Ocriplasmin (Jetrea®)
National Drug Monograph
March/April 2013
VA Pharmacy Benefits Management Services,
Medical Advisory Panel, and VISN Pharmacist Executives

The purpose of VA Pharmacy Benefits Management Services (PBM), Medical Advisory Panel (MAP), and VISN Pharmacist Executives (VPE) drug monographs is to provide a comprehensive drug review for making formulary decisions. These documents will be updated when new clinical data warrant additional formulary discussion. Documents will be placed in the Archive section (http://vaww.pbm.va.gov) when the information is deemed to be no longer current.

Executive Summary:

Efficacy

- The safety and efficacy of ocriplasmin was evaluated in 2 multicenter, randomized, double-blind, phase 3 trials. Study 006 and 007 comprise the Microplasmin for Intravitreous Injection – Traction Release without Surgical Treatment (MIVI-TRUST) clinical program.
- A single injection of ocriplasmin 0.125 mcg or placebo was given via intravitreal injection for the treatment of symptomatic VMA. The primary endpoint was VMA resolution at day 28. Secondary endpoints included: total PVD, nonsurgical closure of a macular hole at day 28, avoidance of vitrectomy, change in BCVA and quality of life with regards to visual function and general health.
- The proportion of patients with nonsurgical resolution of VMA at day 28 was significantly higher in the ocriplasmin vs. placebo arms in each study (p = 0.003 in Study 006 and p < 0.001 in Study 007). Combining data from both studies, 26.5% (123/464) in the ocriplasmin arm vs. 10.1% (19/188) in the placebo arm achieved the primary endpoint at day 28.
- The difference in response between ocriplasmin and placebo groups reached significance at day 7, which was the first follow-up day post-injection. This difference remained significant through month 6.
- Total PVD at day 28 and non-surgical closure of a macular hole was also greater in the ocriplasmin groups.
- Fewer patients in the ocriplasmin group had undergone vitrectomy at 6 months.
- A greater increase in the quality of life vision subscale was noted in the ocriplasmin group (6.1 vs. 2.1 point increase in the ocriplasmin vs. placebo groups; a difference of 4 points; 95% CI, 1.2 - 6.8; p = 0.006).

Safety

- A greater percentage of ocular adverse events were noted in the ocriplasmin vs. placebo groups (68.4 vs. 53.3%) in MIVI-TRUST. Most of these adverse events were mild and transient.
- The most common adverse events (5-20%) were: vitreous floaters, conjunctival hemorrhage, eye pain, photopsia, blurred vision, macular hole, reduced visual acuity, visual impairment and retinal edema.
- Less common adverse events (2-5%) included macular edema, increased intraocular pressure, anterior chamber cell, photophobia, vitreous detachment, ocular discomfort, iritis, cataracts, dry eye, metamorphopsia, conjunctival hyperemia and retinal detachment.
Introduction

Within the eye, the vitreous body is attached to the retina at the macula, or the central part, which is the area where visual acuity is best. As individuals age, the vitreous gel liquefies while vitreoretinal adhesions become weak. This leads to separation of the vitreous from the retina and is also referred to as posterior vitreous detachment (PVD). If the PVD is incomplete, then a partial posterior vitreous detachment may exist. The portion of the posterior vitreous that remains attached to the macula is termed vitreomacular adhesion (VMA). Forces exerted on this adhesion can lead to vitreomacular traction (VMT). VMT can lead to vessel and retinal distortion, which cause retinal swelling, reduced vision and metamorphopsia, or distorted vision. Untreated, VMT can progress to macular hole, which occurs when there is force exerted on the most delicate structure of the eye, the fovea. VMA has been associated with several retinal disorders including macular hole, epiretinal membrane (ERM), Diabetic Macular Edema (DME), retinal venous occlusive disease, neovascular age-related macular degeneration (AMD) and retinal tears/detachment.

The purposes of this monograph are to (1) evaluate the available evidence of safety, tolerability, efficacy, cost, and other pharmaceutical issues that would be relevant to evaluating ocriplasmin for possible addition to the VA National Formulary; (2) define its role in therapy; and (3) identify parameters for its rational use in the VA.

Pharmacology/Pharmacokinetics

Ocriplasmin is a recombinant, truncated form of human plasmin produced in a *pichia pastoris* expression system (a yeast species). The drug is available in a single use glass vial and does not contain preservatives. Each vial contains ocriplasmin 0.5 mg, citric acid 0.21 mg, mannitol 0.75 mg, sodium hydroxide and water for injection.

Mechanism of action

Ocriplasmin works via proteolysis directed at laminin, fibronectin and collagen at the vitreous body/vitreoretinal interface. This results in dissolution of the protein-connector responsible for VMA.

Pharmacokinetics

Ocriplasmin levels are highest immediately post-injection and decrease with time according to a second-order kinetic process. At 24 hours post-injection, vitreous levels were < 3% of the concentration reached immediately post-injection. Due to the small dose of ocriplasmin (0.125 mg) given via intravitreal route, systemic levels of drug are not expected. Via the endogenous protein catabolism pathway, ocriplasmin is inactivated by interactions with protease inhibitor α2-antiplasmin or α2-macroglobulin.

FDA Approved Indication(s)

Ocriplasmin is indicated for the treatment of symptomatic vitreomacular adhesion (VMA).

Potential Off-label Uses

This section is not intended to promote any off-label uses. Off-label use should be evidence-based. See VA PBM-MAP and Center for Medication Safety’s Guidance on “Off-label” Prescribing (available on the VA PBM Intranet site only).
Ocriplasmin is synonymous with microplasmin. There are published trials that have investigated the use of intravenous microplasmin for vascular conditions such as acute ischemic stroke and intra-catheter administration of microplasmin for the restoration of catheter function in long-term venous access catheter thrombosis.

Investigational use of intravitreal plasmin injection and intravitreal tissue plasminogen activator is being studied in Diabetic Macular Edema (DME) associated with VMT. Anticipate that there may be interest in using ocriplasmin in patients with proliferative diabetic retinopathy, neovascular age-related macular degeneration, retinal vein occlusion, or other conditions that were excluded from MIVI-TRUST.

**Current VA National Formulary Alternatives**

There are no VA National Formulary alternatives. Ocriplasmin is the first pharmacotherapeutic option for the treatment of VMA. Pars plana vitrectomy is the standard of care for symptomatic VMA.

Vitrectomies have a very high success rate. Risks include bleeding, infection, progression of cataract and retinal detachment.

**Dosage and Administration**

**General Information**

- Ocriplasmin must be diluted with 0.9% Sodium Chloride Injection, USP (sterile, preservative-free) which is not provided by the manufacturer.
- Drug is for single-use, ophthalmic intravitreal injection to be given by a qualified physician.
- Ocriplasmin is to be stored frozen at or below -4ºF (-20ºC) out of direct light
- Drug is obtained through specialty distribution, including McKesson Plasma & Biologics (MPB) due to storage and temperature requirements. The product will only be sold once an approved freezer is obtained from the Jetrea Collaboration in Access & Reimbursement Essentials (CARE) program.
- The provided freezer is 1.5 cu. ft, which can store up to 34 vials of ocriplasmin.

**VA Process to Obtain Drug (also found at [https://vaww.cmopnational.va.gov/cmop/PBM/Special%20Handling%20Drugs/Forms/AllItems.aspx](https://vaww.cmopnational.va.gov/cmop/PBM/Special%20Handling%20Drugs/Forms/AllItems.aspx))**

1. VA pharmacy should contact MPB and inform the representative of the need to purchase ocriplasmin. The caller will be routed to a MPB representative with experience in the ocriplasmin procurement process
2. MPB will collect basic information including the pharmacy account number and fax number and will contact the Jetrea CARE program if it is the pharmacy’s first ocriplasmin order
3. The Jetrea CARE program will fax the pharmacy the Jetrea CARE freezer order form which also serves as **Transfer of Title, Waiver of Liability and Hold Harmless Agreement Form**. Once the pharmacy completes and faxes the form back to Jetrea CARE, the freezer should be received within 5 to 8 days
4. The pharmacy can then contact MPB to place the ocriplasmin order and confirm arrival and set up of the freezer. Upon receipt of the freezer, the **Confirmation of Freezer Operation Form** will need to be faxed back to the company.
5. MPB will then contact ThromboGenics to have ocriplasmin drop-shipped to the pharmacy with a dry ice coolant for the next business day.
6. The Logistics department of the facility would receive the freezer and catalog the item into inventory. BioMed/Engineering department of the facility will need to certify the unit prior to use.

**Dosing**
- Ocriplasmin dose is 0.125 mg (0.1 ml) via intravitreal injection to the affected eye as a single dose.
- Repeat administration to the same eye is not recommended.

**Preparation for Administration**
The preparation for administration is outlined in the prescribing information, along with figures to illustrate instructions. Please refer to the prescribing information for details concerning preparation. The process to prepare a dose is outlined here.

1. Remove the ocriplasmin vial from the freezer and allow to thaw at room temperature (within a few minutes).
2. Once completely thawed, remove the protective polypropylene flip-off cap from the vial.
3. Disinfect the top of the vial with an alcohol wipe.
4. Using aseptic technique, add 0.2 ml of 0.9% w/v Sodium Chloride Injection, USP (sterile, preservative-free) into the ocriplasmin vial. Gently swirl the vial until the solutions are mixed.
5. Visually inspect the vial for particulate matter. The solution should be clear and colorless without visible particles.
6. Using aseptic technique, withdraw the contents of the vial using a sterile #19 gauge needle, then discard the needle. Slightly tilt the vial to ease withdrawal. Do not use this needle for the intravitreal injection.
7. Replace the needle with a sterile #30 gauge needle. Carefully expel the air bubbles and excess drug from the syringe. Adjust the dose to the 0.1 ml mark on the syringe. This corresponds to the 0.125 mg ocriplasmin dose.
8. **THE SOLUTION SHOULD BE USED IMMEDIATELY AS IT CONTAINS NO PRESERVATIVES.**
9. Discard the vial and any unused portion of the diluted solution after single use.

**Administration and Monitoring**
The intravitreal injection procedure should be carried out under controlled aseptic conditions, which include the use of sterile gloves, a sterile drape and a sterile eyelid speculum (or equivalent). The DUSHOM Ophthalmology Surgical Advisory Board has developed Guidelines for Intravitreal Injections, which can be found at the following:

Adequate anesthesia and a broad spectrum microbiocide should be administered according to standard medical practice.

The injection needle should be inserted 3.5 – 4 mm posterior to the limbus aiming towards the center of the vitreous cavity, avoiding the horizontal meridian. The injection volume of 0.1 ml is then delivered into the mid-vitreous.
Immediately following the intravitreal injection, patients should be monitored for elevation in intraocular pressure. Appropriate monitoring may consist of a check for perfusion of the optic nerve head or tonometry. If required, a sterile paracentesis needle should be available.

Following intravitreal injection, patients should be instructed to report any symptoms suggestive of endophthalmitis or retinal detachment (e.g. eye pain, eye redness, photophobia, blurred or decreased vision) without delay.

Each vial should only be used to provide a single injection for the treatment of a single eye. If the contralateral eye requires treatment, it is not recommended to give ocriplasmin to the contralateral eye within 7 days of the initial injection, to allow time to monitor the original eye post-injection for the potential for decreased vision.

Any unused product should be discarded after the injection.

**Efficacy**

**Efficacy Measures**

Primary endpoint of MIVI-TRUST: Resolution of VMA at day 28

Secondary endpoints:
- Posterior Vitreous Detachment (PVD)
- Non-surgical closure of a macular hold at day 28
- Avoidance of vitrectomy
- Change in Best Corrected Visual Acuity (BCVA)

**Summary of efficacy findings**

- The safety and efficacy of ocriplasmin was evaluated in 2 multicenter, randomized, double-blind, phase 3 trials. Study 006 and 007 comprise the Microplasmin for Intravitreous Injection – Traction Release without Surgical Treatment (MIVI-TRUST) clinical program.
- A total of 654 patients participated in MIVI-TRUST (464 received ocriplasmin and 188 received placebo).
- The study population included adults with focal VMA as seen on OCT and BCVA of 20/25 or less in their affected eye and 20/800 or more in the non-study eye.
- A single injection of ocriplasmin 0.125 mcg or placebo was given via intravitreal injection for the treatment of symptomatic VMA. The primary endpoint was VMA resolution at day 28. Secondary endpoints included: total PVD, nonsurgical closure of a macular hole at day 28, avoidance of vitrectomy, change in BCVA and quality of life with regards to visual function and general health.
- Assessments were made at baseline and on days 7, 14, 28, 90 and 180 days after injection. Patients could receive vitrectomy, per investigator, if their ocular condition or BCVA worsened or if no improvement was noted within 4 weeks.
- Baseline demographics between the ocriplasmin and placebo groups were similar except for the inclusion of more female patients (67.7 vs. 61.2%) and more pseudophakic patients (37.1 vs. 28.2%) in the ocriplasmin group.
- The proportion of patients with nonsurgical resolution of VMA at day 28 was significantly higher in the ocriplasmin vs. placebo arms in each study (p = 0.003 in Study
006 and p < 0.001 in Study 007). The odds ratio was 3.28 (95% CI, 1.93 – 5.84; p < 0.001) for the combined results of Study 006 and Study 007.

- Combining data from both studies, 26.5% (123/464) in the ocriplasmin arm vs. 10.1% (19/188) in the placebo arm achieved the primary endpoint at day 28.
- The difference in response between ocriplasmin and placebo groups reached significance at day 7, which was the first follow-up day post-injection. This difference remained significant through month 6.
- Women appeared to have a greater response than men, achieving resolution of VMA in 30.3 vs. 13% while men achieved resolution in 18.7 vs. 5.5% (ocriplasmin vs. placebo, respectively).
- Patients with pseudophakia did not respond to ocriplasmin as well as those without. The response in those with pseudophakia was 13.4 vs. 3.8% in those without and 34.2 vs. 12.6% in the ocriplasmin vs. placebo groups, respectively.
- A subgroup analysis of those with or without an epiretinal membrane showed that patients without epiretinal membrane had a better nonsurgical response than those with epiretinal membrane.
- Total PVD at day 28 and non-surgical closure of a macular hole was also greater in the ocriplasmin groups.
- Fewer patients in the ocriplasmin group had undergone vitrectomy at 6 months.
- Post hoc subgroup analysis stratified by BCVA noted that at month 6 a gain of ≥ 3 lines was more likely in those with poorer vision (defined as BCVA < 20/50). Among those with BCVA > 20/50 at baseline, the proportion that gained ≥ 3 lines did not differ significantly between the ocriplasmin and placebo groups.
- A greater increase in the quality of life vision subscale was noted in the ocriplasmin group (6.1 vs. 2.1 point increase in the ocriplasmin vs. placebo groups; a difference of 4 points; 95% CI, 1.2 - 6.8; p = 0.006).

For further details on the efficacy results of the clinical trials, refer to Appendix: Clinical Trials (page 12).

**Adverse Events (Safety Data)**

A greater percentage of ocular adverse events were noted in the ocriplasmin vs. placebo groups (68.4 vs. 53.3%) in MIVI-TRUST. Most of these adverse events were mild and transient.

**Deaths and Other Serious Adverse Events**

None known.

**Common Adverse Events**

The most common adverse events (5-20%) were: vitreous floaters, conjunctival hemorrhage, eye pain, photopsia, blurred vision, macular hole, reduced visual acuity, visual impairment and retinal edema.

**Other Adverse Events**

Less common adverse events (2-5%) included macular edema, increased intraocular pressure, anterior chamber cell, photophobia, vitreous detachment, ocular discomfort, iritis, cataracts, dry eye, metamorphopsia, conjunctival hyperemia and retinal detachment.
No acute cataracts were noted. The progression of cataracts in phakic eyes was reported in 8.2 vs. 11.9% of patients treated with ocriplasmin vs. placebo, respectively (p = 0.32). The proportion of patients with cataract progression, who did not undergo vitrectomy, was similar between groups (4.8 vs. 5.2%, respectively; p = 0.97)

**Tolerability**

There were no cases of endophthalmitis observed.

For further details on the safety results of the clinical trials, refer to *Appendix: Clinical Trials* (page 12).
Contraindications

None.

Warnings and Precautions

Decreased Vision
A reduction in Best Corrected Visual Acuity (BCVA) of ≥ 3 lines was noted in 5.6% vs. 3.2% of patients in the clinical trials treated with ocriplasmin vs. vehicle, respectively. In the majority of these cases the reduced visual acuity was due to progressive traction and required surgical intervention. Monitor patients for reduced visual acuity.

Effects associated with the Intravitreal Injection Procedure
Intraocular inflammation and/or infection, intraocular hemorrhage and increased intraocular pressure (IOP) can result from the intravitreal injection procedure. The following table highlights these effects seen in patients participating in the controlled trials:

<table>
<thead>
<tr>
<th></th>
<th>Ocriplasmin arm (%)</th>
<th>Vehicle arm (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intraocular inflammation</td>
<td>7.1</td>
<td>3.7</td>
</tr>
<tr>
<td>Intraocular hemorrhage</td>
<td>2.4</td>
<td>3.7</td>
</tr>
<tr>
<td>IOP</td>
<td>4.1</td>
<td>5.3</td>
</tr>
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</table>

Potential for Lens Subluxation
Lens subluxation was reported in one patient that received 1.4 times the recommended dose. This has also been noted in three animal species (monkey, rabbit, minipig) following a single dose that resulted in vitreous ocriplasmin concentrations that were 1.4 times higher than the recommended dose. A second dose of ocriplasmin, given to monkeys within a 28-day period, resulted in lens subluxation in all treated eyes.

Retinal Breaks
The following data comes from the controlled trials:

<table>
<thead>
<tr>
<th></th>
<th>Ocriplasmin arm (%)</th>
<th>Vehicle arm (%)</th>
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<tbody>
<tr>
<td>During or post-vitrectomy</td>
<td></td>
<td></td>
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<tr>
<td>Retinal detachment</td>
<td>0.9</td>
<td>1.6</td>
</tr>
<tr>
<td>Retinal tear (no detachment)</td>
<td>1.1</td>
<td>2.7</td>
</tr>
<tr>
<td>Pre-vitrectomy</td>
<td></td>
<td></td>
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<tr>
<td>Retinal detachment</td>
<td>0.4</td>
<td>0</td>
</tr>
<tr>
<td>Retinal tear (no detachment)</td>
<td>0</td>
<td>0.5</td>
</tr>
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</table>

Dyschromatopsia
Yellowish vision, or dyschromatopsia, was reported in 2% of all patients treated with ocriplasmin. Approximately half of these patients experienced electroretinographic (ERG) changes.
Special Populations

Pregnancy

Teratogenic Effects
Ocriplasmin is categorized as Pregnancy Category C. There are no well-controlled studies of ocriplasmin in pregnant women. It is not known if administration of ocriplasmin can cause fetal harm or affect reproductive capability. Systemic exposure would be expected to be low given the intravitreal administration route. Assuming a plasma volume of 2700 ml and 100% systemic absorption, the estimated plasma concentration is 46 ng/ml. Ocriplasmin should be used in a pregnant woman only if there is a clear need.

Nursing Mothers
It is not known if ocriplasmin is excreted in human milk, therefore caution should be exercised if considering treatment in a nursing mother.

Geriatric Population
No significant differences were noted with regard to the efficacy and safety of ocriplasmin in the elderly population. A total of 384 and 145 patients in the ocriplasmin vs. vehicle groups, respectively, were ≥ 65 years of age. A total of 192 and 73 patients were ≥ 75 years.

Postmarketing Safety Experience (Optional)
No data available.

Sentinel Events
No data available.

Look-alike / Sound-alike (LA / SA) Error Risk Potential
As part of a Joint Commission standard, LASA names are assessed during the formulary selection of drugs. Based on clinical judgment and an evaluation of LASA information from three data sources (Lexi-Comp, First Databank, and ISMP Confused Drug Name List), the following drug names may cause LASA confusion:

LA/SA for generic name ocriplasmin: Octreotide, Octaplas, Ocupress, Ocutricin

LA/SA for trade name Jetrea: Zencia, Zetia, Jetrex (India)*
*Jetrea: Brand name for ocriplasmin [U.S.] may be confused with Jetrex brand name for dextromethorphan, guaifenesin, bromhexine and chlorpheniramine maleate [India]

Drug Interactions

Drug-Drug Interactions
No known interactions.

Drug-Lab Interactions
No known interactions.
**Acquisition Costs**

Refer to VA pricing sources for updated information.

**Pharmacoeconomic Analysis**

None have been performed to date.

**Conclusions**

Ocriplasmin received FDA-approval for the treatment of symptomatic VMA. Evidence from MIVI-TRUST supports a greater proportion of patients that received ocriplasmin achieved the primary endpoint of VMA resolution at day 28, compared to patients receiving placebo injection.

A greater proportion of patients treated with ocriplasmin achieved secondary endpoints of total posterior vitreous detachment and closure of macular hole at day 28. There was greater improvement in visual acuity with ocriplasmin at 6 months, but the improvement was considered to be modest.

MIVI-TRUST authors note that a limitation of their study was the inclusion of patients with baseline VA that is better than that of patients for whom vitrectomy would typically be recommended. Perhaps this is the reason that visual gains were considered modest.

The effects of ocriplasmin were noted in some, but not all of the patients received benefit from treatment. Ocriplasmin appeared to be more effective than placebo. It is unclear if it is more effective in the treatment of symptomatic VMA than the standard of care, pars plana vitrectomy. At 6 months, approximately 18% of patients treated with ocriplasmin underwent vitrectomy for persistent VMA.

The study population did not include patients with proliferative diabetic retinopathy or neovascular age-related macular degeneration and should not be used in these patients until further evidence supports its use. The Veteran population is likely to have these concomitant conditions.

Ocriplasmin provides a pharmacologic therapeutic option to an otherwise surgically-treated condition.
References


Appendix: Clinical Trials

A literature search was performed on PubMed/Medline (1966 to March 2013) using the search terms ocriplasmin and Jetrea®. The search was limited to studies performed in humans and published in English language. Reference lists of review articles and the manufacturer’s AMCP dossier were searched for relevant clinical trials. All randomized controlled trials published in peer-reviewed journals were included.
## Table 1. Summary of Ocriplasmin Clinical Trials

<table>
<thead>
<tr>
<th>Methods</th>
<th>Eligibility Criteria</th>
<th>Interventions</th>
<th>Patient Population Profile</th>
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<th>Safety Results</th>
<th>Conclusions</th>
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<tr>
<td><strong>Stalmans (2012)</strong>&lt;br&gt;MIVI-TRUST Study Group&lt;br&gt;Study 006 randomized 2:1&lt;br&gt;Age ≥ 18 yrs;&lt;br&gt;Focal VMA;&lt;br&gt;BCVA ≥ 20/25 in study eye and&lt;br&gt;BCVA ≥ 20/800 in nonstudy eye&lt;br&gt;Exclusion: PDR; ARMD; RVO; phakia, high myopia (more than -8 diopters), uncontrolled glaucoma, MH &gt; 400 mcm diameter, vitreous opacification, lenticular/zonular instability; history of retinal detachment; prior vitrectomy; prior laser photoagulation of macula; treatment w/ocular surgery, intravitreal injection or retinal laser photoagulation in prior 3 months&lt;br&gt;Sponsored by ThromboGenics</td>
<td>O via intravitreal injection 125 µg/0.10 ml vs. placebo 0.10 ml&lt;br&gt;F/U Assessments: days 7, 14,28, 90, 180&lt;br&gt;Included eye exam, B-scan US to evaluate status of posterior vitreous cortex, OCT, fundus photograph, FA, NEI-VFQ-25&lt;br&gt;Investigators could proceed to vitrectomy if condition deteriorated, if BCVA worsened by &gt; 2 lines on eye chart or if no improvement within 4 wks of injection</td>
<td>O vs. placebo&lt;br&gt;Groups similar except: more pseudophakia in O group (37 vs. 28%); more women in O group (68 vs. 61%)</td>
<td>O vs. placebo&lt;br&gt;Primary endpoint: proportion of patients with nonsurg resolution of VMA via OCT at day 28&lt;br&gt;Combined results (O vs. placebo): Resolution of VMA 26 vs. 10%; p&lt;0.001; PVD at day 28 13 vs. 4%; p&lt;0.001; Closure of MH 41 vs. 11%; p &lt; 0.001; Between group differences in resolution of VMA noted at day 7 and remained higher through month 6 (odds ratio 5.2; 95% CI, 2.53-12.07; p &lt; 0.001)</td>
<td>O vs. placebo&lt;br&gt;Any ocular AE: 68 vs. 53% (p &lt; 0.001)&lt;br&gt;Most AE mild, transient&lt;br&gt;Common AE: vitreous floaters 17 vs. 8% (p=0.002); Photopsia 12 vs. 3% (p&lt;0.001)&lt;br&gt;Injection-related eye pain 13 vs. 6% (P=0.005)&lt;br&gt;Visual impairment 5.5 vs. 2% (p=0.02)</td>
<td>Enzymatic vitreolysis is a means to resolve VMT and close MH and was superior to placebo.</td>
<td>&lt;br&gt;Applicability limited by exclusion of patients with severe myopia, aphakia, PDR, ARMD.&lt;br&gt;Gains in VA were modest.</td>
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<td><strong>Study 007 randomized 3:1&lt;br&gt;(Ocri vs. placebo)</strong></td>
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*SAE were all non-sig between groups*

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*Updated version may be found at [www.pbm.va.gov](http://www.pbm.va.gov) or [vaww.pbm.va.gov](http://vaww.pbm.va.gov)*
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<td>Underwent vitrectomy by 6 mos: 18 vs. 27% (odds ratio, 0.61; 95% CI 0.40-0.94; P =0.02</td>
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<td>Mean change VFQ-25: ↑ 6.1 vs. ↑ 2.1 points (p=0.006)</td>
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Nr, Number randomized. Add abbreviations, other footnotes