ConectGene TESTES GENÉTICOS

# Laudo de Exame Farmacogenômico

Médico Responsável: Dr. Paulo Magno do Bem Filho
CRM ES 13785

Rua Equador, 43 – Bloco 3 - Sala 1011
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**PACIENTE:** Jane Doe
**DT. NASC.:** 25/01/1985
**REF.:** LCG-1111111

**COLETADO:** 15/10/2018
**RECEBIDO:** 06/11/2018
**REPORTADO:** 20/11/2018

**AMOSTRA:** Bucal
**MÉDICO:** Não informado
**PRÁTICA:** Não informado

## SUMÁRIO RÁPIDO

### TDAH

| | |
|---|---|
| **Anfetamina** (ANFEPRAMONA®, FEMPROPOREX®, ADDERALL®)<br>**Lisdexanfetamina** (VENVANSE®, VYVANSE®) | ✅ Considere a dosagem da bula se não houverem contraindicações. |
| **Atomoxetina** (STRATTERA®) | ⚠ Esteja alerta para efeitos adversos ao medicamento. |
| **Clonidina** (KAPVAY®, CATAPRES®, DURACLON®, NEXICLON ™)<br>**Dextroanfetamina** (DEXEDRINE®, PROCENTRA®, DEXTROSTAT®) | ⚠ Risco de resposta reduzida. |
| **Dexmetilfenidato** (FOCALIN®)<br>**Metilfenidato** (RITALINA®, RITALIN®, CONCERTA®, DAYTRANA®, METADATE®) | ⚠ Risco de efeitos adversos. Risco de tolerância reduzida. |

### IMPORTANTE

Este Sumário Rápido fornece uma visão geral da previsão de resposta do paciente. Estas informações estão baseadas somente nas informações do genótipo e não compõe o perfil completo do paciente. A detecção ou ausência de variantes genéticas não substitui a necessidade de monitoramento terapêutico. Antes de tomar decisões clínicas ou terapêuticas, médicos devem considerar a informação contida na seção Detalhada (disponível apenas em inglês), assim como prescrições atuais, histórico familiar, sintomas apresentados e outros fatores.

✅ Nenhuma observação negativa baseada no genótipo.

⚠ Genótipo pode apresentar maior risco ou menor efetividade. Prescreva com precaução.

⛔ Genótipo pode apresentar maior risco ou menor efetividade. Considere outro medicamento.

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# Pharmacogenetic Test Results

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**PATIENT:** Doe, Jane (F)
**DOB:** 1985-01-01
**PATIENT ID:**

**COLLECTED:** 10/15/2018
**RECEIVED:** 11/06/2018
**REPORTED:** 11/30/2018

**SAMPLE TYPE:** Buccal
**PHYSICIAN:** Not Provided
**PRACTICE:** Not Provided

**ACCESSION:** LGE-9290880938

## QUICK SUMMARY

| ADHD | RESULTS |
|---|---|
| Amphetamine (ADDERALL®)<br>Lisdexamfetamine (VYVANSE®) | ✓ Consider label recommended dosage if no contraindication. |
| Atomoxetine (STRATTERA®) | ⚠ Be alert to adverse drug events. |
| Clonidine (KAPVAY®, CATAPRES®, DURACLON®, NEXICLON™)<br>Dextroamphetamine (DEXEDRINE®, PROCENTRA®, DEXTROSTAT®) | ⚠ Risk of reduced response. |
| Dexmethylphenidate (FOCALIN®)<br>Methylphenidate (RITALIN®, CONCERTA®, DAYTRANA®, METADATE®) | ⚠ Risk of adverse effect. Risk of decreased tolerance. |

**IMPORTANT**

This Quick Summary provides a brief overview of the predicted response of the patient. This information is based solely on the genotype information and is not based on a complete patient profile. Detection or absence of variants does not replace the need for therapeutic monitoring. Physicians should consider the information contained in the Details section, as well as consider current prescriptions, family history, presenting symptoms, and other factors before making any clinical or therapeutic decisions.

✓ No negative assertions based on genotype.

⚠ Genotype may present increased risk or decreased effectiveness; prescribe with caution.

⊘ Genotype may present increased risk or decreased effectiveness; select alternative drug.

## GENE SUMMARY

| GENE | GENOTYPE | PHENOTYPE |
|---|---|---|
| CYP2D6 | *3/*4 | ⊘ Poor Metabolizer |
| COMT | VAL/VAL | ✓ Normal Stimulant Response |

## DETAILED INFORMATION

| | | |
|---|---|---|
| Amphetamine | COMT rs4680 G/G (WT) *Normal stimulant response.* | Evidence ★★ |
| | The patient has the wild-type genotype (VAL/VAL) and should respond well to increased dopamine levels generated by stimulants. Consider label recommended dosage if no contraindication. | |
| | OPRM1 rs2281617 C/C (WT) OPRM1 rs510769 C/T (HET) | Evidence ★ |
| | Patients may have normal Euphoria, Energy and Stimulation scores after amphetamine exposure. Consider label recommended dosage of Amphetamine if no contraindication. | |
| Atomoxetine | CYP2D6 *3/*4 *Poor metabolizer.* | Evidence ★★ |
| | CYP2D6 metabolizers have higher plasma concentrations of atomoxetine compared with individuals who have two copies of normal activity alleles. The DPWG recommends that poor metabolizers be given the standard dose of atomoxetine, but physicians should be aware of adverse drug events. | |
| | SLC6A2 rs12708954 C/C (WT) | Evidence ★ |
| | Patients with the wild-type genotype and ADHD who are treated with atomoxetine may have decreased response as compared to patients with the homozygous genotype. | |
| | SLC6A2 rs3785143 C/C (WT) | Evidence ★ |
| | Consider label recommended dosage of Atomoxetine if no contraindication. | |
| Clonidine | GNB3 rs5443 C/C (WT) | Evidence ★ |
| | Patients with the wild-type genotype have a poorer response to treatment with clonidine as compared to patients with the heterozygous or homozygous genotype. | |
| Dexmethylphenidate | COMT rs4680 G/G (WT) *Normal stimulant response.* | Evidence ★★ |
| | The patient has the wild-type genotype (VAL/VAL) and should respond well to increased dopamine levels generated by stimulants. Consider label recommended dosage if no contraindication. | |
| | DRD1 rs4532 C/C (WT) | Evidence ★ |
| | Patients with the wild-type genotype and attention deficit hyperactivity disorder (ADHD) may have an increased severity of social withdrawal or nausea when treated with methylphenidate as compared to patients with the heterozygous or homozygous genotype. | |
| | DRD3 rs6280 C/T (HET) | Evidence ★ |
| | Patients with the heterozygous genotype and autism spectrum disorders may have a lesser tolerance for methylphenidate treatment as compared to patients with the wild-type genotype. | |
| | ADRA2A rs1800544 G/C (HET) CES1 rs71647871 C/C (WT) | Evidence ★ |
| | Consider label recommended dosage of Methylphenidate if no contraindication. | |
| Dextroamphetamine | COMT rs4680 G/G (WT) *Normal stimulant response.* | Evidence ★★ |
| | The patient has the wild-type genotype (VAL/VAL) and should respond well to increased dopamine levels generated by stimulants. Consider label recommended dosage if no contraindication. | |
| | DRD1 rs4532 C/C (WT) | Evidence ★ |
| | Patients with the wild-type genotype and ADHD may have an increased severity of social withdrawal or nausea when treated with dextroamphetamine as compared to patients with the heterozygous or homozygous genotype. | |

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## DETAILED INFORMATION

| | | | |
|---|---|---|---|
| Lisdexamfetamine | COMT rs4680 G/G (WT) | *Normal stimulant response.* | Evidence ★★ |
| | The patient has the wild-type genotype (VAL/VAL) and should respond well to increased dopamine levels generated by stimulants. Consider label recommended dosage if no contraindication. | | |
| Methylphenidate | COMT rs4680 G/G (WT) | *Normal stimulant response.* | Evidence ★★ |
| | The patient has the wild-type genotype (VAL/VAL) and should respond well to increased dopamine levels generated by stimulants. Consider label recommended dosage if no contraindication. | | |
| | DRD1 rs4532 C/C (WT) | | Evidence ★ |
| | Patients with the wild-type genotype and attention deficit hyperactivity disorder (ADHD) may have an increased severity of social withdrawal or nausea when treated with methylphenidate as compared to patients with the heterozygous or homozygous genotype. | | |
| | DRD3 rs6280 C/T (HET) | | Evidence ★ |
| | Patients with the heterozygous genotype and autism spectrum disorders may have a lesser tolerance for methylphenidate treatment as compared to patients with the wild-type genotype. | | |
| | ADRA2A rs1800544 G/C (HET) CES1 rs71647871 C/C (WT) | | Evidence ★ |
| | Consider label recommended dosage of Methylphenidate if no contraindication. | | |

### KEY FOR VARIANT-DRUG COMBINATION EVIDENCE

| | |
|---|---|
| ★★★ | Replicated in multiple studies with statistical significance and strong effect size. |
| ★★ | Replicated in multiple studies with and without statistical significance and effect size may be minimal. |
| ★ | Not yet replicated or replicated but lacking clear evidence of an association. |
| | Notable information is available and special considerations may be of interest when prescribing for this genotype. |
| | Literature does not indicate additional risks, benefits, or prescription changes to consider for this genotype. |

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## REPORTED GENOTYPES

This panel performs genotyping analysis on key genes and variant hot-spot regions, focused on analyzing loci documented as altering the effectiveness of drug metabolism. Key genotyping results include the following:

**ADRA2A**
rs1800544:G/C Het

**CES1**
rs71647871:C/C Wild

**COMT**
rs4680:G/G Wild

**CYP2D6**
CYP2D6 *3/*4
rs16947:G/G Hom
rs1135840:G/C Het
rs35742686:T/- Het
rs1135824:T/T Wild
rs1065852:G/A Het
rs3892097:C/T Het
rs5030655:A/A Wild
rs5030867:T/T Wild
rs5030865:C/C Wild
rs5030656:CTT/CTT Wild
rs5030863:C/C Wild
rs5030862:C/C Wild
rs72549357:C/C Wild
rs28371706:G/G Wild
rs59421388:C/C Wild
rs769258:C/C Wild
rs28371725:C/C Wild
rs28371696:C/C Wild
rs28371717:C/C Wild

**DRD1**
rs4532:C/C Wild

**DRD3**
rs6280:C/T Het

**GNB3**
rs5443:C/C Wild

**OPRM1**
rs2281617:C/C Wild
rs510769:C/T Het

**SLC6A2**
rs3785143:C/C Wild
rs12708954:C/C Wild

Reported genotype calls are all displayed with respect to the positive DNA strand. Variants indicated as homozygous (Hom) or heterozygous (Het) differ from the GRCh37/hg19 reference sequence (Wild). This report is limited to the following star-alleles: CYP2D6: *1, *2, *3, *3B, *4, *5, *6C, *6, *7, *8, *9, *10, *11, *12, *14A, *14B, *15, *17, *29, *33, *35A, *41, *45A & *46. CYP2C19: *1, *2, *3, *4B, *4, *5, *6, *7, *8, *9, *10, *12 & *17. CYP2C9: *1, *2 & *3. CYP3A5: *1 & *3. CYP3A4: *1, *8, *11, *12, *13, *16, *17 & *22. TPMT: *1, *2, *3A, *3C, *3B & *4. DPYD: *1, *2, *4, *5, *13 & rs67376798A. Any genotype identified as a default star-allele (CYP2D6 *2, CYP2C19 *1, CYP2C9 *1, CYP3A5 *3, CYP3A4 *1, TPMT *1, DPYD *1) indicates the absence only of the other alleles listed and does not imply that other variants in the gene are absent. Full allele deletions and duplications are only analyzed for the CYP2D6 gene. This test does not report polymorphisms other than those specifically listed, and mutations in other genes associated with drug metabolism will not be detected. Rare diagnostic errors may occur if variations occur in primer site locations.

## DISCLAIMER

The information presented on this report is provided as supplementary health information. The results presented are intended for use by a physician, pharmacist or other healthcare professional to advise a patient on the use of prescribed medications. This test is not a 510k cleared test, but managed by CMS and FDA under the Clinical Laboratory Improvement Amendment (CLIA) as a LDT. The ordering physician is responsible for the diagnosis and management of disease and decisions based on the data provided. Results are dependent on adequate specimen collection and processing.

## METHODOLOGY

Genomic DNA is extracted from dry buccal swabs using magnetic particle processing. DNA from patient samples are amplified with primers specific for ADRA2A, CES1, COMT, CYP2D6, DRD1, DRD3, GNB3, OPRM1 & SLC6A2 using Nested Patch PCR (Varley, et. al.). Positive and negative controls are used with each run. Patient samples, positive, and negative controls are sequenced using a MiSeq (Illumina). Sequences are analyzed using alignment and base call algorithms with Kailos Blue Software for the presence or absence of single nucleotide base changes, insertions and deletions. LR-PCR utilized for confirmation of CYP2D6 duplications and deletions. Results and recommendations are compiled as part of a medical report.

Genetic testing was performed in the Kailos Genetics CLIA facility at 601 Genome Way; Huntsville, Al. 35806. CLIA#: 01D2016114. Medical Director: Ronald McGlennen MD, FCAP, FACMG, ABMG.

This report was reviewed and approved for release by CLIA Lab Manager & Supervisor: Michele R. Erickson-Johnson, PhD, MB (ASCP)$^{CM}$

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## REFERENCES

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