

Policy Name	Clinical Policy – Verteporfin (Visudyne)
Policy Number	1345.00
Department	Clinical Product & Development
Subcategory	Medical Management
Original Approval Date	04/07/2021
Current MPC/CCO Approval Date	04/03/2024
Current Effective Date	06/01/2024

Company Entities Supported (Select All that Apply)

- X Superior Vision Benefit Management
 X Superior Vision Services
 X Superior Vision of New Jersey, Inc.
 X Block Vision of Texas, Inc. d/b/a Superior Vision of Texas
 X Davis Vision
- Collectively referred to as 'Versant Health' or 'the Company'

Acronyms	
ARMD	Age Related Macular Degeneration
Anti- VEGF	Vascular Endothelial Growth Factor Receptor Antagonists
CCSC	Chronic Central Serous Choroidopathy
CNV	Choroidal Neovascularization
IVFA	Intravenous Fluorescein Angiography
PDT	Photodynamic Therapy
POHS	Presumed Ocular Histoplasmosis Syndrome

PURPOSE

To provide the clinical criteria to support the indication(s) for verteporfin photodynamic therapy (PDT). Applicable procedure codes are also defined.



D	$\boldsymbol{\cap}$	 IC	v
Г	v	v	•

A. BACKGROUND

Verteporfin (Visudyne) photodynamic therapy (PDT) selectively binds to chorioretinal vascular structures and, in response to subsequent laser therapy, results in occlusion of choroidal vascular anomalies¹ Despite its efficacy, PDT has been replaced largely by Anti-VEGF agents.² However, PDT still has a role in patients who are unresponsive or intolerant to Anti-VEGF agents.

B. Medically Necessary

- 1. PDT is effective in the treatment of the following retinal disorders:
 - a. Age related macular degeneration due to classic choroidal neovascularization (CNV)³
 - b. Degenerative myopia with choroidal neovascularization⁴
 - c. Central serous retinopathy
 - d. Chronic central serous choroidopathy (CCSR)⁵
 - e. Choroidal hemangioma⁶
 - f. Choroidal Metastasis⁷
 - g. Presumed Ocular Histoplasmosis Syndrome8
 - h. Polypoidal choroidal vasculopathy9
 - i. Peripapillary choroidal neovascularization and related disorders¹⁰
 - i. Other choroidal vascular anomalies
- 2. Initial therapy will be considered medically necessary when the following criteria are met:
 - a. Any of the above diagnoses are present; and,
 - b. Patient is 18 years or older.
- 3. Some patients will require retreatment at three (3) month intervals. Retreatment is considered medically necessary when:
 - a. All requirements for initial therapy are still present; and,
 - b. The initial therapy has documented improvement in visual acuity; and,
 - c. Clinical evidence of continued leakage including test results, as applicable.

² Rosenfeld, 2006, Kim, 2006, Brown, 2009, Wong, 2015, and Kang, 2013

⁵ Yannuzzi, 2003, Ober, 2005, Erikitola, 2014, Chan, 2008, Senturk, 2011, Fujita 2011,12, Ergun, 2004

¹ Newman, 2016

³ Schmidt-Erfurt, 2007, Bressler, 2001, Blumenkranz, 2002, Blinder, 2003, Rosenfeld, 2004, Larsen, 2012.

⁴ Wolf, 2014, Wong, 2015

⁶ Alshehri, 2023, Tsipursky, 2011, Ho, 2018, Boixadera, 2009, Blasi, 2010, Porrini, 2003, Singh, 2004, Shields, 2020

⁷ Shields, 2020 (2 articles).

⁸ Busquets, MA, 2003, Ramaiya, 2013

⁹ Uyama, 2002, Eandi, 2007

¹⁰ Jutley, 2011, Rosenblatt, 2005



C. Not Medically Necessary

The combined therapies of PDT plus Anti-VEGF therapy or PDT plus corticosteroid therapy have not demonstrated increased efficacy. Therefore, the combined therapies of PDT and Anti-VEGF or PDT and corticosteroid therapy may not be considered medically necessary¹¹

D. Documentation

Medical necessity must be supported by adequate and complete documentation in the patient's medical record that describes the procedure and the medical rationale. For early retreatment, medical documentation of test results may be required. For any retrospective review, a full operative report and the clinical care plan is needed.

All items must be available upon request to initiate or sustain previous payments. Every page of the record must be legible and include appropriate patient identification information (e.g., complete name, date(s) of service). Services provided or ordered must be authenticated by the physician, in a handwritten or electronic signature. Stamped signatures are not acceptable.

E. Procedural Detail

CPT and HCPCS Codes			
J3396	Injection, verteporfin, 0.1 mg		
67221	Destruction of localized lesion of choroid (e.g., choroidal neovascularization) photodynamic therapy (includes intravenous infusion)		
67225	Destruction of localized lesion of choroid (e.g., choroidal neovascularization); photodynamic therapy, second eye, at single session (List separately in addition to code for primary eye treatment)		

DISCLAIMER and COPYRIGHTS

This clinical policy is provided for information purposes only and does not constitute medical advice. Versant Health, Inc., and its affiliates (the "Company") do not provide health care services and cannot guarantee any results or outcomes. The treating provider is solely responsible for determining what services or treatments to provide to their patients. Patients (members) should always consult their doctor before making any decisions about medical care.

Subject to applicable law, compliance with this clinical policy is not a guarantee of coverage or payment. Coverage is based on the terms of an individual's particular benefit plan document, which may not cover the service(s) or procedure(s) addressed in this clinical policy. The terms of the individual's specific benefit plan are always determinative.

¹¹ Tozer, 2013, Koh, 2012, Antoszyk, 2008, Tong, 2016, Piermarocchi, 2008, Maberley, 2009, Piri, 2014, Koh, 2012.



Every effort has been made to ensure that the information in this clinical policy is accurate and complete, however the Company does not guarantee that there are no errors in this policy or that the display of this file on a website is without error. The company and its employees are not liable for any errors, omissions, or other inaccuracies in the information, product, or processes disclosed herein. Neither the company nor the employees represent that the use of such information, products, or processes will not infringe on privately owned rights. In no event shall the Company be liable for direct, indirect, special, incidental, or consequential damages arising out of the use of such information, product, or process.

COMPANY'S COPYRIGHT STATEMENT Except for any copyrights described below, this clinical policy is confidential and proprietary, and no part of this clinical policy may be copied, distributed or used without Versant Health, or its applicable affiliates, express prior written approval.

AMA COPYRIGHT STATEMENT CPT© is the 2002-2024 copyright of the American Medical Association. All Rights Reserved. CPT™ is a registered trademark of the American Medical Association. Applicable FARS/DFARS Apply to Government Use. Fee schedules, relative value units, conversion factors and/or related components are not assigned by the AMA, are not part of CPT, and the AMA is not recommending their use. The AMA does not directly or indirectly practice medicine or dispense medical services. The AMA assumes no liability for data contained or not contained herein.

RELATED POLICIES	
1317	Intravitreal Injections
1326	Laser Photocoagulation

DOCUMENT HISTORY				
Approval Date	Revision	Effective Date		
04/07/2021	PTD therapy was removed from policy 1317 and republished as a separate policy.	09/01/2021		
04/06/2022	Annual review; no criteria changes.	07/01/2022		
04/12/2023	Add 3 indications for use; delete requirement for OCT or IVFA for initial treatment, add option of ICG test to retreatment criteria.	10/01/2023		
04/03/2024	Annual review; no criteria changes.	06/01/2024		



REFERENCES AND SOURCES

- 1. Alshehri WM, AlAhmadi BO, Alhumaid F, et.al. Safety and Efficacy of Photodynamic Therapy in the Treatment of Circumscribed Choroidal Hemangioma: A Systematic Review. Cureus. 2023 Dec 13;15(12): e50461. doi: 10.7759/cureus.50461. PMID: 38222120; PMCID: PMC10786325.
- 2. Antoszyk AN, Tuomi L, Chung CY, et.al. FOCUS Study Group. Ranibizumab combined with verteporfin photodynamic therapy in neovascular age-related macular degeneration (FOCUS): year 2 results. Am J Ophthalmol. 2008 May;145(5):862-74. doi: 10.1016/j.ajo.2007.12.029. Epub 2008 Mar 5. PMID: 18321465.
- 3. Blinder KJ, Bradley S, Bressler NM, et.al. Treatment of Age-related Macular Degeneration with Photodynamic Therapy study group; Verteporfin in Photodynamic Therapy study group. Effect of lesion size, visual acuity, and lesion composition on visual acuity change with and without verteporfin therapy for choroidal neovascularization secondary to age-related macular degeneration: TAP and VIP report no. 1. Am J Ophthalmol 2003; 136 (3): 407-18.
- 4. Blumenkranz MS, Bressler NM, Bressler SB, et.al. Treatment of Age-Related Macular Degeneration with Photodynamic Therapy (TAP) Study Group. Verteporfin therapy for subfoveal choroidal neovascularization in age-related macular degeneration: three-year results of an open-label extension of 2 randomized clinical trials--TAP Report no. 5. Arch Ophthalmol 2002; 120 (10): 1307-14.
- Boixadera A, García-Arumí J, Martínez-Castillo V, et.al. Prospective clinical trial evaluating the efficacy of photodynamic therapy for symptomatic circumscribed choroidal hemangioma.
 Ophthalmology. 2009 Jan;116(1):100-105.1. doi: 10.1016/j.ophtha.2008.08.029. Epub 2008 Oct 30. Erratum in: Ophthalmology. 2009 May;116(5):822. Arumí, José García [corrected to García-Arumí, José]. PMID: 18973950.
- 6. Bressler NM; Treatment of Age-Related Macular Degeneration with Photodynamic Therapy (TAP) Study Group. Photodynamic therapy of subfoveal choroidal neovascularization in agerelated macular degeneration with verteporfin: two-year results of 2 randomized clinical trials-tap report 2. Arch Ophthalmol 2001; 119 (2): 198-207.
- 7. Brown DM, Michels M, Kaiser PK, et.al. ANCHOR Study Group. Ranibizumab versus verteporfin photodynamic therapy for neovascular age related macular degeneration: Two-year results of the ANCHOR study. Ophthalmology 2009; 116: 57–65.
- 8. Busquets MA. Ocular photodynamic therapy with verteporfin for choroidal neovascularization secondary to ocular histoplasmosis syndrome. Retina 2003 Jun;23(3):299-306.
- 9. Chan WM, Lai TY, Lai RY, et.al., Safety enhanced photodynamic therapy for chronic central serous Chorioretinopathy: one –year results of a prospective study, Retina, 2008 Jan;28(1).
- Ceung CMG, Tan CS, Patalauskaite R, et al. Ranibizumab with or Without Verteporfin Photodynamic Therapy for Polypoidal Choroidal Vasculopathy: Predictors of Visual and Anatomical Response in the EVEREST II Study. Retina. 2021 Feb 1;41(2):387-392. doi: 10.1097/IAE.0000000000002902. PMID: 33475271.
- Cheng CK, Chang CK, Peng CH. Comparison of photodynamic therapy using half-dose of verteporfin or half-fluence of laser light for the treatment of chronic central serous chorioretinopathy. Retina. 2017 Feb;37(2):325-333. doi: 10.1097/IAE.000000000001138. PMID: 27429374.
- 12. Endi CM, Ober MD, Freund KB, et.al. Selective photodynamic therapy for neovascular agerelated macular degeneration with polypoidal choroidal neovascularization. Retina 2007; 27.
- 13. Ergun E, Tittl M, Stur M. Photodynamic therapy with verteporfin in subfoveal choroidal neovascularization secondary to central serous chorioretinopathy. Arch Ophthalmol. 2004 Jan;122(1):37-41. doi: 10.1001/archopht.122.1.37. PMID: 14718292.



- 14. Erikitola OC, Crosby-Nwaobi R, Lotery AJ, et.al. Photodynamic therapy for central serous chorioretinopathy. Eye. 2014;28(8):944-957. doi:10.1038/eye.2014.134.
- 15. Feenstra HMA, van Dijk EHC, Cheung CMG, et.al. Central serous chorioretinopathy: An evidence-based treatment guideline. Prog Retin Eye Res. 2024 Jan 31:101236. doi: 10.1016/j.preteyeres.2024.101236. Epub ahead of print. PMID: 38301969.
- 16. Fujita K, Shinoda K, Imamura Y, et al. Correlation of integrity of cone outer segment tips line with retinal sensitivity after half-dose photodynamic therapy for chronic central serous chorioretinopathy. Am J Ophthalmol. Sep 2012;154(3):579-585. PMID 22818904.
- 17. Fujita K, Yuzawa M, Mori R. Retinal sensitivity after photodynamic therapy with half-dose verteporfin for chronic central serous chorioretinopathy: short-term results. Retina. Apr 2011;31(4):772-778.
- 18. Gao Y, Yu T, Zhang Y, et.al. Anti-VEGF Monotherapy Versus Photodynamic Therapy and Anti-VEGF Combination Treatment for Neovascular Age-Related Macular Degeneration: A Meta-Analysis. Invest Ophthalmol Vis Sci. 2018 Aug 1;59(10):4307-4317. doi: 10.1167/iovs.17-23747. PMID: 30372759.
- 19. Gawęcki M, Kiciński K, Grzybowski A. Crossover to PDT after the unsuccessful micropulse laser treatment of central serous chorioretinopathy. Adv Ophthalmol Pract Res. 2024 Jan 23;4(1):32-38. doi: 10.1016/j.aopr.2024.01.004. PMID: 38406665; PMCID: PMC10891284.
- 20. Gelisken F, Lafout BA, Inhoffen W, et. al., Clinicopathological findings of choroidal neovascularization following verteporfin photodynamic therapy, Br J Ophthal 2004;88:207-211.
- 21. Ho Y-F, Chao A, Chen K-J, et al. (2018) Clinical outcomes and predictors of response to photodynamic therapy in symptomatic circumscribed choroidal hemangioma: A retrospective case series. PLoS ONE 13(5): e0197088. https://doi.org/10.1371/journal.pone.0197088.
- 22. Lazic R, Gabric N. Verteporfin Therapy and Intravitreal Bevacizumab Combined and Alone in Choroidal Neovascularization due to Age-Related Macular Degeneration. American Academy of Ophthamology 2007; 114:1179-1185.
- 23. I Karska-Basta I, Chrzaszcz M, Mackiewicz N, et al. Effect of photodynamic therapy with verteporfin on tumor thickness and best corrected visual acuity in patients with circumscribed choroidal hemangioma: a single-center experience. J Physiol Pharmacol. 2021 Oct;72(5). doi: 10.26402/jpp.2021.5.07. Epub 2021 Feb 12. PMID: 35158334.
- 24. Jurklies B, Anastassiou G, Ortmans S, et al. Photodynamic therapy using verteporfin in circumscribed choroidal haemangioma. Br J Ophthalmol 2003; 87: 84–89.
- 25. Jutley G, Jutley G, Tah V, et al. Treating peripapillary choroidal neovascular membranes: a review of the evidence. Eye 2011; 25: 675–681.
- 26. Kang HM, Koh HJ. Intravitreal anti-vascular endothelial growth factor therapy versus photodynamic therapy for idiopathic choroidal neovascularization. Am J Ophthalmol 2013; 155: 713–719.
- 27. Kang HM, Kim YM, Koh HJ. Five-year follow-up results of photodynamic therapy for polypoidal choroidal vasculopathy. Am J Ophthalmol. Mar 2013;155(3):438-447 e431.
- 28. Koh A, Lee WK, Chen LJ, et.al. EVEREST study: efficacy and safety of verteporfin photodynamic therapy in combination with ranibizumab or alone versus ranibizumab monotherapy in patients with symptomatic macular polypoidal choroidal vasculopathy. Retina 2012; 32: 1453–1464.
- 29. Koh AH, Chen LJ, Chen SJ, et al. Expert PCV Panel. Polypoidal choroidal vasculopathy: evidence-based guidelines for clinical diagnosis and treatment. Retina 2013; 33: 686–716.
- 30. Kraus D, Palasuberniam P, Chen B. Therapeutic Enhancement of Verteporfin-mediated Photodynamic Therapy by mTOR Inhibitors. Photochem Photobiol. 2020 Mar;96(2):358-364. doi: 10.1111/php.13187. Epub 2019 Dec 17. PMID: 31769520; PMCID: PMC7138740.



- 31. Larsen M, Schmidt-Erfurth U, Lanzetta P, et al. Verteporfin plus ranibizumab for choroidal neovascularization in age-related macular degeneration: twelve-month MONT BLANC study results. Ophthalmology. May 2012;119(5):992-1000. PMID 22424834.
- 32. Lim TH, Lai TYY, Takahashi K. et.al. EVEREST II Study Group. Comparison of Ranibizumab with or without Verteporfin Photodynamic Therapy for Polypoidal Choroidal Vasculopathy: The EVEREST II Randomized Clinical Trial. JAMA Ophthalmol. 2020 Sep 1;138(9):935-942. doi: 10.1001/jamaophthalmol.2020.2443. PMID: 32672800; PMCID: PMC7366282.
- 33. Maberley D, Canadian Retinal Trials Group. Photodynamic therapy and intravitreal triamcinolone for neovascular age-related macular degeneration: a randomized clinical trial. Ophthalmology. Nov 2009;116(11):2149-2157 e2141. PMID 19748675.
- 34. Miyamoto N, Mandai M, Oishi A, et.al. Long-term results of photodynamic therapy or ranibizumab for polypoidal choroidal vasculopathy in LAPTOP study. Br J Ophthalmol. 2019 Jun;103(6):844-848. doi: 10.1136/bjophthalmol-2018-312419. Epub 2018 Aug 4. PMID: 30077969.
- 35. Newman DK. Photodynamic Therapy: Current Role in the Treatment of Chorioretinal Conditions. Eye (2016) 30, 202-210.
- 36. Ober MD, Yannuzzi LA, Do DV, et al. Photodynamic therapy for focal retinal pigment epithelial leaks secondary to central serous chorioretinopathy. Ophthalmology. 2005;112(12):2088-2094.
- 37. Nguyen MT, Stacey AW. Photodynamic therapy for the treatment of choroidal metastases: A Case Series and Meta-analysis. Retina. 2022 Jun 1;42(6):1176-1183. doi: 10.1097/IAE.000000000003433. PMID: 35594078.
- 38. Piermarocchi S, Sartore M, Lo Giudice G, et al. Combination of photodynamic therapy and intraocular triamcinolone for exudative age-related macular degeneration and long-term chorioretinal macular atrophy. Arch Ophthalmol. Oct 2008;126(10):1367-1374. PMID 18852414.
- 39. Piri N, Ahmadieh H, Taei R, et al. Photodynamic therapy and intravitreal bevacizumab with versus without triamcinolone for neovascular age-related macular degeneration; a randomized clinical trial. J Ophthalmic Vis Res. Oct-Dec 2014;9(4):469-477. PMID 25709773.
- 40. Porrini G, Giovannini A, Amato G, et.al. Photodynamic therapy of circumscribed choroidal hemangioma. Ophthalmology 2003; 110: 674–680.
- 41. Ramaiya KJ, Blinder KJ, Ciulla T, et al. Ranibizumab versus photodynamic therapy for presumed ocular histoplasmosis syndrome. Ophthalmic Surg Lasers Imaging Retina. Jan-Feb 2013;44(1):17-21.
- 42. Rosenblatt BJ, Shah GK, Blinder K. Photodynamic therapy with verteporfin for peripapillary choroidal neovascularization. Retina 2005; 25: 33–37.
- 43. Rosenfeld PJ, VIM Study Group; Verteporfin in Minimally Classic CNV due to AMD (VIM) Two–Year Results from a Phase II Controlled Clinical Trial. Invest. Ophthalmol. Vis. Sci. 2004;45(13):2273.
- 44. Sachdeva R, Dadgostar H, Kaiser PK, et.al. (2010) Verteporfin photodynamic therapy of six eyes with retinal capillary haemangioma. Acta Ophthalmol 88: e334-e340.
- 45. Schmidt-Erfuth U, Kriechbaum K, Oldag A, Three-dimensional angiography of classic and occult lesion types in choroidal neovascularization, Inv Opth Vis Sci 2007 Apr;48(4):1751-60
- 46. Senturk F, Karacorlu M, Ozdemir H, et al. Micro perimetric changes after photodynamic therapy for central serous chorioretinopathy. Am J Ophthalmol. Feb 2011;151(2):303-309 e301. PMID 21168824.
- 47. Shields CL, Dalvin LA, Lim LA, et. al., Circumscribed Choroidal Hemangioma: Visual Outcome in the Pre-Photodynamic Therapy Era versus Photodynamic Therapy Era in 458 cases, Ophthal Retina 2020:4:100-110.
- 48. Shields CL, Khoo CTL, Mazloumi M, et.al. Photodynamic Therapy for Choroidal Metastasis Tumor Control and Visual Outcomes in 58 Cases: The 2019 Burnier International Ocular



- Pathology Society Lecture. Ophthalmol Retina. 2020 Mar;4(3):310-319. doi: 10.1016/j.oret.2019.10.009. Epub 2019 Oct 28. PMID: 31953111.
- 49. Singh AD, Kaiser PK, Sears JE, et.al. Photodynamic therapy of circumscribed choroidal haemangioma. Br J Ophthalmol 2004; 88:1414–1418.
- 50. Tong Y, Zhao KK, Feng D, et al. Comparison of the efficacy of anti-VEGF monotherapy versus PDT and intravitreal anti-VEGF combination treatment in AMD: a Meta-analysis and systematic review. Int J Ophthalmol. Aug 2016;9(7):1028-1037. PMID 27500113
- 51. Tozer K, Roller AB, Chong LP, et al. Combination therapy for neovascular age-related macular degeneration refractory to anti-vascular endothelial growth factor agents. Ophthalmology 2013; 120: 2029–2034.
- 52. Treatment of Age-Related Macular Degeneration with Photodynamic Therapy (TAP) Study Group. Photodynamic therapy of subfoveal choroidal neovascularization in age related macular degeneration with verteporfin: two-year results of 2 randomized clinical trials. TAP report 2. ArchOphthalmol 2001; 119: 198–207.
- 53. Tsipursky MS, Churgin DS, Conway MD, et.al. (2011) A Review of Photodynamic Therapy for Intraocular Tumors. J Anal Bioanal Tech S1:001. doi: 10.4172/2155-9872.S1-001
- 54. Uyama M, Wada M, Nagai Y, Matsubara T, Matsunaga H, Fukushima I et al. Polypoidal choroidal vasculopathy: natural history. Am J Ophthalmol 2002; 133: 639–648.
- 55. van Dijk EHC, van Rijssen TJ, Subhi Y, et al. Photodynamic Therapy for Chorioretinal Diseases: A Practical Approach. Ophthalmol Ther. 2020 Jun;9(2):329-342. doi: 10.1007/s40123-020-00250-0. Epub 2020 Apr 11. PMID: 32279234; PMCID: PMC7196110.
- 56. van Rijssen TJ, van Dijk EHC, Tsonaka R, et.al. Half-Dose Photodynamic Therapy Versus Eplerenone in Chronic Central Serous Chorioretinopathy (SPECTRA): A Randomized Controlled Trial. Am J Ophthalmol. 2022 Jan; 233:101-110. doi: 10.1016/j.ajo.2021.06.020. Epub 2021 Jun 29. PMID: 34214454.
- 57. Verteporfin in Photodynamic Therapy Study. Group. Verteporfin therapy of subfoveal choroidal neovascularization in age-related macular degeneration: two-year results of a randomized clinical trial including lesions with occult with no classic choroidal
- neovascularization. Verteporfin in photodynamic therapy report 2. Am J Ophthalmol 2001; 131: 541–560.
- 58. Wolf S, Balciuniene VJ, Laganovska G, et al. RADIANCE: a randomized controlled study of ranibizumab in patients with choroidal neovascularization secondary to pathologic myopia. Ophthalmology. Mar 2014;121(3):682-692 e682.
- 59. Wong TY, Ohno-Matsui K, Leveziel N, et al. Myopic choroidal neovascularization: current concepts and update on clinical management. Br J Ophthalmol 2015; 99: 289–296.
- 60. Yannuzzi LA, Slakter JS, Gross NE, et al. Indocyanine green angiography-guided photodynamic therapy for treatment of chronic central serous chorioretinopathy: A pilot study. Retina. 2003;23(3):288-298.

SOURCES

- 1. American Academy of Ophthalmology, Age-Related Macular Degeneration Preferred Practice Patterns. Updated 2015. https://www.aao.org/preferred-practice-pattern/age-related-maculardegeneration-ppp-2015. Accessed February 11, 2021.
- 2. Update on Polypoidal Choroidal Vasculopathy. AAO. https://www.aao.org/eyenet/article/update-on-polypoidal-choroidal-vasculopathy. Accessed 3/2/2023.