CPIC member call

June 4, 2026

1) Housekeeping announcements
2) Guidelines in progress - Kelly Caudle
3) Tacrolimus Guideline - Kelly Birdwell
4) Potential new CPIC level - Kelly Caudle
5) ACMG PGx SIG - Annette Taylor

https://www.pgrn.org/PGRN-Scientific-Meeting-2026

Guidelines in progress

- *CYP3A5* and *CYP3A4*/Tacrolimus – Presenting on CPIC call this Thursday
- *CYP2D6*/Antipsychotics – CPIC review
- *DPYD*/fluoropyrimidines- Drafting guideline text
- *UGT1A1*/irinotecan- Evidence review underway
- *HLA*-authorship plan underway; will include more drugs/alleles
- *CYP2C19*/voriconazole-authorship plan underway
- *NAT2*/isoniazid-starting soon; navigating international collaborations with NIH policy

Iloperidone

Phenotype	Activity Score	Implications	Recommendations	Classification of recommendation	Considerations
CYP2D6 poor metabolizer	0	Although the FDA label for iloperidone recommends a maximum daily dose of 12 mg for CYP2D6 PMs and slower titration with strong CYP2D6 inhibitors, based on pharmacokinetic data and QTc prolongation concerns, there is insufficient clinical evidence to support a genotype-guided prescribing recommendation	No recommendation for therapy due to insufficient or no evidence regarding drug exposure and clinical effectiveness	No recommendation	Clinicians should remain aware of FDA labeling and use clinical judgment when incorporating CYP2D6 genotyping into iloperidone prescribing, particularly in patients at higher QTc risk.

FDA: Do not have access to drug approval documents

Pimozide

Phenotype	Activity Score	Implications	Recommendations	Classification of recommendation	Considerations
CYP2D6 poor metabolizer	0	Although the FDA label for pimozide includes a recommendation that individuals known to be CYP2D6 PMs not exceed a total daily dose of 4 mg based on pharmacokinetic modeling and concerns regarding QTc prolongation, there is insufficient clinical evidence to support genotype-guided prescribing based on this CPIC review.	No recommendation for therapy due to insufficient or no evidence regarding drug exposure and clinical effectiveness	No recommendation	Clinicians should remain aware of FDA labeling and use clinical judgment when incorporating CYP2D6 genotyping into iloperidone prescribing, particularly in patients at higher QTc risk. See the guideline text for additional details.

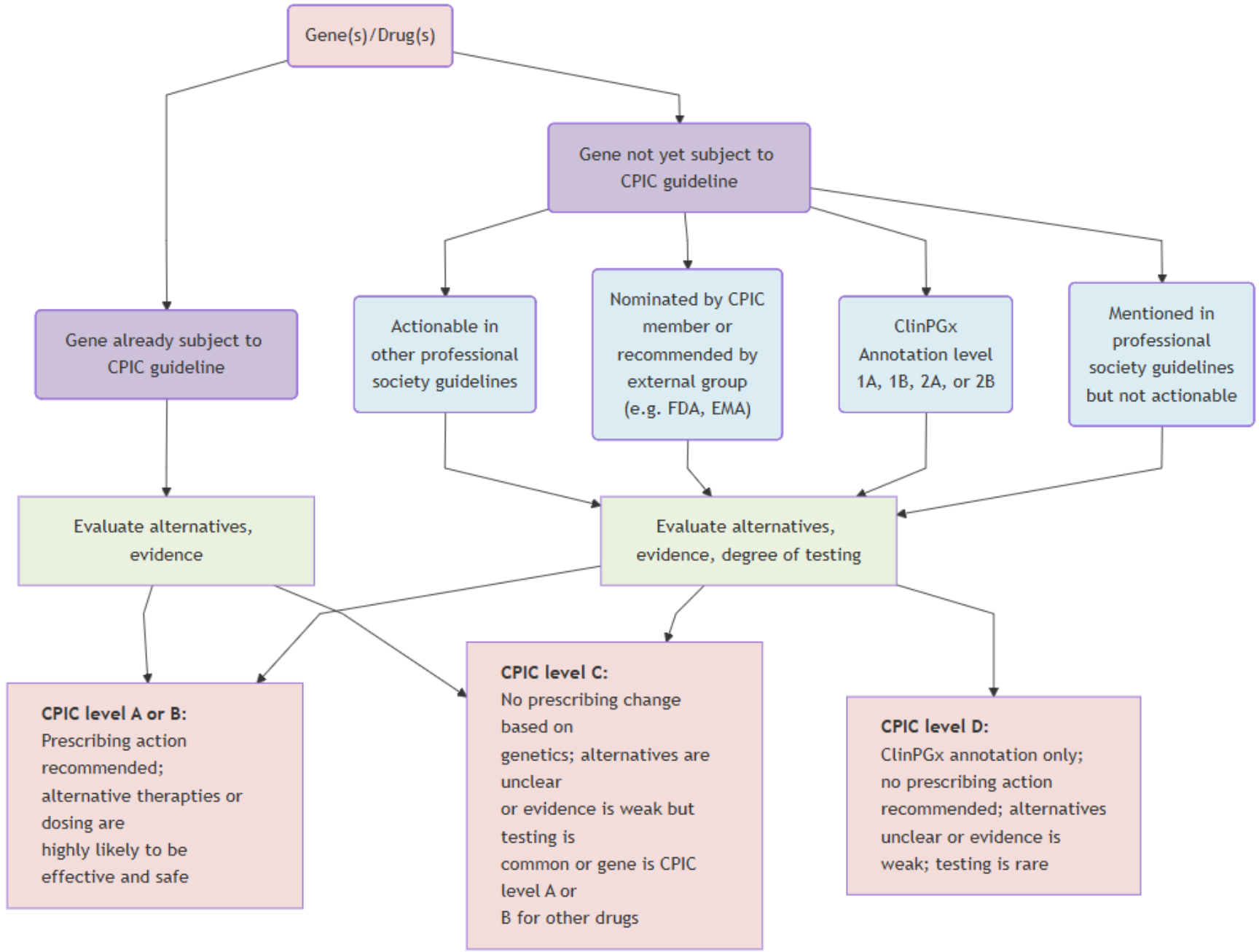
FDA: no genotype data were available, and this was simulated from drug interaction data
CPIC: 5 PK papers but all papers graded weak; one paper on QTc interval changes but not significant

Brexpiprazole

Phenotype	Activity Score	Implications	Recommendations	Classification of recommendation	Considerations
CYP2D6 poor metabolizer	0	Although the FDA and EMA labels for brexpiprazole include recommendations that individuals identified as CYP2D6 poor metabolizers should have their standard dosage reduced by 50%, there is insufficient clinical evidence to support genotype-guided prescribing based on this CPIC review.	No recommendation for therapy due to insufficient or no evidence regarding drug exposure and clinical effectiveness	No recommendation	Clinicians should remain aware of FDA labeling and use clinical judgment when incorporating CYP2D6 genotyping into brexpiprazole prescribing.

- FDA: Coadministration of potent CYP3A4 or CYP2D6 inhibitors resulted in about 2-fold higher exposure and about a 1.5-fold increase in half-life.
- Had 2 PMs with similar PK but dose simulated based on inhibitor data
- CPIC review: based on 3 studies, 2/3 PK modeling ; no clinical outcome data

Considerations for Assignment of CPIC Level for Genes/Drugs



Genes-Drugs in Published Guidelines

316 Pairs

Download

DRUG	GENE	GUIDELINE	CPIC LEVEL	CLINPGX LEVEL OF EVIDENCE	PGX ON FDA LABEL	CPIC PUBLICATIONS (PMID)
vortioxetine	SLC6A4		C		•	37032427
vortioxetine	HTR2A		C		•	37032427
vortioxetine	CYP2C19		C		•	37032427
vitamin k	G6PD		C		•	36049896
vitamin c	G6PD		C		•	36049896
vilazodone	SLC6A4		C		•	37032427
vilazodone	HTR2A		C		•	37032427

Provisional Genes-Drugs

This table includes gene–drug pairs for which no CPIC guideline currently exists and that are therefore assigned a provisional CPIC level. Gene–drug pairs listed as provisional have not yet undergone a comprehensive, in-depth evidence review and should not be considered to have definitive CPIC level assignments.

257 Pairs

Download

DRUG	GENE	CPIC LEVEL	CLINPGX LEVEL OF EVIDENCE	PGX ON FDA LABEL
irinotecan	UGT1A1	A	1A	Testing Recommended
pitolisant	CYP2D6	A		Actionable PGx
siponimod	CYP2C9	A	1A	Testing Required

ClinPgx-GSI tool

CPIC	DPWG	FDA Label Annotations	FDA Table of Pharmacogenetic Associations
chloroquine			
No Recommendation CPIC has no recommendations for chloroquine and G6PD. full annotation	Not Evaluated No DPWG guidance.	Other Guidance "Chloroquine may cause hemolysis in glucose-6 phosphate dehydrogenase (G-6-PD) deficiency. Blood monitoring may be needed as hemolytic anemia may occur, in particular in association with other drugs that cause hemolysis." See label for more information. open details full annotation	Not Evaluated Does not appear in FDA Table of Pharmacogenetic Associations.
chlorpropamide			
No Recommendation CPIC has no recommendations for chlorpropamide and G6PD. full annotation	Not Evaluated No DPWG guidance.	Alternate Drug Other Guidance "Because DIABINESE [chlorpropamide] belongs to the class of sulfonylurea agents, caution should be used in patients with G6PD deficiency and a non-sulfonylurea alternative should be considered." See label for more information. open details full annotation	Not Evaluated Does not appear in FDA Table of Pharmacogenetic Associations.
dabrafenib			
No Recommendation CPIC has no recommendations for dabrafenib and G6PD. full annotation	Not Evaluated No DPWG guidance.	Other Guidance The TAFINLAR (dabrafenib) label states: "TAFINLAR, which contains a sulfonamide moiety, confers a potential risk of hemolytic anemia in patients with glucose-6-phosphate dehydrogenase (G6PD) deficiency. Monitor patients with G6PD deficiency for signs of hemolytic anemia while taking TAFINLAR." See label for more information. open details	Not Evaluated Does not appear in FDA Table of Pharmacogenetic Associations.

Clozapine

- Clozapine is one example where there has been some longstanding info in the labeling about 2D6 that was subsequently largely refuted based on published data.

How should CPIC be handling these situations

- Another CPIC level?
- Continue with current system
- No recommendation but change wording to something like this:

CYP2D6 poor metabolizer	0	The FDA label for iloperidone recommends a maximum daily dose of 12 mg for CYP2D6 PMs and slower titration with strong CYP2D6 inhibitors, based on unpublished pharmacokinetic data and QTc prolongation concerns.	There is insufficient published evidence to provide additional genotype-guided dosing beyond what is recommended in the drug label.	No recommendation	See the guideline text for additional details and context.

New CPIC level

- **Regulatory guidance:** There is limited or insufficient published evidence in the peer-reviewed literature to support a CPIC recommendation, but actionable prescribing guidance is provided in an official regulatory agency drug label (e.g., FDA) and meets these criteria:
  - There are no substantive published evidence demonstrating a lack of association between the genetic variant and the drug-related outcome since the regulatory label was established.
  - The regulatory source must include a clear clinical action (e.g., dose reduction, avoidance, alternative therapy, or enhanced monitoring), rather than solely descriptive pharmacokinetic or pharmacodynamic information.
  - The decision to assign this recommendation category, including the specific regulatory label cited, is made at the discretion of the author group.

ACMG Pharmacogenomics SIG

Goal: To bring together the pharmacogenomics and medical genetics communities to advance ACMG's mission and improve implementation of PGx testing throughout other medical specialties.
The SIG will provide a forum for education, sharing of ideas, and contributions to research and clinical practice to advance pharmacogenomics to standard of care.

Chair: Annette Taylor, PhD, MS, FACMG, Associate VP, Strategic Director, Pharmacogenomics at Labcorp.
ACMG liaison: Josh Deignan, PhD, FACMG, Associate Director of the UCLA Molecular Diagnostic Laboratories.
To join the SIG, please contact Dr. Taylor at Tayla12@labcorp.com.
ACMG membership required, including Affiliate Membership

Formed: 3-10-26
First meeting: 3-10-26 at the 2026 ACMG Annual Clinical Genetics Meeting

Plan: Quarterly virtual meetings
In-person meeting at each ACMG Annual Clinical Genetics Meeting
Working group meetings
Conversations by email to share questions and solutions