- TECHNICAL FEATURES
- INDICATION OF USE
- CLINICAL BENEFITS



Vision Engineering Italy

INNOVATION IN VETERINARY OPHTHALMOLOGY

C

VISIOFLAVIN®



30 mW/cm<sup>2</sup>

10 mW/cm<sup>2</sup>

UV-ALED

Manuak

AMP POWER



#### Vision Engineering Italy srl

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- TECHNICAL FEATURES
  - INDICATION OF USE
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INNOVATION IN VETERINARY OPHTHALMOLOGY

Corneal cross-linking for human use has been developed in Dresden (Germany) for treating KERA-TOCONUS in the late 1990s. Keratoconus is a vision threatening progressive degenerative corneal disease characterized by thinning and bulging of the cornea.

Corneal Cross-Linking (CXL) has been now well established as primary treatment option for keratoconus, avoiding corneal transplantation in most treated cases.

The CXL is a parasurgical treatment with "low invasiveness" and consists in "strengthening" the corneal tissue with the combined use of vitamin B2 (RIBOFLAVIN) and ultraviolet light rays (UV-A).

The CXL induces the generation of new chemical bonds between stromal proteins, thus increasing the tissue mechanical resistance to normal intraocular pressure, thus halting disease progression.

The treatment requires the application of riboflavin (Vitamin B2) before irradiating the cornea with UV-A.



## Corneal phototherapy has been introduced in veterinary medicine by VISION ENGINEERING ITALY s.r.l.

Vision Engineering Italy srl is an innovative company in the Medtech sector. The Company develops new methods and systems for the prevention and treatment of eye diseases with significant socio-economic impact.

Thanks to the expertise in the field of CORNEAL CROSS-LINKING for human use, Vision Engineering Italy has introduced a new treatment paradigm of infectious keratitis and corneal ulcers in veterinary medicine: CORNEAL PHOTOTHERAPY.

CORNEAL PHOTOTHERAPY consists of irradiating the cornea with high UV-A power density, 30 mW/cm<sup>2</sup>, after soaking the tissue with a riboflavin ophthalmic solution.

Unlike standard corneal cross-linking, which is generally performed with UV-A power densities ranging from 3 mW/cm<sup>2</sup> to 10 mW/cm<sup>2</sup>, CORNEAL PHOTOTHERAPY induces a further microbicidal mechanism of action in the diseased cornea.



Dr. Marco Lombardo, eye surgeon, founder of Vision Engineering Italy



Vision Engineering Italy has developed the first UV-A medical device for the CORNEAL PHOTOTHERAPY of infectious keratitis and corneal ulcers. For veterinary use only.







In a randomized controlled multicenter study, corneal phototherapy with VETUVIR® has been shown to be on average 80% more effective than topical antimicrobial therapies for the treatment of septic corneal ulcers in dogs and horses. CORNEAL PHOTOTHERAPY How does it work?

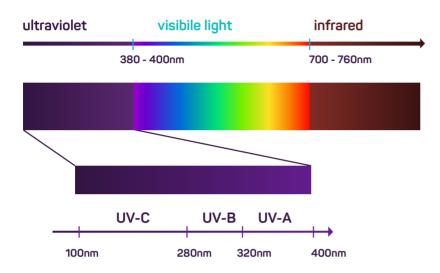
#### **COMBINED USE OF:**

VITAMIN B2 (RIBOFLAVIN): 10 minutes (EQUIRVIS) 20 minutes (VISIOFLAVIN) ULTRAVIOLET RAYS (UV-A): 3 minutes (30 mW/cm<sup>2</sup>) 9 minutes (10 mW/cm<sup>2</sup>)

DIRECT, NON SELECTIVE, MICROBICIDAL ACTION inducing PEROXIDATION of cell membranes of bacteria viruses - fungi – protozoa 115

STRENGTHENING ACTION in the CORNEAL STROMA induced by PHOTO-POLYMERIZATION OF STROMAL PROTEINS, which contrasts the collagenolytic proteases' activity

## Microbicide mechanism



• Ultraviolet light is an electromagnetic radiation with wavelengths shorter than visible light.

• In combination with photo-sensitizing substances, like riboflavin, UV-A radiation triggers photo-oxidative reactions that damage the cells.

• The photo-chemical action triggered by UV-A rays and the photo-sensitizing substance is instantaneous and acts directly onto the cellular components of microorganisms.

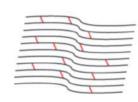
 No microorganism can resist to the photo-oxidative damage generated by UV-A rays and riboflavin.
 The corneal photo-therapy mechanism can virtually inactivate and kill all living microorganisms.





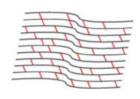
Cross-linking mechanism





Less cross-linking bonds: *weaker cornea* 

The "cross-links" are chemical bonds between corneal stromal proteins



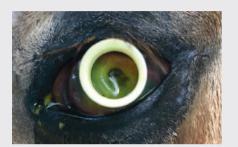
More cross linking bonds: stronger cornea

Main advantages of the mechanism of action of **corneal phototherapy** on infective agents compared to antimicrobial topical therapy:

- Photo-chemical mechanism of action;
- Not selective;
- It does not induce resistance to antibiotics;
- Strengthens the corneal structure.

### How does it work?

Corneal phototherapy consists in illuminating the cornea, after the tissue has been administered with a riboflavin ophthalmic, such as Visioflavin<sup>®</sup> or Equirvis<sup>®</sup>, using the Vetuvir<sup>®</sup> UV-A device.

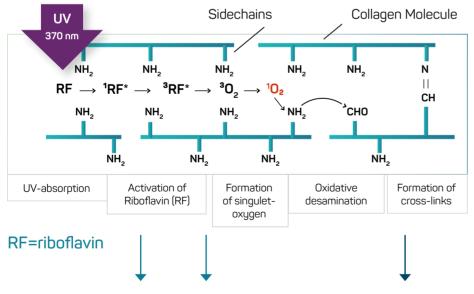


1 - Administer riboflavin (Equirvis o Visioflavin)



2 - Illuminate the cornea with Vetuvir

#### Corneal phototerapy reaction



#### Peroxidation of cell membranes

Direct bactericidal action on microbes caused by peroxidation of cell membranes.

#### Strengthening of the corneal stroma

Strengthens the biomechanics and microstructure of the corneal tissue by photopolymerization of stromal proteins (which also counteracts the collagenolytic activity of bacteria). The medical devices Vetuvir<sup>®</sup>, Visioflavin<sup>®</sup> and Equirvis<sup>®</sup> are for exclusive use in veterinary medicine. They are registered trademarks of Vision Engineering Italy srl.



## YETUYK<sup>®</sup>

## Unique technical features

- Selectable light irradiance:
  10 mW/cm<sup>2</sup>, 30 mW/cm<sup>2</sup>
- Portable
- Ease of use
- Bluetooth remote control

### Indications of use

- Corneal infection (30 mW/cm<sup>2</sup>)
- Corneal ulcer (30 mW/cm<sup>2</sup>)
- Bullous keratopathy (10 mW/cm²)

#### Advantages

- Rapid procedure
  (it takes a few minutes)
- Effective in monotherapy
- Superior to topical therapy for the treatment of corneal ulcers (RCT VEI\_vet01)
- Does not induce antibiotic resistance

## EQUIRVIS

#### Highly concentrated riboflavin ophthalmic solution

#### Solostano onalmica 0.22% riboflavin ophthalmic solutio 0.22% EQUIRVIS Soluzione oftalmica 0.22% riboflavina per fototerapia corneale in medicina veterinaria. 0.22% riboflavin ophthalmic solution for corneal phototherapy. For use by veterinary practioners only. 1 1 3 ml Dispositivo Medico. Medical Device. C VISION JUIRV riboflavina soluzion Per fototerapia corneale 0,22% riboflavin ophthalm

lution for corneal photoin

**UNIQUE TECHNICAL FEATURES** 

Riboflavin 0.22%

Hypotonic

Volume 3 ml

High cost-benefit ratio

#### **INDICATIONS FOR USE**

- Corneal infection
- Corneal ulcer
- Bullous keratopath

#### **ADVANTAGES**

 Reduces the time of administration

#### (10 min.)

 Further improves efficacy of corneal phototherapy

 Greater protection of the corneal tissue in case of deep ulcers

Innovation in veterinary ophthalmology



#### Corneal phototherapy Clinical cases



**French Bulldog** with corneal *melting* and descemetocele. **Resistant to antibiotic therapy.** *Kind courtesy of Prof. C. Perruccio* 



1 day after treatment (No more descemetocele)

2 weeks after treatment (The cornea begins to become somewhat transparent)

1 month after treatment (Visual function is restored)



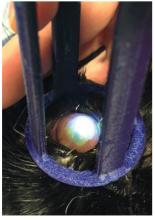








**Persian cat** with septic corneal *ulcer*. *Courtesy of Dr. C. Giordano* 



1 month after treatment (Neovascularization)

2 months after treatment (The cornea is almost completely transparent)







### Corneal phototherapy Clinical cases



**Horse** with septic corneal abscess (pseudomonas+ and streptococcus+). **Resistant to antibiotic therapy.** *Kind courtesy of Prof. R. Gialletti* 





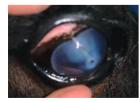
1 week after treatment with VETUVIR® (almost complete resolution of the abscess)







It is never too late to treat a corneal ulcer with Vetuvir®



Deep ulcer in a horse treated with Ceftriazone based on the antibiogram.



Because of the quick worsening of the ulcer, the surgeon performed a conjunctival flap, which however could not restore vision.



Corneal phototherapy was performed with Vetuvir (30 mW/cm<sup>2</sup>) and Visioflavin.



After 3 days from corneal phototherapy, new vessels and granulation tissue were capping the corneal ulcer.



9 days after corneal phototherapy, the corneal epithelium was intact and the neovascolarization begun to withdraw.



# **VETUK**®

- Produced by Vision Engineering Italy research.
- Proprietary technology.
- Specific for veterinary medicine.
- Wide spectrum of efficacy: bacteria, fungi, viruses, protozoa.
- Non-selective mechanism of action that does not create antimicrobial resistance.
- Improves corneal tissue's integrity.

- Clinically proven: performance better than standard of care (studio clinico VEI\_vet01).
- Save the eye.
- High quality: durable device.
- Simple to use.
- Easy compliance to therapy:
- effective with a single treatment.

From left to right: Dr. Sebastiano Serrao, Eng. Giuseppe Lombardo, Dr. Marco Lombardo. Giuseppe and Marco Lombardo are brothers and co-founders of Vision Engineering Italy srl

INNOVATION IN VETERINARY OPHTHALMOLOGY

3. 9. %

"Solutions to unmet needs in eye care"

## **VISION ENGINEERING ITALY SRL**

#### Innovative company in the Medtech sector

- Biomedical company specialized in research
- Focus on ophthalmology
- Made in Italy
- Compliant with the European regulatory and quality requirements



- Holds proprietary and patented technologies
- Has created products specifically for veterinary use
- Corneal phototherapy has been shown to be 80% more effective than standard topical antimicrobial therapy for the treatment of corneal ulcers and infectious keratitis (study VEI\_vet01)<sup>1,3</sup>



CORNEAL PHOTOTHERAPY effective and safe therapy of corneal infections



#### Bibliography

**1.** Marchegiani A. et al. **Corneal photochemotherapy for the treatment of deep septic corneal ulcer in dogs. Veterinary Ophthalmology 2019;** E81-E89. Abstracts: Annual Scientific Meeting of the European Society of Veterinary Ophthalmology, Dublin, Ireland 3-6 Oct 2019.

2. Perrazzi A. et al. An Assay System to Evaluate Riboflavin/UV-A Corneal Phototherapy Efficacy in a Porcine Corneal Organ Culture Model. Animals (Basel) 2020; 10(4): E730.

**3.** Orzalesi C. et al. **Use of cross-linking technique in bacterial and mycotic keratitis of the horse.** World Equine Veterinary Association Congress, Verona, Italy 3-5 Oct 2019.

3. Lombardo, G., Micali, N.L., Villari, V., Serrao, S., Lombardo, M., 2016. All-Optical Method 422 to Assess Stromal Concentration of Riboflavin in Conventional and Accelerated UV-A 423 Irradiation of the Human Cornea. Invest Ophthalmol Vis Sci 57, 476. 424.

**4.** Lombardo G et al. **Assessment of stromal riboflavin concentration-depth profile in nanotechnology-based transepithelial corneal cross-linking.** J Cataract Refract Surg 2017;43(5):680-686.

5. Lombardo M et al. Randomized controlled trial comparing transepithelial corneal cross-linking using iontophoresis with the Dresden protocol in progressive keratoconus. Ophthalmology 2017; 124: 804–812.

.6.Labate C et al. Biomechanical strengthening of the human cornea induced by nanoplatform-based transepithelial riboflavin/UV-A corneal cross-linking. Invest Ophthalmol Vis Sci 2017; 58(1): 179-184.

7. Lombardo M et al. Novel technique of transepithelial corneal cross-linking using iontophoresis in progressive keratoconus. J Ophthalmology 2016; 7472542.

8. Lombardo M et al. All-optical method to assess stromal concentration of riboflavin in conventional and accelerated UV-A irradiation of the human cornea. Invest Opthalmol Vis Sci 2016; 57(2): 476-483.

**9.** Lombardo M et al. **Ultraviolet A - visible spectral absorbance of the human cornea after transepithelial soaking with dextran-enriched and dextran-free riboflavin 0.1% ophthalmic solutions** J Cataract Refract Surg 2015; 41: 2283-2290.

**10.** Labate C et al. **Multiscale investigation of the depth-dependent mechanical anisotropy of the human corneal stroma.** Invest Ophthalmol Vis Sci 2015; 56: 4053-4060.

11. Labate C et al. Understanding of the Viscoelastic Response of the Human Corneal Stroma Induced by Riboflavin/UV-A Cross-Linking at the Nano Level. PLoS One 2015; 10(4): e0122868.

**12.** Lombardo M et al. **Corneal light backscattering following transepithelial corneal cross-linking using iontophoresis in donor human corneal tissues.** J Cataract Refract Surg 2015; 41(3): 635-643.

**13.** Lombardo M et al. Interaction of ultraviolet light with the cornea- clinical implications for corneal crosslinking. J Cataract Refract Surg 2015; 41(2):446-459.

14. Lombardo M et al. Analysis of the viscoelastic properties of the human cornea using Scheimpflug imaging in inflation experiment of eye globes. PloS ONE 2014; 9(11): e112169.

**15.** Lombardo M et al. **Biomechanical changes of the human cornea following transepithelial corneal cross-linking using iontopho***resis.* J Cataract Surg 2014; 40(10): 1706-1715.

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