BIODECODE | İstanbul Genetik Grubu

Neuropsychiatry panel

Pharmacogenomic Report

67 gene regions and 49 active substances; according to CPIC, DPWG and FDA guidelines.

Name	Date of birth / sex	Requesting physician	Report date
			18 Nov 2026
Protocol / sample	**National ID no.**	**Specimen type**	**Specimen received**
		Peripheral blood (K3-EDTA)	

Sequencing ID ORNEK_L01_00 Panel Twist BIODECODE PGx V2

Result

The genotype changes the treatment decision for **16 of 49** active substances.

Recommendations (p. 5) are given in the guideline's own wording.

7	✕ **Alternative drug** Choose another drug	amitriptyline, clomipramine, doxepin and 4 more (p. 5)	3 genes
9	▲ **Dose adjustment** Adjust the dose	desipramine, nortriptyline, paroxetine and 6 more (p. 5)	CYP2D6 · CYP2C9
3	◆ **Standard start, monitor** Monitor response	citalopram, escitalopram, sertraline	CYP2C19 · CYP2B6
30	● **Standard use** No change needed	Genotype requires no change; full list in the drug guide (p. 2).	

≠ Guidelines diverge For 2 active substances the followed guideline advises no change; another authority defines one (p. 10).

Genotype

enzymes that determine the verdicts; all (p. 19)

CYP2B6	CYP2C19	CYP2C9	CYP2D6	CYP3A4
***4/*5**	***17/*38**	***1/*3**	***2/*4**	***1/*1**
Rapid	**Rapid**	**Intermediate** AS 1.0	**Intermediate** AS 1.0	Normal

Basis of this result

Seven analyses were assessed together.

67 gene regions	67 regions	10 genes with altered function.	(p. 19)
Exon and intron reading	whole gene	Whole-gene reading; 2 genes not readable.	(p. 19)
Loss-of-function screening	54 variants	ACMG-based screening; no finding to report.	(p. 18)
HLA analysis	5 / 5 negative	HLA-A and HLA-B typed; no risk allele detected.	(p. 15)
CYP2D6 confirmation	3 algorithms	2 independent algorithms agree; confirmation advised.	(p. 15)
CPIC, DPWG and FDA	19 active substances	Recommendations in the guidelines' own wording.	(p. 5)
Phenoconversion	4 active substances	If added, other recommendations change; ask first.	(p. 17)

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A clinical decision-support tool; to be interpreted together with the diagnosis, history, concomitant drugs and the physician's judgment. For research use · not IVD-approved.

Clinical section

Drug guide

49 active substances: use in this patient, by drug class. The mark tells you what to do.

Antidepressants

19 active substances

✕ **Alternative drug**	amitriptyline≠, clomipramine≠, doxepin≠, imipramine≠, trimipramine	CYP2C19, CYP2D6
▲ **Dose adjustment**	desipramine, nortriptyline, paroxetine≠	CYP2D6
◆ **Standard start, monitor**	citalopram, escitalopram	CYP2C19
	sertraline	CYP2B6, CYP2C19
● **Standard use**	amoxapine, bupropion, fluoxetine, fluvoxamine≠, mirtazapine, protriptyline, venlafaxine≠, vortioxetine	

Antipsychotics

12 active substances

✕ **Alternative drug**	thioridazine	CYP2D6
▲ **Dose adjustment**	pimozide, zuclopenthixol	CYP2D6
● **Standard use**	aripiprazole, aripiprazole lauroxil, brexpiprazole, clozapine, haloperidol, iloperidone, perphenazine, quetiapine, risperidone	

Antiepileptics and anxiolytics

8 active substances

▲ **Dose adjustment**	fosphenytoin≠, phenytoin≠	CYP2C9
● **Standard use**	brivaracetam, carbamazepine, clobazam, diazepam, lamotrigine, oxcarbazepine	

ADHD and addiction treatment

3 active substances

▲ **Dose adjustment**	atomoxetine	CYP2D6
● **Standard use**	amphetamine, lofexidine	

Neurology, other

7 active substances

✕ **Alternative drug**	siponimod≠	CYP2C9
▲ **Dose adjustment**	tetrabenazine	CYP2D6

Clinical section

Drug guide cont.

Standard use	deutetrabenazine, donepezil, galantamine, pitolisant, valbenazine

≠ Guidelines diverge; views in the drug recommendations (p. 10). Guideline texts for the 19 active substances with a recommendation (p. 5). Alphabetical list of all active substances (p. 4). Not in this guide: 13 active substances without a pharmacogenetic guideline. Names are active substance names; brand names are not used.

Clinical section

Drug list

All 49 active substances in the panel, alphabetically; each row gives the verdict and its determining gene.

≠ Active substance on which guidelines diverge (p. 10). Recommendation texts (p. 5). The Gene column shows the gene behind the verdict; gene results for this sample (p. 19).

Active substance	Verdict	Gene
✕ Amitriptyline≠	Alternative drug	CYP2C19, CYP2D6
● Amoxapine	Standard use	CYP2D6
● Amphetamine	Standard use	CYP2D6
● Aripiprazole	Standard use	CYP2D6
● Aripiprazole Lauroxil	Standard use	CYP2D6
▲ Atomoxetine	Dose adjustment	CYP2D6
● Brexpiprazole	Standard use	CYP2D6
● Brivaracetam	Standard use	CYP2C19
● Bupropion	Standard use	CYP2B6
● Carbamazepine	Standard use	HLA-A, HLA-B, SCN1A
◆ Citalopram	Standard start, monitor	CYP2C19
● Clobazam	Standard use	CYP2C19
✕ Clomipramine≠	Alternative drug	CYP2C19, CYP2D6
● Clozapine	Standard use	CYP2D6
▲ Desipramine	Dose adjustment	CYP2D6
● Deutetrabenazine	Standard use	CYP2D6
● Diazepam	Standard use	CYP2C19
● Donepezil	Standard use	CYP2D6
✕ Doxepin≠	Alternative drug	CYP2C19, CYP2D6
◆ Escitalopram	Standard start, monitor	CYP2C19
● Fluoxetine	Standard use	CYP2D6
● Fluvoxamine≠	Standard use	CYP2D6
▲ Fosphenytoin≠	Dose adjustment	CYP2C9

Active substance	Verdict	Gene
● Galantamine	Standard use	CYP2D6
● Haloperidol	Standard use	CYP2D6
● Iloperidone	Standard use	CYP2D6
✕ Imipramine≠	Alternative drug	CYP2C19, CYP2D6
● Lamotrigine	Standard use	HLA-B
● Lofexidine	Standard use	CYP2D6
● Mirtazapine	Standard use	CYP2D6
▲ Nortriptyline	Dose adjustment	CYP2D6
● Oxcarbazepine	Standard use	HLA-B
▲ Paroxetine≠	Dose adjustment	CYP2D6
● Perphenazine	Standard use	CYP2D6
▲ Phenytoin≠	Dose adjustment	CYP2C9
▲ Pimozide	Dose adjustment	CYP2D6
● Pitolisant	Standard use	CYP2D6
● Protriptyline	Standard use	CYP2D6
● Quetiapine	Standard use	CYP3A4
● Risperidone	Standard use	CYP2D6
◆ Sertraline	Standard start, monitor	CYP2B6, CYP2C19
✕ Siponimod≠	Alternative drug	CYP2C9
▲ Tetrabenazine	Dose adjustment	CYP2D6
✕ Thioridazine	Alternative drug	CYP2D6
✕ Trimipramine	Alternative drug	CYP2C19, CYP2D6
● Valbenazine	Standard use	CYP2D6
● Venlafaxine≠	Standard use	CYP2D6
● Vortioxetine	Standard use	CYP2D6
▲ Zuclopenthixol	Dose adjustment	CYP2D6

Clinical section

Drug recommendations

19 active substances with a guideline recommendation. Each row is the named guideline's own recommendation; its strength is on the right.

✖ Alternative drug

7 active substances

Amitriptyline CYP2C19 rapid CYP2D6 intermediate CPIC guideline · PMID 27997040	CPIC	**CYP2C19 · CYP2D6:** Consider alternative drug not metabolized by CYP2C19; If amitriptyline is warranted, utilize therapeutic drug monitoring to guide dose adjustment. Utilizing therapeutic drug monitoring to guide dose adjustments is strongly recommended.	optional
	DPWG	**CYP2D6:** Use 75% of the standard dose and monitor the efficacy and side effects or the plasma concentrations of amitriptyline and nortriptyline in order to set the maintenance dose	
Clomipramine CYP2C19 rapid CYP2D6 intermediate CPIC guideline · PMID 27997040	CPIC	**CYP2C19 · CYP2D6:** Consider alternative drug not metabolized by CYP2C19; If clomipramine is warranted, utilize therapeutic drug monitoring to guide dose adjustment. Utilizing therapeutic drug monitoring to guide dose adjustments is strongly recommended.	optional
	DPWG	**CYP2D6:** Use 70% of the standard dose and monitor the effect and side effects or the plasma concentrations of clomipramine and desmethylclomipramine.	
Doxepin CYP2C19 rapid CYP2D6 intermediate CPIC guideline · PMID 27997040	CPIC	**CYP2C19 · CYP2D6:** Consider alternative drug not metabolized by CYP2C19; If doxepin is warranted, utilize therapeutic drug monitoring to guide dose adjustment. Utilizing therapeutic drug monitoring to guide dose adjustments is strongly recommended.	optional
	DPWG	**CYP2D6:** Use 80% of the standard dose and monitor the effect and side effects or the plasma concentrations of doxepin and nordoxepin in order to set the maintenance dose.	
Imipramine CYP2C19 rapid CYP2D6 intermediate CPIC guideline · PMID 27997040	CPIC	**CYP2C19 · CYP2D6:** Consider alternative drug not metabolized by CYP2C19; If imipramine is warranted, utilize therapeutic drug monitoring to guide dose adjustment. Utilizing therapeutic drug monitoring to guide dose adjustments is strongly recommended.	optional
	DPWG	**CYP2D6:** Use 70% of the standard dose and monitor the effect and side effects or the plasma concentrations of imipramine and desipramine in order to set the maintenance dose.	

Clinical section

Drug recommendations cont.

Siponimod
CYP2C9
DPWG guideline

FDA: CYP2C9 genotyping is required before starting treatment · CYP2C9 — this patient's CYP2C9 result is available in this report

DPWG Use 50% of the normal maintenance dose. Reconsider the choice and the potential benefit of siponimod if the patient is also using a moderate CYP3A4 inducer, such as modafinil, or a strong CYP3A4 inducer. For this gene variation, a moderate or strong CYP3A4 inducer results in a reduction in the exposure of siponimod by 49%, according to a pharmacokinetic model.

FDA The MAYZENT (siponimod) label states: "Initiate MAYZENT with a 4-day titration, as shown in Table 2... Do not use the starter pack for patients who will be titrated to the 1-mg maintenance dosage." "In patients with a CYP2C9 *1/*3 or *2/*3 genotype, after treatment titration (see Treatment Initiation), the recommended maintenance dosage of MAYZENT is 1 mg taken orally once daily starting on Day 5." See label for more information. *

Basis — CYP2C9 — FDA labeling contains a genetic testing requirement; there is no published CPIC guideline

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Thioridazine
CYP2D6
FDA labeling

FDA "...thioridazine is contraindicated...in patients, comprising about 7% of the normal population, who are known to have a genetic defect leading to reduced levels of activity of P450 2D6." See label for more information. *

Trimipramine
CYP2C19 rapid
CYP2D6 intermediate
CPIC guideline · PMID 27997040

CPIC Consider alternative drug not metabolized by CYP2C19; If trimipramine is warranted, utilize therapeutic drug monitoring to guide dose adjustment. Utilizing therapeutic drug monitoring to guide dose adjustments is strongly recommended.

optional

▲ Dose adjustment

9 active substances

Atomoxetine
CYP2D6 intermediate
CPIC guideline · PMID 30801677

CPIC **Adults:** Initiate with a dose of 40 mg/day and increase to 80 mg/day after 3 days. If no clinical response and in the absence of adverse events after 2 weeks, consider increasing dose to 100 mg/day. If no clinical response observed after 2 weeks, consider obtaining a peak plasma concentration (1 to 2 hours after dose administered). If <200 ng/mL, consider a proportional increase in dose to approach 400 ng/mL. Dosages greater than 100 mg/day may be needed to achieve target concentrations.

moderate

Clinical section

Drug recommendations cont.

Atomoxetine cont.		**Pediatrics:** Initiate with a dose of 0.5 mg/kg/day and increase to 1.2 mg/kg/day after 3 days. If no clinical response and in the absence of adverse events after 2 weeks, consider obtaining a peak plasma concentration (1 to 2 hours after dose administered). If < 200 ng/mL, consider a proportional increase in dose to approach 400 ng/mL.	moderate
	DPWG	In the event of side effects occurring and/or a response later than 9 weeks: reduce the dose and check whether the effect is conserved The plasma concentration of atomoxetine is a factor of 2-3 times higher for IM than for NM at the same dose.	
Desipramine CYP2D6 intermediate CPIC guideline · PMID 27997040	CPIC	Consider a 25% reduction of recommended starting dose. Titrate dose to observed clinical response with symptom improvement and minimal (if any) side effects. Utilize therapeutic drug monitoring to guide dose adjustments.	optional
Fosphenytoin CYP2C9 intermediate HLA-B risk alleles screened: *15:02 negative · *57:01 negative · *58:01 negative CPIC guideline · PMID 32779747	CPIC	**PHT naive · PHT use >3mos:** For first dose, use typical initial or loading dose. For subsequent doses, use approximately 25% less than typical maintenance dose. Subsequent doses should be adjusted according to therapeutic drug monitoring, response and side effects. An HLA-B*15:02 negative test does not eliminate the risk of phenytoin-induced SJS/TEN, and patients should be carefully monitored according to a usual standard.	moderate
	FDA	"Consider avoiding CEREBYX [fosphenytoin] as an alternative to carbamazepine in patients who are positive for HLA-B*1502 or in CYP2C9*3 carriers. Should CEREBYX [fosphenytoin] be utilized for CYP2C9*3 carriers, consider starting at the lower end of the dosage range...[P]atients who are known to be intermediate or poor metabolizers may ultimately require lower doses to maintain similar steady-state concentrations compared to normal metabolizers. In patients who are known to be carriers of the decreased function CYP2C9*2 or *3 alleles (intermediate and poor metabolizers), consider starting at the low end of the dosage range and monitor serum concentrations to maintain total phenytoin concentrations of 10 to 20 mcg/mL." See label for more information. *	
Nortriptyline CYP2D6 intermediate CPIC guideline · PMID 27997040	CPIC	Consider a 25% reduction of recommended starting dose. Titrate dose to observed clinical response with symptom improvement and minimal (if any) side effects. Utilize therapeutic drug monitoring to guide dose adjustments.	optional

Clinical section

Drug recommendations cont.

Nortriptyline cont.	**DPWG**	Use 60% of the standard dose and monitor the effect and side effects or the plasma concentration of nortriptyline in order to set the maintenance dose.	
Paroxetine CYP2D6 intermediate CPIC guideline · PMID 37032427	**CPIC**	Consider a lower starting dose and slower titration schedule as compared to normal metabolizers.	optional
	DPWG	NO action is needed for this gene-drug interaction.	
Phenytoin CYP2C9 intermediate HLA-B risk alleles screened: *15:02 negative · *57:01 negative · *58:01 negative CPIC guideline · PMID 32779747	**CPIC**	**CYP2C9 · HLA-B · PHT naive · PHT use >3mos:** For first dose, use typical initial or loading dose. For subsequent doses, use approximately 25% less than typical maintenance dose. Subsequent doses should be adjusted according to therapeutic drug monitoring, response and side effects. An HLA-B*15:02 negative test does not eliminate the risk of phenytoin-induced SJS/TEN, and patients should be carefully monitored according to a usual standard.	moderate
	DPWG	**CYP2C9:** The loading dose does not need to be adjusted. For the other doses, use 70% of the standard dose and assess the dose based on effect and serum concentration after 7–10 days. For patients with gene variant HLA-B*1502, take the extra increase in the risk of life threatening cutaneous adverse events into account while weighing the risks of phenytoin against the benefits. Dose reduction probably does not lower this risk. Advise the patient to report side effects (such as ataxia, nystagmus, slurred speech, sedation or, especially in Asian patients, rash).	
	FDA	**CYP2C9 · HLA-B:** "Patients who are intermediate or poor metabolizers of CYP2C9 substrates (e.g., *1/*3, *2/*2, *3/*3) may exhibit increased phenytoin serum concentrations compared to patients who are normal metabolizers (e.g., *1/*1). Thus, patients who are known to be intermediate or poor metabolizers may ultimately require lower doses of phenytoin to maintain similar steady-state concentrations compared to normal metabolizers...Consider avoiding DILANTIN [phenytoin] as an alternative to carbamazepine in patients who are positive for HLA-B*1502 or in CYP2C9*3 carriers." See label for more information. *	
Pimozide CYP2D6 DPWG guideline		**FDA: CYP2D6 genotyping is required at doses above 4 mg/day in adults and 0.05 mg/kg/day in children · CYP2D6 — this patient's CYP2D6 result is available in this report**	

Clinical section

Drug recommendations cont.

Pimozide cont.	**DPWG**	Use no more than the following doses (80% of the normal maximum dose): 12 years and older: 16 mg/day younger than 12 years: 0.08 mg/kg per day to a maximum of 3 mg/day Basis — CYP2D6 — FDA labeling contains a genetic testing requirement; there is no published CPIC guideline
Tetrabenazine CYP2D6 FDA labeling		**FDA: CYP2D6 genotyping is required before exceeding 50 mg/day · CYP2D6 — this patient's CYP2D6 result is available in this report**
	FDA	"Genotyped patients who are identified as extensive (EMs) or intermediate metabolizers (IMs) of CYP2D6, who need doses of XENAZINE [tetrabenazine] above 50 mg per day, should be titrated up slowly at weekly intervals by 12.5 mg daily, to allow the identification of a tolerated dose that reduces chorea. Doses above 50 mg per day should be given in a three times a day regimen. The maximum recommended daily dose is 100 mg and the maximum recommended single dose is 37.5 mg. If adverse reactions such as akathisia, parkinsonism, depression, insomnia, anxiety or sedation occur, titration should be stopped and the dose should be reduced. If the adverse reaction does not resolve, consideration should be given to withdrawing XENAZINE [tetrabenazine] treatment or initiating other specific treatment." See label for more information * Basis — CYP2D6 — FDA labeling contains a genetic testing requirement; there is no published CPIC guideline
Zuclopenthixol CYP2D6 DPWG guideline	**DPWG**	Use 75% of the normal dose.

◆ Standard start, monitor

3 active substances

Citalopram, Escitalopram CYP2C19 rapid CPIC guideline · PMID 37032427	**CPIC**	Initiate therapy with recommended starting dose. If patient does not adequately respond to recommended maintenance dosing, consider titrating to a higher maintenance dose or switching to a clinically appropriate alternative antidepressant not predominantly metabolized by CYP2C19.	optional
Sertraline CYP2B6 rapid · CYP2C19 rapid CPIC guideline · PMID 37032427	**CPIC**	Initiate therapy with recommended starting dose. If patient does not adequately respond to recommended maintenance dosing, consider titrating to a higher maintenance dose or switching to a clinically appropriate alternative antidepressant not predominantly metabolized by CYP2C19 or CYP2B6.	optional

Clinical section

Drug recommendations cont.

Active substances on which guidelines diverge

10 active substances

The guidelines differ for the same genotype. This report's verdict comes from the highest-priority source: CPIC, then DPWG, then FDA labeling. Which to apply is the physician's decision.

Active substance	Verdict in this report	Source of the verdict	Diverging view
Amitriptyline	✕ **Alternative drug**	CPIC: consider alternative drug not metabolized by CYP2C19; If amitriptyline is warranted, utilize therapeutic drug monitoring to guide dose adjustment.	DPWG: dosing information
Clomipramine	✕ **Alternative drug**	CPIC: consider alternative drug not metabolized by CYP2C19; If clomipramine is warranted, utilize therapeutic drug monitoring to guide dose adjustment.	DPWG: use 70% of the standard dose and monitor the effect and side effects or the plasma concentrations of clomipramine and desmethylclomipramine.
Doxepin	✕ **Alternative drug**	CPIC: consider alternative drug not metabolized by CYP2C19; If doxepin is warranted, utilize therapeutic drug monitoring to guide dose adjustment.	DPWG: dosing information
Imipramine	✕ **Alternative drug**	CPIC: consider alternative drug not metabolized by CYP2C19; If imipramine is warranted, utilize therapeutic drug monitoring to guide dose adjustment.	DPWG: dosing information
Siponimod	✕ **Alternative drug**	DPWG: use 50% of the normal maintenance dose.	FDA: the MAYZENT (siponimod) label states: "Initiate MAYZENT with a 4-day titration, as shown in Table 2...
Fosphenytoin	▲ **Dose adjustment**	CPIC (PHT naive): for first dose, use typical initial or loading dose.	FDA: consider avoiding CEREBYX [fosphenytoin] as an alternative to carbamazepine in patients who are positive for HLA-B*1502 or in CYP2C9*3 carriers.

Clinical section

Drug recommendations cont.

Active substance	Verdict in this report	Source of the verdict	Diverging view
Paroxetine	▲ **Dose adjustment**	CPIC: consider a lower starting dose and slower titration schedule as compared to normal metabolizers.	DPWG: no action needed
Phenytoin	▲ **Dose adjustment**	CPIC (PHT naive): for first dose, use typical initial or loading dose.	DPWG: the loading dose does not need to be adjusted.; FDA: alternative drug
Fluvoxamine	● **Standard use**	CPIC: no action needed	FDA: other guidance
Venlafaxine	● **Standard use**	CPIC: no action needed	DPWG: it is not possible to offer adequately substantiated advice for dose reduction based on the literature.

What may change this interpretation

ask before prescribing

Concomitant drug	In this report, four active substances, if added to treatment, change other recommendations: bupropion, fluoxetine, paroxetine, fluvoxamine. Details (p. 17).
Non-drug factors	Pregnancy (CYP2D6) · Severe inflammation / acute infection (CYP2D6) · St John's wort (CYP2C19, CYP3A4) · Oral contraceptive (ethinylestradiol) (CYP2C19) · Grapefruit and citrus juice (CYP3A4) · Smoking / tobacco smoke (CYP1A2) · Chargrilled meat, cruciferous vegetables (CYP1A2): may change drug levels.
Organ function, age, pregnancy	Genotype-based advice is weighed with liver and kidney function, age and pregnancy.
Guideline update	Antipsychotics × CYP2D6 / CYP3A4 / CYP2C19: The CPIC antipsychotic guideline is under development. Recommendations for these active substances come from FDA labeling and DPWG and are not shown as CPIC guidance.

Versions of the DPWG and FDA texts (p. 21), source publications (p. 22).

Clinical section

Pharmacodynamic findings

Variants linked to an active substance's effect and what to watch in follow-up. Not a guideline recommendation; changes no verdict in the guide (p. 2).

An associated allele was detected in 7 of 18 associations.

Detected variants

7 associations, watch during follow-up

Active substance	Gene and detected genotype	Point to watch
Antipsychotics (studied at class level) aripiprazole, aripiprazole lauroxil, brexpiprazole, clozapine, haloperidol, iloperidone, perphenazine, pimozide, quetiapine, risperidone, thioridazine, zuclopenthixol	**DRD2** −141C Ins/Del: Ins/Del **Detected allele: Del, one copy**	Do not set expectations of antipsychotic response on the basis of this result. Basis: In a meta-analysis (6 studies, 687 patients) −141C Del carriage was linked to poorer antipsychotic response than Ins/Ins; single studies conflict. Consistency: inconsistent, 3 sources.
Clozapine	**HTR2A** His452Tyr: His452/Tyr452 heterozygous **Detected allele: 452Tyr, one copy**	Do not change antidepressant or antipsychotic choice or dose because of this result. Basis: The 452Tyr allele was associated with poor clozapine response in two candidate-gene studies; in one, significance at genotype level was lost after correction for multiple comparisons. Not clinically validated. Consistency: inconsistent, 2 sources.
Oxazepam	**UGT2B15** *2 (Asp85Tyr): *2/*2 (homozygous) **Detected allele: *2, two copies**	Do not change the oxazepam or lorazepam dose; if unexpected sedation occurs, reduced clearance is one possible explanation. Basis: The *2 allele is linked to a copy-number-proportional fall in oxazepam clearance (about half in *2/*2); no genotype-related difference in sedation or cognitive measures has been shown. Consistency: partly consistent, 3 sources.
Lorazepam	**UGT2B15** *2 (Asp85Tyr): *2/*2 (homozygous) **Detected genotype: *2/*2**	Do not change the oxazepam or lorazepam dose; if unexpected sedation occurs, reduced clearance is one possible explanation. Basis: In *2/*2 the systemic clearance of intravenous lorazepam was 0.58-fold that in *1/*1; no pharmacodynamic difference was reported at baseline. Consistency: partly consistent, 1 source.

Clinical section

Pharmacodynamic findings cont.

Active substance	Gene and detected genotype	Point to watch
Naltrexone	**OPRM1** 118A>G (Asn40Asp): Asn40/Asp40 (heterozygous) **Detected allele: 118G, one copy**	Do not base the opioid starting dose or the naltrexone decision on this result. Basis: A genotype-stratified randomized trial (221 patients) found no genotype–treatment interaction; a meta-analysis of seven randomized trials left it uncertain whether the 118G allele predicts naltrexone response. Consistency: partly consistent, 2 sources.
Opioid analgesics morphine, oxycodone, codeine, tramadol, hydrocodone, hydromorphone, fentanyl, alfentanil, remifentanil, sufentanil, buprenorphine, methadone, levomethadone	**OPRM1** 118A>G (Asn40Asp): Asn40/Asp40 (heterozygous) **Detected allele: 118G, one copy**	Do not base the opioid starting dose or the naltrexone decision on this result. Basis: In a meta-analysis (39 studies, 7,455 patients) opioid requirement in the first 24–48 hours after surgery was slightly higher in 118G carriers; the effect is small and does not allow individual prediction. Consistency: partly consistent, 1 source.
Opioid analgesics morphine, oxycodone, codeine, tramadol, hydrocodone, hydromorphone, fentanyl, alfentanil, remifentanil, sufentanil, buprenorphine, methadone, levomethadone	**COMT** Val158Met: Met158/Met158 (homozygous) **Detected allele: Met158, two copies**	Do not change the dose of any opioid, antipsychotic or stimulant because of this result. Basis: The Met158 allele was associated with lower postoperative opioid consumption (meta-analysis, 39 studies); the effect is small. A randomized trial comparing morphine with oxycodone reported that genotype alone was not discriminating. Consistency: partly consistent, 2 sources.

Not detected or not determined

11 associations

Active substance	Gene and detected genotype	Result
SSRI and SNRI antidepressants	**HTR2A** rs7997012: A/G; 102T/C: C/C; −1438A/G: G/G	No specific allele is defined in the studies; genotype given for information. Topic: treatment response and adverse effects. Consistency: inconsistent, 3 sources.
	SLC6A4 5-HTTLPR: cannot be determined with short reads (a targeted test is needed)	No specific allele is defined in the studies; genotype given for information. Topic: treatment response and tolerability. Consistency: inconsistent, 5 sources.
Citalopram	**HTR2A** rs7997012: A/G	A/A genotype not detected. Topic: treatment response. Consistency: inconsistent, 1 source.

Clinical section

Pharmacodynamic findings cont.

Active substance	Gene and detected genotype	Result
P-glycoprotein substrate antidepressants amitriptyline, citalopram, escitalopram, paroxetine, venlafaxine	**ABCB1** 2677G>T/A: G/G; 1236C>T: C/C; rs2032583: T/C; rs2235015: G/T	No specific allele is defined in the studies; genotype given for information. Topic: treatment response (remission). Consistency: inconsistent, 4 sources.
	HTR2A His452Tyr: His452/Tyr452 heterozygous	No specific allele is defined in the studies; genotype given for information. Topic: adverse effect (tardive dyskinesia). Consistency: inconsistent, 1 source.
Risperidone	**DRD2** −241A/G: A/A	No specific allele is defined in the studies; genotype given for information. Topic: treatment response. Consistency: inconsistent, 2 sources.
Olanzapine	**HTR2C** Cys23Ser: Cys23/Cys23 (X-linked gene; single copy in males)	No specific allele is defined in the studies; genotype given for information. Topic: adverse effect (weight gain). Consistency: largely negative, 1 source.
Clozapine, Olanzapine, Risperidone	**HTR2C** Cys23Ser: Cys23/Cys23 (X-linked gene; single copy in males)	No specific allele is defined in the studies; genotype given for information. Topic: adverse effect (weight gain). Consistency: largely negative, 2 sources.
Temazepam	**UGT2B15** *2 (Asp85Tyr): *2/*2 (homozygous)	No specific allele is defined in the studies; genotype given for information. Topic: drug metabolism (in vitro). Consistency: partly consistent, 1 source.
Methylphenidate	**CES1** Gly143Glu: Gly143/Gly143	Glu143 allele not detected. Topic: drug exposure. Consistency: partly consistent, 3 sources.
Antiepileptics (drug-resistant epilepsy)	**ABCB1** 3435C>T: CC	No specific allele is defined in the studies; genotype given for information. Topic: treatment resistance. Consistency: largely negative, 3 sources.

“Consistency” is how far studies replicate the association; it is not a CPIC level of evidence. A “detected allele” alone does not predict risk or response. References (p. 22). Other active substances mapped to these genes: COMT (citalopram, escitalopram). This report covers its own clinical area; pharmacodynamic associations in other areas are in the general report.

Analytical evidence

CYP2D6 confirmation and HLA analysis

The two regions hardest for short reads get their own method and checks.

CYP2D6 confirmation

three independent algorithms

Three algorithms gave the same result: ***2/*4**, intermediate metabolizer.

Algorithm	Approach	Diplotype	Result
BIODECODE CYP2D6 module	Matching to star-allele definitions; among 5 candidates	***2/*4**	**concordant**
Independent algorithm 1	Read depth and structural variant model	***2/*4**	**concordant**
Independent algorithm 2	Joint resolution of allele combinations	***2/*4C**	**concordant**

Concordance is assessed at core-allele level: *2/*4C — the suballele letter denotes the same core allele (*2/*4).

Activity score

1.0 intermediate metabolizer

0	0.25 – 1	1.25 – 2.25	above 2.25
poor	**intermediate**	**normal**	**ultrarapid**

Copy number

2 copies depth ratio 1.04



one copy two copies three copies

Other candidates not excluded	4 candidates — 2 candidates with activity score 0.25–1 · 2 candidates with a (rare) allele of unassigned function
Coverage	1 defining position below 20× depth — the reason the candidates could not be separated
Copy number estimate	Consistent with two copies: no evidence of gene deletion or duplication (read depth ratio 1.04 · compared with 28 samples from the same run). Copy-neutral structural rearrangements cannot be excluded with this method.
Quality control	3 heterozygous positions checked for allele fraction and alignment quality; all consistent with germline heterozygosity.

Short-read data alone could not distinguish between 5 candidate diplotypes. Two independent star-allele callers gave the same diplotype; as this diplotype is in the BIODECODE candidate set, it was passed to the BIODECODE PGx engine. Phenotype follows the CPIC activity score table; the guideline verdict follows CPIC/DPWG/FDA. For CYP2D6 substrates the verdict rests on this phenotype; see the drug recommendations. The diplotype rests on the concordance of independent callers; as CYP2D6 coverage is limited in this sample, for drugs with a narrow therapeutic range a CYP2D6-specific confirmatory test is advised before the decision.

Analytical evidence

CYP2D6 confirmation and HLA analysis cont.

HLA analysis

drug hypersensitivity risk alleles

None of the five risk alleles was detected.

Risk allele	Result	Related active substances	Source
HLA-B*57:01	negative	abacavir	CPIC
HLA-B*15:02	negative	carbamazepine, oxcarbazepine, phenytoin, fosphenytoin, lamotrigine	CPIC
HLA-A*31:01	negative	carbamazepine	CPIC
HLA-B*58:01	negative	allopurinol	CPIC
HLA-B*13:01	negative	dapsone	DPWG/literature

HLA-A A*25:01 (homozygous) · **HLA-B** B*44:02 / B*49:02

A risk allele is counted as positive when it is seen in all typing solutions; if the solutions diverge the result is reported as “uncertain”, not as negative.

Analytical evidence

Phenoconversion and LoF screening

The genotype does not change; concomitant drugs and rare variants can change the result.

Phenoconversion

effect of concomitant drugs

The main focus is **CYP2D6**: if a strong or moderate inhibitor is added, the recommendation changes for 16 active substances.

Gene, result	If added	The gene behaves as	Recommendation changes for
CYP2D6 intermediate	Strong inhibitor: **bupropion**, **fluoxetine**, **paroxetine**, quinidine, terbinafine Moderate inhibitor: abiraterone, cinacalcet, duloxetine, mirabegron	**intermediate → poor**	desipramine, fluvoxamine, nortriptyline, venlafaxine, vortioxetine: **alternative drug**; aripiprazole, brexpiprazole, clozapine, deutetrabenazine, haloperidol, iloperidone, pitolisant, risperidone, valbenazine: **dose adjustment**; fluoxetine, lofexidine: **standard start, monitor**
CYP2C19 rapid	Strong inhibitor: **fluoxetine**, **fluvoxamine**, fluconazole, ticlopidine	**rapid → poor**	citalopram, escitalopram, sertraline: **alternative drug**; brivaracetam, clobazam: **dose adjustment**
	Moderate inhibitor: voriconazole	**rapid → intermediate**	amitriptyline, citalopram, clomipramine, doxepin, escitalopram, imipramine, trimipramine: **dose adjustment**; sertraline: **standard use**
	Strong inducer: rifampicin	**rapid → ultrarapid**	citalopram, escitalopram: **alternative drug**
CYP3A4 normal	Strong inhibitor: clarithromycin, itraconazole, ketoconazole, ritonavir, voriconazole	**normal → poor**	quetiapine: **alternative drug**
	Moderate inhibitor: **fluvoxamine**, diltiazem, erythromycin, fluconazole, verapamil	**normal → intermediate**	none
	Strong inducer: **carbamazepine**, **fosphenytoin**, **phenytoin**, rifampicin	**normal → rapid**	quetiapine: **level falls**; not defined in the guideline
CYP1A2 not genotyped	Inhibitor: **fluvoxamine**, ciprofloxacin, mexiletine, vemurafenib, zileuton; smoking cessation	activity decreases	clozapine: **level rises**

Analytical evidence

Phenoconversion and LoF screening cont.

Gene, result	If added	The gene behaves as	Recommendation changes for
CYP1A2 not genotyped	Inducer: **carbamazepine**, **fosphenytoin**, **phenytoin**, rifampicin, teriflunomide; smoking / tobacco smoke	activity increases	clozapine: **level falls**

Do not change the class	Alone, these active substances in this report do not change the phenotype class; effects may add up. CYP2D6: citalopram, clobazam, escitalopram, fluvoxamine, haloperidol, sertraline · CYP2C19: carbamazepine, fosphenytoin, oxcarbazepine, phenytoin, sertraline · CYP3A4: clobazam, oxcarbazepine.
Shift not calculated	These active substances in this report inhibit or induce the enzyme, but the effect size is too poorly documented to assign a phenotype class; monitor clinically when combined. CYP2D6: perphenazine, thioridazine.
Non-drug factors	Pregnancy: CYP2D6 activity increases · Severe inflammation / acute infection: CYP2D6 activity decreases · St John's wort: CYP2C19, CYP3A4 activity increases · Oral contraceptive (ethinylestradiol): CYP2C19 activity decreases · Grapefruit and citrus juice: CYP3A4 activity decreases · Smoking / tobacco smoke: CYP1A2 activity increases · Chargrilled meat, cruciferous vegetables: CYP1A2 activity increases.

Bold: active substances in this report. Changes are derived by looking up the guideline data with the shifted phenotype and applying the report's verdict rules. The patient's current medication is not part of the analysis; ask before prescribing, including over-the-counter and herbal products. The table does not add up two simultaneous factors. Shift rules: Literature-based activity-score multiplier (strong ×0 · moderate ×0.5 · weak ×1). Neither CPIC nor DPWG has published a phenoconversion rule.

Loss-of-function (LoF) screening

36 genes outside HLA, exons and introns

No loss-of-function finding; two variants could not be scored.

36	› 54	› 52	› 0 + 2
genes screened	**variants examined**	**benign**	**reported, not scorable**
regions outside HLA; two genes partly read	outside the star-allele definitions	population frequency or in-silico evidence	no variant to report

Variants are scored with the BIODECODE ACMG scoring system. They do not change the recommendation; phenotype is assigned only from a confirmed allele. For 2 unscorable variants, data are insufficient for classification; these variants are not counted as benign. Score and class thresholds (p. 20).

Analytical evidence

67 gene regions

Status of each panel region in this sample. No result is never counted as normal; the reason is given.



33	21	9	2	2
genotype determined diplotype or genotype call	**passed loss-of-function screening** regions without a star-allele call	**HLA region** outside risk screening	**targeted test** cannot be resolved with short reads	**not readable** no result in this sample

Each region is read with its exons and introns; a result is given where read depth is at least 20×.

Regions with a determined genotype

33 regions

Altered function 10	**CYP2B6** *4/*5 rapid · **CYP2C9** *1/*3 intermediate · **CYP2C19** *17/*38 rapid · **CYP2D6** *2/*4 intermediate · **CYP3A5** *1/*3 expresser (partial) · **NAT2** *5/*6 poor · **UGT1A1** *1/*80+*28 intermediate · **ABCG2** rs2231142 G/T decreased function · **SLCO1B1** *15/*37 decreased function · **DPYD** c.85T>C (*9A) + c.1129-5923C>G, c.1236G>A (HapB3) intermediate
Function at expected level 8	CYP3A4 · NUDT15 · TPMT · CACNA1S (uncertain susceptibility) · CFTR (ivacaftor non-responsive) · VKORC1 (-1639 GG) · HLA-A (no risk allele) · HLA-B (no risk allele)
Genotype reported only 15	CYP4F2 *1/*17 · IFNL3 rs12979860 C/T · CYP2C8 R139K absent, K399R absent · COMT Met158/Met158 (homozygous) · ITPA Pro32/Pro32 · UGT2B15 *2/*2 · ABCB1 3435 CC · ADRB2 Arg16/Arg16, Gln27/Gln27 · DRD2 −141C Ins/Del, −241 A/A · HTR2A His452/Tyr452 heterozygous · HTR2C Cys23 · OPRM1 Asn40/Asp40 (heterozygous) · BCHE atypical variant absent · CES1 Gly143/Gly143 · F5 Leiden absent. The guidelines define no class such as “poor” or “normal” for these genes; follow-up notes (p. 12).

Regions without a star-allele call

23 regions

No call does not mean “reference”; these regions go through loss-of-function screening.

No variant to report 21	CYP1A2 · CYP2A6 · CYP2E1 · CYP2J2 · CYP3A7 · POR · GSTA1 · UGT2B7 · ABCC2 · ABCC4 · SLC22A1 · SLC22A2 · SLC22A6 · SLC22A8 · SLC47A1 · SLC47A2 · SLCO1B3 · SLCO2B1 · ADH1B · ALDH2 · SCN1A
Not readable in this sample 2	G6PD · RYR1: some defining positions are below 20×; the result is not considered confirmed. Active substances depending on these genes show “No result” in the guide.

Regions that give no result with this method

11 regions

HLA, outside risk screening 9	HLA-C: no defined risk allele. HLA-DPA1 · DPB1 · DQA1 · DQB1 · DRB1 · DRB3 · DRB4 · DRB5: not typed in this panel.
Targeted test required 2	GSTM1 (copy number) · SLC6A4 (5-HTTLPR length). Targeted test on request.

Technical appendix

Methods and limitations

How the result is produced, what each step checks and what the method cannot see.

1 **Sample** peripheral blood, genomic DNA

› 2 **Sequencing** targeted capture, NGS; 67 regions

› 3 **Alignment** GRCh38 reference genome; variant calling, quality recalibration

› 4 **Allele and phenotype** star-allele diplotype, CPIC phenotype

› 5 **Recommendation** from CPIC, DPWG, FDA tables; doses not calculated

Method

step by step

Reading rule	A position read at a depth of at least 20× with no variant record counts as the reference allele. A position below the threshold is reported as “not readable”, never assumed normal.
CYP2D6	Resolved by a separate module: allele-combination matching, allele-fraction and alignment-quality checks and read-based phasing, compared with two independent algorithms. Copy number is estimated from read depth normalized within the run; if not two copies, no diplotype or phenotype is reported.
HLA	Risk alleles are screened on the HLA-A and HLA-B typing solutions. An allele present in all solutions is positive, in none negative; if solutions diverge the result is uncertain and is not reported as negative.
Loss-of-function screening	Variants outside star-allele definitions are scored with the BIODECODE ACMG scoring system: each gets ACMG/AMP criterion codes and a total score. Missense variants are also scored with REVEL and AlphaMissense, as supporting evidence only. A variant seen in over 5% of the population counts as benign. HLA regions are not screened.

−6 and below	−5 to 0	1 to 6	8 to 10	12 and above
benign	**likely benign**	**uncertain**	**likely pathogenic**	**pathogenic**

Limitations of the method

what this test cannot see

- Phasing is applied only in CYP2D6; elsewhere two variants cannot be assigned to the same chromosome.
- CYP2D6 copy number is not independently confirmed; hybrid alleles and four or more copies cannot be determined. If critical, use MLPA or long-read sequencing.
- SLC6A4 5-HTTLPR, GSTM1 copy number, HLA-C and HLA class II give no result here.
- Genes outside the panel and rare variants cannot be excluded; an unreported allele is not proven absent.
- Seven active substances linked only to genes outside the panel are not in this report: l-methylfolate, amisulpride, paliperidone, ziprasidone, divalproex sodium, valproic acid, caffeine.

Technical appendix

Definitions and source versions

Phenotype classes, guideline evidence levels and the knowledge base used.

Phenotype classes

by gene class

Enzymes

Ultrarapid	enzyme activity markedly increased
Rapid	activity above normal
Normal	expected activity
Intermediate	activity partly reduced
Poor	activity severely reduced or absent

Transporters and other genes

Increased function	activity above expected
Normal function	works at the expected level
Decreased function	exposure may change
Poor function	severely reduced activity
Expresser	used instead of “normal” for CYP3A5 and CYP3A7

Direction depends on the active substance: for an active drug, slow metabolism causes accumulation and fast metabolism loss of effect. For prodrugs (codeine, tramadol) the reverse holds.

CPIC levels of evidence

actionability tier

A	Guideline recommends a genotype-based prescribing change; a dose or drug recommendation exists.
B	Guideline offers a genotype-based change as an option; the alternative is at least as effective and safe.
C	No prescribing change is recommended; evidence is limited.
D	Evidence is insufficient; no clinical action defined.

The letter rates how actionable the gene–active substance pair is, not measurement reliability. Recommendation strength (strong, moderate, optional) is a separate axis, shown at the right of each row.

Knowledge base versions

biodecode-kb 2.0, build 14 Nov 2026

Source	Updated
CPIC gene–drug pairs list	5 Aug 2026
CPIC provisional list	5 Aug 2026
BIODECODE curated drug database	22 Apr 2026
DPWG guideline pairs	10 Nov 2026
BIODECODE PGx engine guideline data	14 Nov 2026
Report template	version 5.0, 15 Nov 2026

Pending update: Antipsychotics × CYP2D6 / CYP3A4 / CYP2C19: The CPIC antipsychotic guideline is under development. Recommendations for these active substances come from FDA labeling and DPWG and are not shown as CPIC guidance.

Technical appendix

References

Guideline publications behind the recommendations, research bibliography, local context.

Guideline publications

used in this report

Topic	Source	PMID
Amitriptyline, clomipramine, desipramine, doxepin and 3 more: CYP2C19, CYP2D6	CPIC guideline	23486447 · 27997040
Atomoxetine: CYP2D6	CPIC guideline	30801677
Carbamazepine, oxcarbazepine: HLA-A, HLA-B	CPIC guideline	23695185 · 29392710
Citalopram, escitalopram, fluoxetine, fluvoxamine and 4 more: CYP2C19, CYP2D6, HTR2A, SLC6A4, CYP2B6	CPIC guideline	25974703 · 37032427
Fosphenytoin, phenytoin: CYP2C9, HLA-B	CPIC guideline	25099164 · 32779747
Quetiapine: CYP3A4	DPWG guideline	37002327
CYP2D6 genotype-to-phenotype standard	CPIC and DPWG 2020	31647186
Variant classification criteria	ACMG/AMP 2015	25741868

DPWG recommendations come from the DPWG guideline pairs, FDA ones from the pharmacogenomic biomarker table and labeling; versions on (p. 21). Allele names follow PharmVar nomenclature.

Research bibliography

sources of the pharmacodynamic findings, PMID

HTR2A	33097827 · 23733030 · 37032427 · 16642436 · 15857569 · 8916101 · 9629566
SLC6A4	17146470 · 20615496 · 22137564 · 32421611 · 34945806
ABCB1	18215618 · 36681895 · 18382661 · 33147643 · 20605481 · 19178561 · 25550900
DRD2	20194480 · 9858029 · 33147643 · 18855532 · 28696411
HTR2C	22967772 · 20504252 · 42480244
UGT2B15	19916996 · 15044558 · 12386133 · 15961980 · 40543327
CES1	28087982 · 18485328 · 41567292
OPRM1	25760804 · 31961981 · 37774182
COMT	37774182 · 36426809

Local context

use in Türkiye

Product information	Recommendations are from CPIC, DPWG and the FDA. For any product prescribed in Türkiye, also check the current TİTCK SmPC.
Population	Allele frequencies vary between populations. Ancestry does not replace genotyping; findings rest on the patient's measured genotype.
Numerical doses	Dose statements are quoted from the source guideline; re-check at the bedside against product, indication, age, organ function and concomitant drugs.

Technical appendix

Institutional information and responsibility

Who produces and approves the report, sample details, conditions of use.

1 **Sample receipt and storage**
İstanbul Genetik Grubu

› 2 **Laboratory analysis**
İstanbul Genetik Grubu

› 3 **Bioinformatics and interpretation**
BIODECODE

› 4 **Medical approval**
İstanbul Genetik Grubu

Responsible parties

chain of responsibility

Responsible medical genetics diagnostic center

İstanbul Genetik Grubu Sağlık Hizmetleri Ltd. Şti.
Genetic Diseases Evaluation Center

Türkali Mah. Nüzhetiye Cad. No: 38/A Beşiktaş, İstanbul
Tel 0212 227 52 54 · igg@istanbulgenetik.com

Medically approves the report and holds clinical responsibility. Clinical and result queries go to this center.

Software, interpretation and report generation

BIODECODE
Clinical Pharmacogenomics

Runs the bioinformatic analysis and produces the report. Approval lies with the center.

Commercial distribution: PHARMADECODE. No part in analysis, interpretation or approval; not responsible for medical content.

Sample and method details

ORNEK_L01_00

Specimen **Peripheral blood (K3-EDTA)**	Date received _____	Test **Neuropsychiatry panel**	Method **Targeted sequencing (NGS)**
Panel **BIODECODE PGx, 67 regions**	Reference genome **GRCh38**	Interpretation source **CPIC, DPWG, FDA**	Active substances assessed **49**

Approval and signature

report date 18 Nov 2026

Medical approval

Dr. Rıdvan Seçkin Özen
Head of the Genetic Diseases Evaluation Center · Dok.Dip.No: 94
İstanbul Genetik Grubu

Report prepared by

Asst. Prof. Burak Berber
Molecular Biologist · Head of BIODECODE
BIODECODE

Valid clinically with the medical approval signature; the preparer's signature records the analysis.

Conditions of use

legal and ethical responsibilities

- For research use; not IVD-approved. The results are used as clinical decision support.
- No substitute for diagnosis, history, concomitant drugs or the physician's judgment.
- Drug response also depends on non-genetic factors: drug interactions, liver and kidney function, age, pregnancy, smoking. A sample taken after stem-cell transplantation or recent transfusion may not reflect the patient's genotype.
- The physician must consult current product information and relevant clinical guidelines.
- Special-category health data under Turkish Law No. 6698; shared only with the patient's explicit consent or as legislation provides.