ophtha futur®

01000-1-1

01000-2-1

Dear valued customer

This catalogue introduces a new brand: ʿ**ophthafutur**®.

ʿ**ophthafutur**® is more than just a standard product line. The brand faces all current and future challenges in the ophthalmic sector. It offers unique and smart solutions, supported and counselled by a multidisciplinary group of experts. These experts come from the fields of ophthalmology, chemistry, pharmacy, biology and physics.

The primary goal of the brand is the generation of new product ideas, development, registration and marketing of related products.

The introduction of the new European guidelines and other requirements from around the world results in a rise of expectations from all stakeholders: international health authorities, notified bodies, as well as surgeons and patients asking for products manufactured to the highest pharmaceutical and regulatory standards, offering outstanding quality. The ʿ**ophthafutur**® product line responds to this market demand.

The co-operation of clinicians and scientists with an experienced manufacturer enables a rational problem solving approach, aided by a very successful history of 25 years in pharmaceutical production, quality control, device manufacturing and drug synthesis. We aim to offer superior quality products conforming to the most demanding requirements. Further benefits are ease of use, modern packaging and clear labeling.

One source for innovation will be the adaption of new surgical techniques, high-tech engineering, novel materials and developments around well-established products.
A better understanding of the interaction of medical devices with tissues during surgery, as well as their newly defined bio-chemical and physical impact will offer new opportunities.

ʿ**ophthafutur**® represents an innovative and creative environment in which you can become an important part. We invite you to join with us in your role as surgeon or scientist.

Please contact the ʿ**ophthafutur**® team with your ideas and needs. We can then discuss and evaluate your thoughts for successful inclusion into the ʿ**ophthafutur**® concept.

ʿ**ophthafutur**®
nomen est omen –
the name says it all

Your ʿ**ophthafutur**® team

Information as of: 01/2019

01000-3-2

01000_1

ophtha futur®

research & development

novel approaches to **illuminate the eye**

Currently, light fibres connected to external light sources are used to illuminate the posterior chamber of the eye.

Controlling the light intensity reaching the retina, the distance to the retina, as well as the exposure time of light is currently not possible using these fibres.

Novel approaches using specially designed light sources within the eye are very promising. In addition the interaction of illumination with tissues and ophthalmic liquids is currently being studied.

novel approaches to **tissue removal**

As various media are used during surgery, the interaction of energy (induced by Laser or ultra-sound) with these media and the intra-ocular tissue must be well understood.

A consortium of six partners with a broad experience in the fields of ophthalmic surgery, optics, engineering, industrial manufacturing and design of medical devices investigates the possibility of removing delicate tissues in and around the eye.

The technology is based on a novel 2.94 µm approach for very efficient use of laser light as a surgical tool.

novel approaches to **package design & labeling**

Packaging and labeling require constant attention. Up to date packaging must be accurate, environmentally friendly, user friendly and attractive.

It is very challenging to combine all these features with non-verbal communication, safe labeling, coding (UDI: unique device identification) and forgery protective elements.

ophthafutur® shows new ways and develops creative, safe and convenient packaging.

ophtha futur®

Coming soon

THE ISSUE

Inferior retinal detachments are currently treated by heavy mixtures of silicone oils and semifluorinated additives.
Due to the toxic profile of the additives, which are masked by the silicone oil, new substances are needed.

Inhomogenities are reported.

At low temperatures the components of the mixtures can potentially separate from each other.

A one part heavy liquid is needed.

OUR ANSWER

Avoiding additives in silicone oil is the first step to developing an alternative product. Chemically binding fluor atoms to the silicone oil backbone network also avoids the usage of mixtures.

All volatile components are removed by the application of a proprietary purification processes.

ophtha futur®

sil heavy

- Avoids head down position
- Additive free
- Safe and easy application
- Heavier than water
- Chemically stable
- Highly purified

ophthafutur® sil heavy is a one part liquid with a density of 1.07 g/cm³. The product has been purified applying Pharmpur silicone oil purification technology.

Heavy oil can be used in the treatment of inferior retinal detachment without the worry of low temperature storage or interaction of additives with the intraocular tissue.

01100-8-1

ophtha futur®

products

Product	Article-Nr.	Spec.-Nr.	Units per box	Filling quantity [ml]	Dimension [mm x mm x mm]	Weight [g]	Shelf Life [months]
ophthafutur®							
deca	500500	0500	1 Vial	5	80 x 40 x 155	54	36
	500501	0501	1 Vial	7	80 x 40 x 155	58	36
	500502	0502	1 Syringe	5	120 x 35 x 195	68	36
	500503	0503	1 Syringe	7	120 x 35 x 195	72	36
octa	500504	0504	1 Vial	5	80 x 40 x 155	55	36
	500505	0505	1 Vial	7	80 x 40 x 155	59	36
	500506	0506	1 Syringe	5	120 x 35 x 195	69	36
	500507	0507	1 Syringe	7	120 x 35 x 195	73	36
sf6	500512	0512	1 Syringe	15	80 x 60 x 240	n.n.	24
c2f6	500513	0513	1 Syringe	12	80 x 60 x 240	n.n.	24
c3f8	500514	0514	1 Syringe	9	80 x 60 x 240	n.n.	24
sil 1000	500508	0508	1 Syringe	10	80 x 40 x 155	71	36
sil 2000	500509	0509	1 Syringe	10	80 x 40 x 155	71	36
sil 5000	500510	0510	1 Syringe	10	80 x 40 x 155	71	36
hpmc	500518	0518	1 Syringe	2	80 x 26 x 150	33	24
coming soon ...							
sil heavy	500511	0511	1 Syringe	10	80 x 40 x 155	n.n.	36

ophtha futur®

purity

01000-10-1

ophtha futur®

octa & deca

THE ISSUE

manufacturing-related impurities

H_{value} >> 10 ppm

Perfluorooctane and Perfluorodecaline are both liquids consisting from carbon and fluorine atoms only. For use as a medical device, it is essential that no other atoms (like Hydrogen: H) are bound in the molecules. Such alterations in the atomic structure can result in very reactive molecules, subsequently leading to tissue interaction. Incompletely fluorinated molecules can potentially damage the sensitive tissues within the eye.

A measure for the purity of a Perfluorocarbon is the H-Value. The H-value summarizes all impurities which relate to the presence of Hydrogen (H) containing compounds. A whole library of such compounds can be present even in incomplete purified products and each of these compounds can create a severe adverse reaction. Standard procedures of purifying and analytical controls are not sufficient to separate or detect the toxic impurities.

ophtha futur®

octa & deca purity

OUR ANSWER

multi-step ultra-purification process

H_{value} ≤ 10 ppm

our response: ultra-purified perfluorocarbon liquids

ophthafutur® octa and deca are highly purified by a unique and multi-step process. During the ultra-purification, all potential impurities are removed down to a level of not more than 10 ppm, which represents the limit of quantification. The in-process controls are very strict during manufacturing and analytics of **ophthafutur®** products. This results in a product which is finally purified to the highest extent.

The purification steps are monitored and the success of the purification process is verified. Final products are only accepted if the H-value is below 10 ppm.

01000-12-2

ophtha futur®

octa & deca usability

intended use

Perfluorocarbon liquids (PFCL) are used for intraoperative unfolding and repositioning / fixation of a detached retina. Furthermore, these liquids simplify the removal of luxated lenses and foreign bodies from the vitreous.

handling

PFCL, due to their high density, sink to the bottom of the eye. When applied, the liquid should be slowly injected over the papilla until a small bubble forms.
The tip of the injection cannula should then be kept within the bubble, gently enlarging it.

When removing PFCL, the user should ensure complete removal.

Remnants of PFCL may cause adverse reactions such as inflammation and could lead to interactions with subsequently filled silicone oil.

It is not recommended to directly exchange the PFCL with silicone oil to avoid direct contact between the two substances.

novel high performance polymer syringes (HPPS)

As glass syringes add considerable weight (uncomfortable for the surgeon) and PFCL can possibly interact with the lubrication of glass syringes, we introduced a novel filling technology.

Using HPPS syringes avoids contact between the perfluorocarbon liquid and the standard lubrication used in glass syringes.
This measure increases safety and reduces the likelihood of sticky effects or emulsification.

Preloaded syringes offer an ideal solution for the surgeon: They are easy to prepare and use. An ergonomically designed fingerplate was created to aid control and comfort.

ophtha futur®

octa & deca

facts

Parameters

Tamponade	**Perfluoro-n-octane C_8F_{18}**	**Perfluorodecalin $C_{10}F_{18}$**
Total Fluorinated Compounds	100 %	100 %
Perfluoro-N-Octane	≥ 95 %	–
Perfluorodecalin	–	≥ 95 % (cis + trans isomerism)
Refractive Index n_D^{20}	1.27	1.31
Density (20 °C)	1.77 g/ml	1.93 g/ml
H_{value} (Concentration of C-H Compounds)	< 10 ppm	< 10 ppm
Boiling Point	104 °C	141 °C
Bacterial Endotoxins	≤ 0.5 EU/ml	≤ 0.5 EU/ml

Product Sterility	Sterile Filtration	Sterile Filtration
Outer Surface Sterility	Steam Sterilisation	Steam Sterilisation

Cell Toxicity (%)	0	8	14	36	72	87	92
H_{value} (ppm)	≤ 10	175	350	700	1,400	2,100	2,800

Menz D-H, Feltgen N, Menz H, et al. How to ward off retinal toxicity of perfluorooctane and other perfluorocarbon liquids? *Invest Ophthalmol Vis. Sci.* 2018; 59: 4841-4846.

Compound	Surface Tension mN/m
Perfluoro-n-octane	14
1H-Perfluoro-n-octane	15
Perfluorodecalin	19

	Interfacial Tension Against Water mN/m
Perfluoro-n-octane	54
1H-Perfluoro-n-octane	32
Perfluorodecalin	53

Presentation

	Filling Volume	Container	Sterile Barrier
ophthafutur® deca	5 ml / 7 ml	vial	pouch
ophthafutur® deca	5 ml / 7 ml	syringe	pouch
ophthafutur® octa	5 ml / 7 ml	vial	pouch
ophthafutur® octa	5 ml / 7 ml	syringe	pouch

01000-14-2

ophtha futur®

octa & deca products

- High patient and product safety
- Multi-step proven & tested ultra-purification process
- Safe, biocompatible, sterile, endotoxin-free products
- 3 years shelf life
- Novel high performance polymer syringes (HPPS)

01000-15-1

ophtha futur®

environment

01000-16-1

ophtha futur®

gas

sf6 | c2f6 | c3f8

THE ISSUE

CO_2 emissions

The specific global warming potential of SF_6 is approximately 22.000 higher when compared to CO_2

Due to their impact on our environment, fluorinated gases have been banned from a wide range of industrial applications.
However, some gases are still available for medical purposes.

As the demand for gas is constantly increasing, the challenge is to support and preserve our environment.
The aim must be to release as little gas as possible during the surgical procedure.

Premixed gases, as well storage containers currently used (bottles, cans) can raise legal and/or stability concerns.

ophtha futur®

gas environment

OUR ANSWER

effective dose

borosilicate glass container

In borosilicate glass containers, the gas is stored in a non-pressurized state. The glass container is gas tight and does not allow any exchange with the external environment. The gentle sterilization process allows safe storage of the gas.

The system helps to protect the environment by offering only the quantities which are needed in the OR, thus minimizing waste.

The surgeons can adjust the gas concentration mixture to their needs without releasing too much gas into the environment.

01000-18-2

ophtha futur®

gas usability

Quick guide to assist surgical practice

SF_6, C_2F_6 and C_3F_8 are chemically and physiologically inert, colourless, and odourless gases for tamponading retinal detachments after vitrectomy.

application system

ophthafutur® gas is supplied in glass containers. The system also includes a preassembled sterile plastic syringe to prepare the gas mixture and a small gauge needle to facilitate the injection. A patient information card and a patient bracelet are also included.

preparation of gas mixtures

The illustration shows the single steps of the preparation of gas / air mixtures including handling instructions.
The gas is offered in a non-pressurized glass container. The pure gas is drawn into the larger sterile plastic syringe (see step 1–4 of the illustration). After the transfer, the surgeon can mix the gas with filtered ambient air.

Prior to mixing the excess of the pure gas which is not needed to prepare the mixture is expelled from the syringe. Ambient air is then drawn in through the filter into the plastic syringe. The amount of air determines the resulting mix ratio (step 5 – 8 of the illustration).

application

Ensure the vitreous body has been completely removed before applying SF_6, C_2F_6 or C_3F_8.

It should be considered that pure gases will expand, when purely injected into the eye. There is an equilibrium between gas and ambient air at which the gas mixture will not expand. Values from the literature are given to indicate possible non-expansive mixtures. Please be aware to carefully check the mixing process.

A small gauge needle is included to aid the injection of gas. This allows the surgeon to finally adjust the gas pressure within the eye after removing all surgical accessories. Patients who have received gas should be provided with the patient information card and a bracelet should be attached to their wrist.
Patients should be made aware of the possible hazards when a gas bubble is present in the eye.

warnings

Patients with a gas tamponade must not be exposed to pressure variations (flying, diving, etc.).
Nitrous oxide anaesthesia must be interrupted at least 20 minutes before applying SF_6, C_2F_6 or C_3F_8.

ophtha futur®

gas facts

Composition

SF_6 consists of sulfur hexafluoride with an initial purity of > 4.5 (Mass fraction > 99.995%) and density of 6.07 kg/m³ (1 bar, 20 °C).

C_2F_6 consists of hexafluoroethane with an initial purity of > 5.0 (Mass fraction > 99.999%) and density of 5.84 kg/m³ (1 bar, 15 °C).

C_3F_8 consists of octafluoropropane with an initial purity of > 4.0 (Mass fraction > 99.99%) and density of 8.17 kg/m³ (1 bar, 15 °C).

Properties

Filling quantity glass reservoir	SF_6: 15 ml	C_2F_6: 12 ml	C_3F_8: 9 ml
Total syringe volume	60 ml		

Possible effective tamponade duration of the gases [days]:

SF_6: 6
C_2F_6: 15
C_3F_8: 30

Possible retention time ot the gases [days]:

SF_6: up to 14
C_2F_6: up to 35
C_3F_8: up to 65

Packaging aid: quick guide, patient safety card and patient bracelet (including individuell insert), injection needle, instruction of use and product stickers.

01000-20-2

ophtha futur®

gas products

- High purity
- Improved convenience
- Adjustable gas concentration
- Environmental friendly
- Enhanced safety

ophtha futur®

purity

01000-22-1

ophtha futur®

sil

1000 | 2000 | 5000

THE ISSUE

manufacturing-related impurities

risks of silicone oil endotamponades

With silicone oils, as with all polymers, the characteristics are determined by chain length and chain length distribution.
Risks originate from volatile and short-chained components which are generated during production. These components can penetrate into tissue and damage cells.

Due to the combination of hydrophobicity and polarity, silicone oils can act as a trap for many impurities that can destabilize the tamponade ("emulsification"), even in low concentrations.

ophtha futur®

sil purity

OUR ANSWER

multi-step ultra-purification process

our response: ultra-purified silicon liquids

ophthafutur® silicone oils are ultra-purified according to a multi-step FDA approved process, which is succesfully performed since 1998. By combining extraction, thermal treatment and filtration, all critical impurities are separated.
The materials of the primary containers are selected to prevent any recontamination during manufacturing and storage.

purity criteria for silicone oils

In addition to the well-established GC-MS methods, the control of the removal of short-chained compounds by gel permeation chromatography (SEC) is an **ophthafutur®** standard.

ophtha futur®

sil usability

intended use

Silicone oils are used as ocular endotamponades in cases of severe retinal detachment, e.g. solid proliferative vitreo-retinopathy, traumatic detachment and giant tears, as well as other detachments of the retina, which cannot be treated with other forms of therapy.

Silicone oil can be injected into the eye with the support of vitrectomy machines. An adapter kit of the **ophthafutur®** line will support the oil injection.

Silicone oils exhibit a density < 1 g/cm³. For this reason the oil will float on water.

The eye should be completely filled with silicone oil to avoid cavities which may still contain water or gas.

To avoid high intraocular pressure, the patient should be monitored postoperatively. Due to the lower density, an iridectomy at 6 o'clock should be considered.

Emulsifications are one of the known side effects of oil injections and can be triggered by various reasons.
In addition to the precondition of the patient, the quality of the injected oil may play a role. The likelihood of emulsifications can be reduced by using ultrapurified oil.

The standard glass syringe, which is widely used in ophthalmology has a plastic luer lock at the tip. For added protection of the luerlock and safer handling, a mechanical support tube is shrunk over the tip.

ophtha futur®

sil facts

Parameters

Tamponade	Poly (Dimethylsiloxane)		
Viscosity (mPas, 25 °C)	5,000	2,000	1,000
Molar Mass (kDa)	54	41	34

Density (25 °C)	0.97 g/cm³
Interfacial Tension vs. Water (35 °C)	39 mN/m

Silanol Content	< 100 ppm
Content Volatile Oligosiloxanes (HS-GC/MS)	
DMCPS/D5	≤ 10 ppm
DMTS/MD2M	≤ 10 ppm
HMDS/MM	≤ 10 ppm
HMCTS/D3	≤ 10 ppm
OMCTS/D4	≤ 10 ppm
OMTS/MDM	≤ 10 ppm
∑	≤ 25 ppm
Acetone Content (HS-GC/MS)	< 10 ppm

Mass Loss	≤ 0.1%
Polydispersity	1.0 – 2.3
Refractive Index n_D^{25}	1.404

Filling Volume	10 ml Syringe
Sterilisation	Steam Sterilisation
Bacterial Endotoxins	≤ 0.5 EU/ml

01000-26-2

ophtha futur®

sil products

High patient and product safety

Multi-step proven and tested ultra-purification process

Safe, biocompatible, sterile, endotoxin-free products

3 years shelf life

ophtha futur®

safety

01000-28-1

ophtha futur®

hpmc

THE ISSUE

bacterial endotoxins and injectability

The world-wide ambition to reduce the acceptable concentration of bacterial endotoxins is a major challenge in manufacturing, especially for products derived from natural raw materials.

HPMC (Hydroxypropylmethylcellulose) is made from natural cellulose. Microbial impurities are therefore a major concern.

The main goal during ophthalmic surgery is to obtain an unobstructed view through the clear media of the eye. Bubbles contained in any liquid product may considerably obstruct the surgeon's view. The supply of HPMC having a sufficiently high viscosity paired with an easy and simple injectability represents an additional challenge.

ophtha futur®

hpmc safety

OUR ANSWER

GMP environment

advanced filling technology

our response: scientifically-based engineering

ophthafutur® hpmc is a dispersive ophthalmic viscosurgical device (OVD). Characterized by good wetting properties, excellent tissue and endothelium protection, efficient volume replacement and quick removal.

ophthafutur® viscoelastics are in compliance to the standards of pharmaceutical products and are manufactured according to the relevant GMP guidelines in a fully controlled clean room environment.
The filling is performed under pharmaceutical class A conditions avoiding any product contamination.
Vacuum technology enables bubble free filling.

01000-30-1

ophtha futur®

hpmc usability

fields of application are:

ophthafutur® hpmc can be used for various purposes.
The product can be used either intraocularly or extraocularly.
It allows excellent visualization when used during surgery due to the absence of bubbles.

ophthafutur® hpmc can be used to wet the cornea during cataract, corneal or retinal procedures.
The syringe allows an easy application of the product under a microscope.

The product may also be used to lubricate the surfaces of IOL injectors or IOL cartridges.

The patient should be monitored accordingly after surgery, as elevated intraocular pressure may occur.

ophtha futur®

hpmc facts

Parameters

OVD	Hydroxypropylmethylcellulose (HPMC)	
Molar Mass	80	kDa
Filling Volume	≥ 2.0	ml
HPMC Content	2	% (m/m)
pH	7.0	
Bacterial Endotoxins	≤ 0.2	EU/mL
Osmolality	285	mOsm/kg
Viscosity (20 °C)	3,500 – 6,000	mPas
Sterility	Steam Sterilisation	
Refractive Index n_D^{35}	1.336	

Injection of hpmc was investigated by using a variety of injection needles. To ensure safe injection, the surgeon should select the appropriate needle due to the variances of inner diameters between manufacturers of 23g outer needles.

23 G Cannulas – The Inner Diameter Makes The Difference

Type	Viscoflow	4001B	1274A	M3909	4001CTW
Inner Diameter (mm)	0.30	0.32	0.33	0.42	0.42

01000-32-2

ophtha futur®

hpmc

product

- Crystal clear view
- Endotoxin free
- Preloaded syringe

quality standards

The whole product life cycle of the **ophthafutur®** product lines is controlled by an integrated management system incorporating the activities of all partners involved.

The products are manufactured strictly according to the relevant GMP standards, especially

EU GMP Guideline,
ISO 13485,
21CFR 820 and 211,
CAN/CSA-ISO 13485,
ANVISA RDC 59/2000,
KGMP (Korea),
I.R. Iran GMP

Medical Device manufacturer according to Council Directive 93/42/EEC, certified by DQS Medizinprodukte GmbH (CE 0297)

Manufacturing authorization for Medicinal Products (Regierung von Oberbayern DE_BY_04_MIA_2011_0023).

FDA listed contract manufacturer (www.fda.gov, FDA FEI number 3005689226).

A modular system of manufacturing as well as documentation processes enables optimized and highly efficient validation and qualification procedures of all relevant processes and equipment. On this basis, medical devices and pharmaceuticals can be manufactured on an equivalent quality level. This was and is frequently confirmed by inspections of the world leading health agencies over the last two decades.

The whole **ophthafutur®** team intends to maintain and further improve the high level of the integrated quality system and to support our customers with related results and experiences.

01000-34-2

ophtha futur®

manufacturing

about the manufacturer

Pharmpur GmbH is the exclusive manufacturer of the **ophthafutur®** products. Pharmpur can look back to a 25 years successful history with the focus on contract manufacturing. Millions of units of ophthalmic liquids manufactured at Pharmpur have been used all over the world.

Pharmpur is one of the European pioneers of purifying perfluorocarbon liquids and silicone oils for ophthalmic use. The chemist Dr. D.-H. Menz played the leading role as managing partner as well as inventor and developer of products and processes of Pharmpur, reflected in numerous papers and patents.

Over the years the company was organically developed into a state of the art organisation with expertise in analytics, manufacturing of medical devices and pharmaceuticals, product development and quality management.
A young and highly educated staff ensures the continuous further development of the company.

manufacturing excellence – made in germany

The concept of combining all critical production steps under one roof guarantees conformity and excellent quality. The quality of the raw materials, which are synthesized and ultra-purified according to proprietary processes, meets the highest standards in international comparison.

Pharmpur maintains validated procedures for compounding, aseptic filling, autoclaving and dry heat sterilization. These procedures are completed by all associated packaging processes. A dense network of quality controls is performed per batch in own, fully equipped laboratories.

product-portfolio

Pharmpur is specialized in the fill-finish manufacturing of ready-to-use syringes and vials.

The product range covers gases, products of low and high viscosity and gel-type media (viscoelastic substances). The manufacturing processes, as well as the documentation processes, are based on a modular system which allows an efficient process management employing optimized validation strategies.

Pharmpur GmbH

Messerschmittring 33
86343 Königsbrunn
Germany

Tel. + 49 8231 9577 - 0
Fax + 49 8231 9577 - 22

info@pharmpur.de
www.pharmpur.de

Office Dornstadt

Hauffstrasse 21
89160 Dornstadt
Germany

Tel. +49 7348 4 07 70 11

www.ophthafutur.de

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