Clinical Policy: Clomipramine (Anafranil)

Reference Number: PA.CP.PMN.197
Effective Date: 4.17.19
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Revision Log

Description
Clomipramine (Anafranil™) is a tricyclic antidepressant.

FDA Approved Indication(s)
Anafranil is indicated for the treatment of obsessions and compulsions in patients with obsessive-compulsive disorder (OCD).

Policy/Criteria
Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with PA Health & Wellness® that Anafranil is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Obsessive-Compulsive Disorder (must meet all)**:**

1. Diagnosis of OCD;
2. Failure of 2 selective serotonin reuptake inhibitors (SSRIs), each used for at least 4 weeks at up to maximally indicated doses unless contraindicated or clinically significant adverse effects are experienced;
3. Dose does not exceed 250 mg/day.

Approval duration: 12 months

B. Autistic Disorder (off-label) (must meet all)**:**

1. Diagnosis of autistic disorder;
2. Failure of a 4 week trial of fluoxetine at up to maximally indicated doses unless contraindicated or clinically significant adverse effects are experienced;
3. Dose does not exceed 250 mg/day.

Approval duration: 12 months

C. Other diagnoses/indications:

1. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53 for Medicaid

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II. Continued Therapy

A. All Indications in Section I (must meet all)**:**

1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.LTSS.PHAR.01) applies;
2. Member is responding positively to therapy;

3. If request is for a dose increase, new dose does not exceed :
   a. OCD or autistic disorder: 250 mg/day;

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.LTSS.PHAR.01) applies.
   Approval duration: Duration of request or 12 months (whichever is less); or
2. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off-label use policy – refer to PA.CP.PMN.53

B. Premature Ejaculation

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

FDA: Food and Drug Administration
OCD: obsessive-compulsive disorder
SSRI: selective serotonin reuptake inhibitor

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
citalopram (Celexa®)	OCD*: 40 mg PO/day	40 mg/day
escitalopram (Lexapro®)	OCD*: 20 mg PO/day	40 mg/day
fluoxetine (Prozac®)	OCD: 20-60 mg PO/day Autistic disorder*: 20-40 mg PO/day	80 mg/day
fluvoxamine (Luvox®)	OCD: 100-200 mg PO/day	300 mg/day
paroxetine (Paxil®, Pexeva®)	OCD: 40-60 mg PO/day	60 mg/day
sertraline (Zoloft®)	OCD: 50-200 mg PO/day	200 mg/day

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.
**Off-label*

Appendix C: Contraindications

- Contraindication(s): coadministration with an MAO, including linezolid and intravenous methylene blue, or within 14 days of MAOI discontinuation due to increase risk of serotonin syndrome, hypersensitivity to clomipramine or other tricyclic antidepressants, and during the acute recovery period after a myocardial infarction,
- Boxed Warning(s): Antidepressants increased the risk compared to placebo of suicidal thinking and behavior in children, adolescents, and young adults in short-term studies of major depressive disorder and other psychiatric disorders. Anyone considering the use of clomipramine hydrochloride or any other antidepressant in a child, adolescent, or young adult must balance this risk with the clinical need. Short-term studies did not show an increase in the risk of suicidality with antidepressants compared to placebo in adults beyond age 24; there was a reduction in risk with antidepressants compared to placebo in adults aged 65 and older. Depression and certain other psychiatric disorders are themselves associated with increases in the risk of suicide. Patients of all ages who are started on antidepressant therapy should be monitored appropriately and observed closely for clinical worsening, suicidality, or unusual changes in behavior. Families and caregivers should be advised of the need for close observation and communication with the prescriber. Clomipramine hydrochloride is not approved for use in pediatric patients except for patients with obsessive compulsive disorder.

Appendix D: General Information

- Contraindications:
  - Concurrent use with a monoamine oxidase inhibitor or within 14 days of stopping a monoamine oxidase inhibitor due to the increased risk of serotonin syndrome
  - Concurrent use with linezolid or intravenous methylene blue due to the increased risk of serotonin syndrome
  - Use during the acute recovery period after a myocardial infarction due to cardiovascular effects (e.g., decrease in blood pressure, tachycardia, electrocardiogram changes)
- Per the American Psychiatric Association guidelines for OCD, first-line therapies are serotonin reuptake inhibitors, which include clomipramine and all SSRIs. SSRIs are generally preferred prior to clomipramine due to their better safety profile.
  - While some meta-analyses of placebo-controlled trials suggest greater efficacy for clomipramine than for fluoxetine, fluvoxamine, and sertraline, the results of head-to-head trials directly comparing clomipramine and SSRIs do not support this.
- Per the American Academy of Child and Adolescent Psychiatry guidelines for autism spectrum disorder, pharmacotherapy may be used when there is a specific target symptom or comorbid condition. Clomipramine and fluoxetine are both serotonin reuptake inhibitors which have been shown to decrease repetitive behaviors in randomized controlled trials.
  - Citalopram is another serotonin reuptake inhibitor which was evaluated in a randomized controlled trial; however, there was no significant difference in repetitive behaviors compared to placebo.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose

OCD	Adults: Initially 25 mg PO QD; increase as tolerated to 100 mg during the first 2 weeks Pediatrics: Initially 25 mg PO QD; increase as tolerated to 3 mg/kg or 100 mg, whichever is smaller, during the first 2 weeks	Adults: 250 mg/day Pediatrics: 3 mg/kg/ day or 200 mg/day, whichever is smaller
Autistic disorder*	Adults: Initially 25 mg PO QD; increase if needed to 75-100 mg Pediatrics: Initially 25 mg PO QD; increase if needed to 3 mg/kg or 200 mg, whichever is smaller	Adults: 250 mg/day Pediatrics: 3 mg/kg/ day or 200 mg/day, whichever is smaller

**Off-label*

VI. Product Availability

Capsules: 25 mg, 50 mg, 75 mg

VII. References

1. Anafranil Prescribing Information. Hazelwood, MO: Mallinckrodt Inc; September 2018. Available at: https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=4074b555-7635-41a9-809d-fae3b3610059. Accessed February 14, 2019.
2. Koran LM, Hanna GL, Hollandar E, et al. Practice guideline for the treatment of patients with obsessive-compulsive disorder. Arlington, VA: American Psychiatric Association; July 2007. Available at: http://www.psychiatryonline.org/guidelines. Accessed March 5, 2018.
3. Dixon L, Perkins D, Calmes C. Guideline watch (March 2013): practice guideline for the treatment of patients with obsessive-compulsive disorder. Arlington, VA: American Psychiatric Association; March 2013. Available at: http://www.psychiatryonline.org/guidelines. Accessed February 14, 2019
4. Volkmar F, Siegel M, Woodbury-Smith M, et al. Practice parameter for the assessment and treatment of children and adolescents with autism spectrum disorder. J Am Acad Child Adolesc Psychiatry. 2014; 53(2): 237-257.
5. American Geriatrics Society 2019 Beers Criteria Update Expert Panel: American Geriatrics Society 2019 Updated AGS Beers Criteria for Potentially Inappropriate Medication Use in Older Adults. J Am Geriatr Soc 2019; 00:1-21,2019

Reviews, Revisions, and Approvals	Date	P&T Approval Date
New policy created	04.17.19	