

Clinical Policy: Clomipramine (Anafranil)

Reference Number: HIM.PA.149

Effective Date: 03.13.18

Last Review Date: 05.18

Line of Business: HIM

[Revision Log](#)

See [Important Reminder](#) at the end of this policy for important regulatory and legal information.

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 Centene Corporation[®] 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. Premature Ejaculation (off-label) (must meet all):

1. Diagnosis of premature ejaculation;
2. Failure of 2 of the following SSRIs: fluoxetine, paroxetine, or sertraline, each used at up to maximally indicated doses unless contraindicated or clinically significant adverse effects are experienced;
3. Dose does not exceed 25 mg prior to intercourse (no more than 4 capsules/month).

Approval duration: 12 months

D. Other diagnoses/indications

1. Refer to HIM.PHAR.21 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

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

1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
2. Member is responding positively to therapy;
3. If request is for a dose increase, new dose does not exceed (a or b):
 - a. OCD or autistic disorder: 250 mg/day;
 - b. Premature ejaculation: 25 mg prior to intercourse (no more than 4 capsules/month).

Approval duration: 12 months

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

1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.

Approval duration: Duration of request or 12 months (whichever is less); or

2. Refer to HIM.PHAR.21 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

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 – HIM.PHAR.21 or evidence of coverage documents.

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 Premature ejaculation*: 5-20 mg PO/day	80 mg/day
fluvoxamine (Luvox [®])	OCD: 100-200 mg PO/day	300 mg/day

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
paroxetine (Paxil [®] , Pexeva [®])	OCD: 40-60 mg PO/day Premature ejaculation*: 10-40 mg PO/day or 20 mg PO 3-4 hours before intercourse	60 mg/day
sertraline (Zoloft [®])	OCD: 50-200 mg PO/day Premature ejaculation*: 25-200 mg PO/day or 50 mg PO 4-8 hours before intercourse	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: 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.
- Per the American Urological Association guidelines for premature ejaculation, the following serotonin reuptake inhibitors have demonstrated benefit over placebo in clinical trials: fluoxetine, paroxetine, sertraline, and clomipramine.
 - Studies suggest that nefazodone, citalopram, and fluvoxamine, on the other hand, are ineffective for premature ejaculation.
 - Both continuous (daily) and situational (prior to intercourse) dosing regimens are used to manage premature ejaculation. One has not been shown to be more effective than the other.

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
Premature ejaculation*	25-50 mg PO QD or 25 mg PO 4-24 hours prior to intercourse**	See regimen

*Off-label

**Note: Only the situational (prior to intercourse) dosing regimen is covered

VI. Product Availability

Capsules: 25 mg, 50 mg, 75 mg

VII. References

1. Anafranil Prescribing Information. Hazelwood, MO: Mallinckrodt Inc; June 2014. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/019906s040lbl.pdf. Accessed March 5, 2018.
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 March 5, 2018.
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. Montague DK, Jarow J, Broderick GA, et al. AUA guideline on the pharmacologic management of premature ejaculation. J Urol. 2004; 172(1): 290-294.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created	03.13.18	05.18

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted

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CLINICAL POLICY
Clomipramine



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