MASSACHUSETTS

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Medical Policy

Photodynamic Therapy for Choroidal Neovascularization

Table of Contents

Policy Number: 599

BCBSA Reference Number: 9.03.08 (For Plan internal use only)
NCD/LCD: National Coverage Determination (NCD) for Photodynamic Therapy (OPT) (80.2)

Related Policies

Intraocular Radiotherapy for Age-Related Macular Degeneration, #610

Policy

Commercial Members: Managed Care (HMO and POS), PPO, and Indemnity

Verteporfin photodynamic therapy as monotherapy may be considered **MEDICALLY NECESSARY** as a treatment of:

- Choroidal neovascularization (CNV) associated with age-related macular degeneration, or
- Pathologic myopia, or
- Presumed ocular histoplasmosis
- Chronic central serous chorioretinopathy, or
- Choroidal hemangioma.

Verteporfin photodynamic therapy is considered **INVESTIGATIONAL** as monotherapy for other ophthalmologic disorders.

Verteporfin photodynamic therapy is considered **INVESTIGATIONAL** when used in combination with one or more of the antivascular endothelial growth factor therapies: pegaptanib (Macugen®), ranibizumab (Lucentis®), bevacizumab (Avastin®), or aflibercept (Eylea™) as a treatment of:

- CNV associated with age-related macular degeneration,
- Pathologic myopia,
- Presumed ocular histoplasmosis,
- Central serous chorioretinopathy,
- Choroidal hemangioma, or
- For other ophthalmologic disorders.

Medicare HMO Blue℠ and Medicare PPO Blue℠ Members

Medical necessity criteria and coding guidance can be found through the link below.

National Coverage Determinations (NCDs)

National Coverage Determination (NCD) for Photodynamic Therapy (OPT) (80.2)

Note: To review the specific NCD, please remember to click "accept" on the CMS licensing agreement at the bottom of the CMS webpage.

Prior Authorization Information

Inpatient

- For services described in this policy, precertification/preauthorization **IS REQUIRED** if the procedure is performed **inpatient**.

Outpatient

- For services described in this policy, see below for situations where prior authorization **might be required** if the procedure is performed **outpatient**.

	Outpatient
Commercial Managed Care (HMO and POS)	Prior authorization is **not required**.
Commercial PPO and Indemnity	Prior authorization is **not required**.
Medicare HMO Blue℠	Prior authorization is **not required**.
Medicare PPO Blue℠	Prior authorization is **not required**.

CPT Codes / HCPCS Codes / ICD Codes

Inclusion or exclusion of a code does not constitute or imply member coverage or provider reimbursement. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage as it applies to an individual member.

Providers should report all services using the most up-to-date industry-standard procedure, revenue, and diagnosis codes, including modifiers where applicable.

The following codes are included below for informational purposes only; this is not an all-inclusive list.

The above medical necessity criteria MUST be met for the following codes to be covered for Commercial Members: Managed Care (HMO and POS), PPO, and Indemnity:

CPT Codes

CPT codes:	Code Description
67221	Destruction of localized lesions of choroid (e.g., choroidal neovascularization); photodynamic therapy (includes intravenous infusion)
67225	Destruction of localized lesions of choroid (e.g., choroidal neovascularization); photodynamic therapy, second eye, at single session (list separately in addition to code

The following ICD Diagnosis Codes are considered medically necessary when submitted with the CPT codes above if medical necessity criteria are met:

ICD-10 Diagnosis Codes

ICD-10-CM Diagnosis codes:	Code Description
B39.9	Histoplasmosis, unspecified
D18.09	Hemangioma of other sites
H32	Chorioretinal disorders in diseases classified elsewhere
H35.051	Retinal neovascularization, unspecified, right eye

H35.052	Retinal neovascularization, unspecified, left eye
H35.053	Retinal neovascularization, unspecified, bilateral
H35.059	Retinal neovascularization, unspecified, unspecified eye
H35.30	Unspecified macular degeneration
H35.3110	Nonexudative age-related macular degeneration, right eye, stage unspecified
H35.3111	Nonexudative age-related macular degeneration, right eye, early dry stage
H35.3112	Nonexudative age-related macular degeneration, right eye, intermediate dry stage
H35.3113	Nonexudative age-related macular degeneration, right eye, advanced atrophic without subfoveal involvement
H35.3114	Nonexudative age-related macular degeneration, right eye, advanced atrophic with subfoveal involvement
H35.3120	Nonexudative age-related macular degeneration, left eye, stage unspecified
H35.3121	Nonexudative age-related macular degeneration, left eye, early dry stage
H35.3122	Nonexudative age-related macular degeneration, left eye, intermediate dry stage
H35.3123	Nonexudative age-related macular degeneration, left eye, advanced atrophic without subfoveal involvement
H35.3124	Nonexudative age-related macular degeneration, left eye, advanced atrophic with subfoveal involvement
H35.3130	Nonexudative age-related macular degeneration, bilateral, stage unspecified
H35.3131	Nonexudative age-related macular degeneration, bilateral, early dry stage
H35.3132	Nonexudative age-related macular degeneration, bilateral, intermediate dry stage
H35.3133	Nonexudative age-related macular degeneration, bilateral, advanced atrophic without subfoveal involvement
H35.3134	Nonexudative age-related macular degeneration, bilateral, advanced atrophic with subfoveal involvement
H35.3190	Nonexudative age-related macular degeneration, unspecified eye, stage unspecified
H35.3191	Nonexudative age-related macular degeneration, unspecified eye, early dry stage
H35.3192	Nonexudative age-related macular degeneration, unspecified eye, intermediate dry stage
H35.3193	Nonexudative age-related macular degeneration, unspecified eye, advanced atrophic without subfoveal involvement
H35.3194	Nonexudative age-related macular degeneration, unspecified eye, advanced atrophic with subfoveal involvement
H35.3210	Exudative age-related macular degeneration, right eye, stage unspecified
H35.3211	Exudative age-related macular degeneration, right eye, with active choroidal neovascularization
H35.3212	Exudative age-related macular degeneration, right eye, with inactive choroidal neovascularization
H35.3213	Exudative age-related macular degeneration, right eye, with inactive scar
H35.3220	Exudative age-related macular degeneration, left eye, stage unspecified
H35.3221	Exudative age-related macular degeneration, left eye, with active choroidal neovascularization
H35.3222	Exudative age-related macular degeneration, left eye, with inactive choroidal neovascularization
H35.3223	Exudative age-related macular degeneration, left eye, with inactive scar
H35.3230	Exudative age-related macular degeneration, bilateral, stage unspecified
H35.3231	Exudative age-related macular degeneration, bilateral, with active choroidal neovascularization
H35.3232	Exudative age-related macular degeneration, bilateral, with inactive choroidal neovascularization
H35.3233	Exudative age-related macular degeneration, bilateral, with inactive scar
H35.3290	Exudative age-related macular degeneration, unspecified eye, stage unspecified

H35.3291	Exudative age-related macular degeneration, unspecified eye, with active choroidal neovascularization
H35.3292	Exudative age-related macular degeneration, unspecified eye, with inactive choroidal neovascularization
H35.3293	Exudative age-related macular degeneration, unspecified eye, with inactive scar
H35.711	Central serous chorioretinopathy, right eye
H35.712	Central serous chorioretinopathy, left eye
H35.713	Central serous chorioretinopathy, bilateral
H35.719	Central serous chorioretinopathy, unspecified eye
H44.20	Degenerative myopia, unspecified eye
H44.21	Degenerative myopia, right eye
H44.22	Degenerative myopia, left eye
H44.23	Degenerative myopia, bilateral
H44.2A1	Degenerative myopia with choroidal neovascularization, right eye
H44.2A2	Degenerative myopia with choroidal neovascularization, left eye
H44.2A3	Degenerative myopia with choroidal neovascularization, bilateral eye
H44.2A9	Degenerative myopia with choroidal neovascularization, unspecified eye
H44.2B1	Degenerative myopia with macular hole, right eye
H44.2B2	Degenerative myopia with macular hole, left eye
H44.2B3	Degenerative myopia with macular hole, bilateral eye
H44.2B9	Degenerative myopia with macular hole, unspecified eye
H44.2C1	Degenerative myopia with retinal detachment, right eye
H44.2C2	Degenerative myopia with retinal detachment, left eye
H44.2C3	Degenerative myopia with retinal detachment, bilateral eye
H44.2C9	Degenerative myopia with retinal detachment, unspecified eye
H44.2D1	Degenerative myopia with foveoschisis, right eye
H44.2D2	Degenerative myopia with foveoschisis, left eye
H44.2D3	Degenerative myopia with foveoschisis, bilateral eye
H44.2D9	Degenerative myopia with foveoschisis, unspecified eye
H44.2E1	Degenerative myopia with other maculopathy, right eye
H44.2E2	Degenerative myopia with other maculopathy, left eye
H44.2E3	Degenerative myopia with other maculopathy, bilateral eye
H44.2E9	Degenerative myopia with other maculopathy, unspecified eye

Description

Vision Loss

Severe vision loss can occur with ocular neovascularization, the growth of abnormal blood vessels in the retina or choroid. Neovascularization occurs in a number of ocular diseases, including age-related macular degeneration.

Age-Related Macular Degeneration

Age-related macular degeneration is a degenerative disease of the retina that results in loss of central vision. Two distinctive forms, known as dry and wet degeneration, may be observed. The dry form (also known atrophic or areolar) is more common and is often a precursor of the wet form (also known as exudative neovascular or disciform). The wet form is more devastating and characterized by serous or hemorrhagic detachment of the retinal pigment epithelium and development of choroidal neovascularization, which greatly increases the risk of developing severe irreversible loss of vision. Choroidal neovascularization is categorized as classic or occult. Classic choroidal neovascularization appears as an initial lacy pattern of hyperfluorescence followed by more irregular patterns as the dye leaks into the subretinal space. Occult choroidal neovascularization lacks the characteristic angiographic pattern. Classic choroidal neovascularization carries a worse prognosis for vision than occult choroidal

neovascularization, suggesting that the proliferative response that obscures new vessels may also favorably alter the clinical course of age-related macular degeneration.

Pathologic Myopia
Pathologic myopia refers to an abnormal elongation of the eye associated with severe near-sightedness. It generally occurs among people older than 30 years of age and can result in a progressive, severe loss of vision, frequently related to the development of choroidal neovascularization. Verteporfin photodynamic therapy has also been investigated in patients with choroidal neovascularization related to pathologic myopia. Antivascular endothelial growth factor therapy is now considered a first-line intervention in patients with myopic choroidal neovascularization.

Presumed Ocular Histoplasmosis
Presumed ocular histoplasmosis may be the second most common cause of blindness in patients younger than 50 years of age in certain endemic areas (Ohio and Mississippi River Valleys in the United States). This condition is characterized by a positive skin test for histoplasmosis, miliary opacities of the lungs, tiny choroidal scars, peripapillary disruption of the choriocapillaris, and exudation or hemorrhage from choroidal lesions in or near the macula. The condition is asymptomatic and benign, unless the choroidal neovascularization lesions, which may develop many years after chorioretinal scarring has taken place, affect the macula.

Central Serous Chorioretinopathy
Central serous chorioretinopathy refers to an idiopathic disease in which there is a serous detachment of the macula due to leakage of fluid from the choriocapillaris through the retinal pigment epithelium. This condition is avascular; however, neovascularization can occur as a secondary complication. In most cases, central serous chorioretinopathy resolves spontaneously in 3 to 4 months. However, in a few cases, chronic progression or recurrence can lead to the progressive decline of visual acuity. Central serous chorioretinopathy has been treated with medication and laser photocoagulation, but these treatments have limited efficacy. Multiple definitions have been used in the literature to classify central serous chorioretinopathy as acute or chronic based cutoff time points (eg, persistent fluid for <3, 4 or 6 months) or less frequently based on the timing of treatment. For example, acute central serous chorioretinopathy defined as the first attempted treatment to improve visual acuity, and chronic central serous chorioretinopathy is defined as being refractory to treatment. Further, multiple verteporfin photodynamic therapy strategies that use either reduced-dose or half-fluency have been evaluated for the treatment of central serous chorioretinopathy because full-dose verteporfin photodynamic therapy used in age-related macular degeneration has shown a potentially higher risk of developing choroidal ischemia and retinal atrophic changes.

Polypoidal Choroidal Vasculopathy
Polypoidal choroidal vasculopathy arises primarily from abnormal choroidal circulation, resulting in characteristic lesions comprising well-defined vascular networks of vessels ending in polyp-like structures. A less common subtype is polypoidal choroidal neovascularization, and it may be considered a subtype of age-related macular degeneration. Eyes that develop a cluster of grape-like polypoidal dilations are at high risk for severe vision loss.

Choroidal Hemangioma
Choroidal hemangioma is an uncommon, benign vascular tumor, manifesting as an orange-red mass in the posterior pole of the eye. Visual loss may be progressive and irreversible because of chronic foveal detachment.

Angioid Streaks
Angioid streaks result from crack-like breaks in the Bruch membrane (the innermost layer of the choroid) and occur in patients spontaneously or due to blunt trauma or associated with some systemic diseases such as pseudoxanthoma elasticum, Paget disease of bone, or sickle hemoglobinopathy. Vision loss in eyes with angioid streaks occurs most frequently as a result of choroidal neovascularization.

Treatment
Available therapeutic options for choroidal neovascularization include antivascular endothelial growth factor inhibitors, verteporfin photodynamic therapy, antioxidants, thermal laser photocoagulation, and corticosteroids. The safety and efficacy of each treatment depends on the form and location of the neovascularization.

Verteporfin photodynamic therapy is a treatment modality designed to selectively occlude ocular choroidal neovascular tissue. The therapy is a 2-step process, consisting of an injection of the photosensitizer verteporfin, followed 15 minutes later by laser treatment to the targeted sites of retinal neovascularization. The laser treatment selectively damages the vascular endothelium and occludes the neovacularized tissue. Patients may be retreated if leakage from choroidal neovascularization persists.

Monotherapy with vascular endothelial growth factor inhibitors is now standard treatment of choroidal neovascularization due to age-related macular degeneration and pathologic myopia. Combining verteporfin photodynamic therapy with antivascular endothelial growth factor inhibitors, concurrently or sequentially, has a biologic basis and has been investigated in multiple trials particularly in the treatment of choroidal neovascularization due to age-related macular degeneration and pathologic myopia.

The use of verteporfin photodynamic therapy in choroidal neovascularization has decreased substantially with the availability of antivascular endothelial growth factor therapy. Subsequent to U.S. Food and Drug Administration (FDA) approval of verteporfin photodynamic therapy in 2000, the FDA approved pegaptanib in 2004 and ranibizumab in 2006 for treatment of age-related macular degeneration related choroidal neovascularization. The approval of pegaptanib was based on a sham-controlled RCT[1,2,] while ranibizumab was approved based on a head-to-head comparison with verteporfin photodynamic therapy in the Anti-VEGF Antibody for the Treatment of Predominantly Classic Choroidal Neovascularization in Age-Related Macular Degeneration (ANCHOR) trial.[3,] Intravitreal injections of antivascular endothelial growth factor drugs such as ranibizumab and bevacizumab have shown superior efficacy compared with verteporfin photodynamic therapy in multiple head-to-head trials. Currently, verteporfin photodynamic therapy is used for patients in whom vascular endothelial growth factor inhibitors are contraindicated or for those who fail to benefit from vascular endothelial growth factor inhibitors.

Summary
Verteporfin photodynamic therapy is a treatment modality designed to selectively occlude ocular choroidal neovascular tissue. The therapy is a 2-step process, consisting of an injection of the photosensitizer verteporfin, followed 15 minutes later by laser treatment to the targeted sites of retinal neovascularization. The laser treatment selectively damages the vascular endothelium, thereby occluding choroidal neovascularization tissue. Patients may be retreated if leakage from choroidal neovascularization persists.

Age-Related Macular Degeneration
For individuals who have classic choroidal neovascularization due to age-related macular degeneration who receive verteporfin photodynamic therapy, the evidence includes randomized controlled trials (RCTs) and systematic reviews of controlled trials. Relevant outcomes are symptoms, change in disease status, functional outcomes, and quality of life. Multiple RCTs have supported the superiority of verteporfin photodynamic therapy in reducing vision loss and decreasing retinal thickness compared with placebo or sham procedure. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have choroidal neovascularization due to age-related macular degeneration who receive verteporfin photodynamic therapy plus antivascular endothelial growth factor therapy, the evidence includes 2 confirmatory RCTs (and their multiple analyses), multiple smaller RCTs, and a meta-analysis of existing trials. Relevant outcomes are symptoms, change in disease status, functional outcomes, and quality of life. This evidence does not demonstrate improvements in visual acuity using combination therapy compared with antivascular endothelial growth factor monotherapy. Combination therapy may reduce the number of intravitreal injections needed, but this result has not been consistently

reported across studies. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have choroidal neovascularization due to age-related macular degeneration who receive verteporfin photodynamic therapy plus corticosteroids and/or antivascular endothelial growth factor therapy, the evidence includes 3 small RCTs. Relevant outcomes are symptoms, change in disease status, functional outcomes, and quality of life. The evidence does not demonstrate improvements in visual acuity with combination therapy. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Pathologic Myopia
For individuals who have choroidal neovascularization due to pathologic myopia who receive verteporfin photodynamic therapy, the evidence includes a subgroup analysis from a large RCT. Relevant outcomes are symptoms, change in disease status, functional outcomes, and quality of life. The subgroup analysis showed verteporfin photodynamic therapy was more effective than placebo in preventing vision loss at one year but not in the second year. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have choroidal neovascularization due to pathologic myopia who receive verteporfin photodynamic therapy plus antivascular endothelial growth factor therapy, the evidence includes a small RCT and a retrospective cohort study. Relevant outcomes are symptoms, change in disease status, functional outcomes, and quality of life. The single RCT was likely underpowered to detect a clinically meaningful change in visual acuity outcomes. The retrospective cohort study did not demonstrate improvements in visual acuity with combination treatment. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Presumed Ocular Histoplasmosis
For individuals who have choroidal neovascularization due to presumed ocular histoplasmosis who receive verteporfin photodynamic therapy, the evidence includes a small RCT and a prospective cohort study. Relevant outcomes are symptoms, change in disease status, functional outcomes, and quality of life. Lack of a control arm in the prospective cohort study and 50% lost to follow-up in the RCT preclude a meaningful interpretation of data of observed improvements in visual acuity outcomes. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Central Serous Chorioretinopathy
For individuals who have choroidal neovascularization due to acute central serous chorioretinopathy who receive verteporfin photodynamic therapy, the evidence includes 2 RCTs. Relevant outcomes are symptoms, change in disease status, functional outcomes, and quality of life. Although the evidence has demonstrated that full and reduced doses of verteporfin photodynamic therapy result in a small improvement in visual acuity outcomes, the improvements did not meet clinically meaningful thresholds. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have choroidal neovascularization due to chronic central serous chorioretinopathy who receive verteporfin photodynamic therapy, the evidence includes multiple retrospective studies. Relevant outcomes are symptoms, change in disease status, functional outcomes, and quality of life. Although this relatively large body of retrospective studies has shown that half-dose verteporfin photodynamic therapy yields positive functional and anatomic outcomes while, at the same time, reducing the potential adverse events associated with conventional verteporfin photodynamic therapy, data from RCTs for multiple verteporfin photodynamic therapy strategies are lacking. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Polypoidal Choroidal Vasculopathy

For individuals who have choroidal neovascularization due to polypoidal choroidal vasculopathy who receive verteporfin photodynamic therapy, the evidence includes several prospective cohort studies and a meta-analysis of 2 RCTs. Relevant outcomes are symptoms, change in disease status, functional outcomes, and quality of life. Prospective cohort studies have reported favorable anatomic and visual acuity outcomes for patients treated with verteporfin photodynamic therapy. However, RCTs comparing verteporfin photodynamic therapy with antivascular endothelial growth factor therapies have reported no statistically significant differences in visual acuity outcomes. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have choroidal neovascularization due to polypoidal choroidal vasculopathy who receive verteporfin photodynamic therapy plus antivascular endothelial growth factor therapy, the evidence includes 2 small RCTs, a meta-analysis, and 2 retrospective cohort studies. Relevant outcomes are symptoms, change in disease status, functional outcomes, and quality of life. Results of the 2 RCTs failed to demonstrate statistically significant differences in visual acuity outcomes. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Choroidal Hemangioma
For individuals who have choroidal neovascularization due to choroidal hemangioma who receive verteporfin photodynamic therapy, the evidence includes a systematic review of case series and a prospective cohort study. Relevant outcomes are symptoms, change in disease status, functional outcomes, and quality of life. Although the prospective cohort suggested a favorable effect of verteporfin photodynamic therapy on various visual acuity and anatomic outcomes in patients with choroidal hemangioma, data from RCTs are lacking. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Angioid Streaks
For individuals who have choroidal neovascularization due to angioid streaks who receive verteporfin photodynamic therapy, the evidence includes a systematic review of case series. Relevant outcomes are symptoms, change in disease status, functional outcomes, and quality of life. Data from multiple case series have shown conflicting results for visual acuity outcomes. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Inflammatory Chorioretinal Conditions
For individuals who have choroidal neovascularization due to inflammatory chorioretinal conditions who receive verteporfin photodynamic therapy, the evidence includes a systematic review of case reports. Relevant outcomes are symptoms, change in disease status, functional outcomes, and quality of life. Methodologic limitations limit the conclusions drawn from 15 case reports (total N=115 patients) of multiple disease indications. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Policy History

Date	Action
4/2022	Annual policy review. Description, summary, and references updated. Policy statements unchanged.
4/2021	Annual policy review. Description, summary, and references updated. Policy statements unchanged.
5/2020	Annual policy review. Description, summary, and references updated. Policy statements unchanged.
4/2019	Annual policy review. Description, summary, and references updated. Policy statements unchanged.
5/2018	Annual policy review. Description, summary, and references updated. Policy statements unchanged. Prior Authorization Information reformatted.
10/2017	Clarified coding information.

5/2017	Annual policy review. Description, summary, and references updated. Policy statements unchanged.
10/2016	Clarified coding information.
4/2016	Annual policy review. New references added.
8/2015	Annual policy review. New references added.
9/2014	Annual policy review. New references added.
6/2014	Updated Coding section with ICD10 procedure and diagnosis codes. Effective 10/2015.
12/2013	Removed ICD-9 diagnosis codes 363.43 and 367.1 as they do not meet the intent of the policy and added 228.09 and 362.41 as they do meet the intent of the policy.
7/2013	Coverage for Medicare Advantage clarified. Effective 4/3/2013.
3/2013	Annual policy review. New medically necessary indications described. Effective 3/1/2013.
11/2011-4/2012	Medical policy ICD 10 remediation: Formatting, editing and coding updates. No changes to policy statements.
2/2011	Reviewed - Medical Policy Group - Psychiatry and Ophthalmology. No changes to policy statements.
4/2010	Annual policy review. No changes to policy statements.
2/2010	Reviewed - Medical Policy Group - Psychiatry and Ophthalmology. No changes to policy statements.
12/2009	Annual policy review. No changes to policy statements.
2/2009	Reviewed - Medical Policy Group - Psychiatry and Ophthalmology. No changes to policy statements.
2/2008	Reviewed - Medical Policy Group - Psychiatry and Ophthalmology. No changes to policy statements.
2/2007	Reviewed - Medical Policy Group - Psychiatry and Ophthalmology. No changes to policy statements.

Information Pertaining to All Blue Cross Blue Shield Medical Policies

Click on any of the following terms to access the relevant information:
Medical Policy Terms of Use
Managed Care Guidelines
Indemnity/PPO Guidelines
Clinical Exception Process
Medical Technology Assessment Guidelines

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