epirubicin	D
GSTP1	epirubicin	D
HAS3	epirubicin	D
NQO1	epirubicin	D

DYNC2H1	etoposide	D
GSTP1	fluorouracil	D
NQO1	fluorouracil	D
TYMS	fluorouracil	D
UMPS	fluorouracil	D
FKBP5	fluoxetine	D
CRHR1	fluticasone propionate	D
CRHR1	fluticasone/salmeterol	D
CETP	fluvastatin	D
LPA	fluvastatin	D
ADD1	furosemide	D
NT5C2	gemcitabine	D
NEDD4L	hydrochlorothiazide	D
PRKCA	hydrochlorothiazide	D
YEATS4	hydrochlorothiazide	D
CBR3	idarubicin	D
HAS3	idarubicin	D
C8orf34	irinotecan	D
SEMA3C	irinotecan	D
UGT1A4	lamotrigine	D
PTGFR	latanoprost	D
C11orf65	metformin	D
ATIC	methotrexate	D
MTRR	methotrexate	D
CYB5R1	metoclopramide	D
CYB5R2	metoclopramide	D
CYB5R3	metoclopramide	D
CYB5R4	metoclopramide	D
FKBP5	mirtazapine	D
CCHCR1	nevirapine	D
CHRNA3	nicotine	D
ANKK1	olanzapine	D
GSTM1	oxaliplatin	D
GSTP1	oxaliplatin	D
FKBP5	paroxetine	D
HTR1A	paroxetine	D

VDR	peginterferon alfa-2b	D
CETP	pravastatin	D
HMGCR	pravastatin	D
KIF6	pravastatin	D
LPA	pravastatin	D
FDPS	raloxifene	D
VDR	ribavirin	D
FDPS	risedronate	D
ANKK1	risperidone	D
FCGR3A	rituximab	D
COQ2	rosuvastatin	D
LPA	rosuvastatin	D
ADRB2	salbutamol	D
COL22A1	salbutamol	D
CRHR2	salbutamol	D
ADRB2	salmeterol	D
GNB3	sildenafil	D
CETP	simvastatin	D
HMGCR	simvastatin	D
LPA	simvastatin	D
ADD1	spironolactone	D
ABCC4	tenofovir	D
CRHR1	triamcinolone	D
FKBP5	venlafaxine	D
CALU	warfarin	D
GGCX	warfarin	D
PROC	warfarin	D
PROS1	warfarin	D

Change Log

Document Version	Major or Minor Revision?	Date	Name	Comments
1.0	New	02/22/2025	Stefanie Caswell	New