V8. 21/12/06- suite téléconférence avec AFSSAPS

OBJET : arrêt définitif de commercialisation, rappel de produits et suivi de patients implantés
Lentilles intraoculaires de presbytie NEWLIFE® / VIVARTE® PRESBYOPIC
Lentilles intraoculaires de myopie GBR® / VIVARTE® MYOPIC

CE BULLETIN D'INFORMATION NECESSITE VOTRE COLLABORATION

Cher Docteur,

Suite à notre dernière communication de Mars 2006, nous soulignons l'importance de ce message et, nous nous permettons de solliciter votre implication active.

Concernant les lentilles de presbytie NEWLIFE® / VIVARTE® PRESBYOPIC

Dans notre précédent message nous portions à votre connaissance des pertes endothéliales rencontrées avec les implants Newlife® et Vivarte® Presbyopic, tous deux implants de presbytie implantés en chambre antérieure. Ces pertes endothéliales apparaissaient dans les 2 ou 3 ans suivant l'implantation. Chez certains de ces patients, elle était suffisamment importante pour conduire à une explantation. Ces incidents avaient conduit Ioltech à suspendre la promotion et la commercialisation de l'implant Newlife®, la commercialisation de Vivarte® presbyopic étant arrêtée depuis décembre 2005.

A la suite de notre courrier, en accord avec l'Agence Française de Sécurité Sanitaire des Produits de Santé (AFSSAPS), nous avons réalisé une étude rétrospective portant sur 150 patients (270 yeux) ayant au moins un implant Newlife ou Vivarte presbyopic depuis en moyenne 18.76 mois [0.26-54.47]. Cette étude rétrospective montre que le risque de chute de la densité endothéliale augmente dans les 2 ou 3 ans qui suivent l'implantation, cette chute pouvant nécessiter l'explantation de la lentille. Néanmoins aucune cause spécifique n'a pu être clairement identifiée.
Les résultats de l'étude confirment notre décision (voir Synopsis joint). La commercialisation du Newlife® est en conséquence définitivement arrêtée.

Concernant les lentilles de myopie GBR® / VIVARTE® MYOPIC

Par ailleurs, deux implants destinés à la correction de la myopie, GBR® et Vivarte® myopique, présentent une conception similaire aux implants de presbytie et sont implantables en chambre antérieure de l'œil phaque. Bien que moins fréquents, plusieurs cas de pertes de cellules endothéliales ayant nécessité une explantation nous ont été rapportés pour ces implants.

En accord avec l'AFSSAPS, Ioltech prend volontairement la décision de rappeler le GBR® et d'arrêter définitivement sa commercialisation, la commercialisation du Vivarte® myopique étant arrêtée depuis décembre 2005.

Notre personnel entrera en contact avec vos collaborateurs afin de savoir, si vous êtes encore en possession de GBR® et facilitera leur rapatriement chez Ioltech dans les meilleurs délais.

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Suivi des patients implantés

En accord avec l'AFSSAPS, pour tous les patients ayant un implant Newlife®, Vivarte® presbyopic, GBR® ou Vivarte® myopic, nous recommandons que la fréquence du comptage endothélial par microscopie spéculaire soit augmentée à un contrôle semestriel, au lieu d'un contrôle annuel. Dans le cas où vous observeriez une perte endothéliale supérieure à 30 % par comparaison au comptage cellulaire préopératoire et / ou une densité cellulaire inférieure à 1500 cellules / mm², l'opportunité d'une explantation devra être envisagée en concertation avec le patient, l'explantation pouvant être uni ou bilatérale.

Toute perte endothéliale de niveau telle que précisée ci-dessus et/ou toute explantation doit faire l'objet d'une déclaration de matériovigilance auprès de l'AFSSAPS.

Par ailleurs, en accord avec l'AFSSAPS, Ioltech continuera le suivi de la cohorte de patients inclus dans l'étude rétrospective mentionnée ci-dessus, afin de dégager d'éventuels facteurs de risque de façon significative et/ou d'adapter les recommandations de suivi des patients implantés.

Ioltech continuera à vous tenir informé sur le sujet, n'hésitez pas à nous contacter directement pour toutes questions que vous jugeriez utiles.

Nous vous prions d'agréer cher Docteur, l'assurance de notre plus haute considération.

Pascal Bernard
Directeur Recherche Avancée
Correspondant Matériovigilance

Marielle Fournier
Responsable Affaires Réglementaires

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RE : Definitive stop of marketing, product recall and follow-up of implanted patients
Presbyopic intraocular lenses NEWLIFE® / VIVARTE® PRESBYOPIC

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Myopic intraocular lenses GBR® / VIVARTE® MYOPIC

ACTION REQUIRED

Dear Doctor,

This message is a very important update from our March 2006 communication and will require action on your part.

Concerning presbyopic intraocular lenses, NEWLIFE® / VIVARTE® PRESBYOPIC

As background, in March we informed you of concerns brought to our attention regarding endothelial cell loss with the Newlife® or Vivarte® Presbyopic intraocular lens, both implants being presbyopic lenses implanted in the anterior chamber. At that time we reported endothelial cell loss that started occurring after two to three years post-implantation. In these patients the loss was great enough that it lead to explantation of the lens. Consequently to these incidents, Ioltech discontinued the sales and marketing of the Newlife® intraocular lens (marketing of Vivarte® Presbyopic intraocular lens was stopped in December 2005).

Since March, in agreement with the our local French authority**,** the French Health Products Safety Agency (AFSSAPS), a retrospective investigation involving 150 patients (270 eyes) having received at least one implant Newlife® or Vivarte® presbyopic with a mean follow-up of 18.76 months [0.26-54.47] has been performed. This study shows that the risk of endothelial cell loss increases after two to three years of implantation. The level of cell loss may necessitate explantation of the lens. However, no specific cause for this endothelium cell loss has been clearly identified.

The study results support our decision (see attached synopsis). As a result, sales and marketing of Newlife® will not be resumed again.

Concerning myopic intraocular lenses, GBR® / VIVARTE® MYOPIC

Two other implants used in myopic correction, GBR® and Vivarte® myopic, have a similar design and are also implanted in the anterior chamber in phakic eyes. Several cases of endothelial cell loss that may necessitate explantation, although less frequent, have been reported so far.

In agreement with our local French authority AFSSAPS, Ioltech voluntarily and definitively stops selling the GBR® (marketing of Vivarte® myopic intraocular lens was stopped in December 2005).

One of our staff will be contacting your practice to determine if you have any remaining product still in stock and to facilitate the return to Ioltech as soon as possible.

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Follow-up of implanted patients

In agreement with our local French authority AFSSAPS, for the patients having been implanted so far, we recommend that the periodic monitoring of corneal endothelium performed by cell count using specular microscopy after implantation is increased from yearly to every 6 months. In the case that you observe greater than a 30% endothelial cell loss (when compared to the preoperative cell count) and/or count below 1500 cells/mm², the opportunity of an explantation should be evaluated in concert with the patient ; explantation may be uni- or bilateral.

Any loss of endothelial cells at a level such as described here above and/or any explantation must be reported to your local authorities.

Moreover, in agreement with our local French authority AFSSAPS, Ioltech will continue the follow-up of the patients cohort included in the retrospective study mentioned above, in order to identify significant potential risk factors and/or to adapt the follow-up recommendations for implanted patients.

Ioltech, will continue to keep you updated on this matter. If you have any questions regarding this notice please do not hesitate to contact us directly.

Best Regards,

Pascal Bernard
Advanced Research Director
Adverse Event correspondent

Marielle Fournier
Head of Regulatory Affairs

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Name of sponsor/Company IOLTECH SA A company of Carl Zeiss Meditec AG	**Name of product** NEWLIFE (VIVARTE Presbyopic)	**Common designation** Intra-ocular lens for Presbyopic surgery (anterior chamber)
Title of study	Observational study of tolerance of Newlife implant	
Investigator(s)	Pr Baikoff - Dr Bosc - Dr Simorre - Dr Gauthier - Dr Hachet - Pr Lagoutte / Dr Chastang	
Study centre(s)	6 centres	
Publication (reference)	NA	
Studied period (years) April 2006 – September 2006	Phase of development Post-marketing phase	
Objectives	Following several cases of important loss of endothelial cells after 2-3 year implantation that may lead to corneal damage and explantation of Newlife®. In agreement with local authorities, AFSSAPS, observational study in order to understand the phenomenon and/or risk factors.	
Methodology	Surgeons having implanted the most important numbers of Newlife implant have received a letter explaining the need and objectives of post-operative data analysis. Data have been collected by independent clinical research associates at the centres. Data sheets were completed: - pre-operative data - per-operative data - post-operative data at each control visit When data relative to endothelial cell count were not available at any post-operative visit, patient was not enrolled. An information note has been also provided to the center for the concerned patients, explaining the data collection.	
Number of patients	150 patients (277 eyes) Compliance to eligibility conditions of patients to be implanted with a Newlife has been checked versus surgical protocol recommended by Ioltech.	
Diagnosis and main criteria	See methodology	
Test product	Newlife	
Duration of implantation	Duration of implantation range from 0.26 to 54.47 months (mean = 18.76 months)	
Criteria for evaluation	- endothelial cell count, pre-operative and post-operative - variation of endothelial cell count - ACD - Duration of implantation	
Statistical method	Double data record on Alpha/Open VMS Criteria analysis mainly descriptive. Numeric variables are means, standard deviations, median, 95% confidence interval and extreme values. Qualitative variables are numbers and %.	
Summary/Conclusion	Over the 270 eye data collected, 25 were explanted, among which 6 were explanted due to endothelial cell loss. Mean duration of implantation observed for the explanted population due to endothelial cell loss is 11 month longer compared to the mean duration of implantation of the global population (29.56 months and 18.76 months respectively). It seems that a « low » endothelial cell count at pre-operative visit (between 1800 and 2000 c/mm²) is not predictive of pathological cell loss after implantation. - none of the explanted case has a pre-operative count below 2000 c/mm² - none of the global population case having a low pre-operative cell count has been explanted to date for endothelial cell loss and all of them remained stable all over the follow-up. The potential effect of the diameter of the implant has been also assessed but data collected does not allow to conclude as diameter of the implant	

	and size of irido-corneal angle are both available for only 20.85% of the cases. The depth of anterior chamber seems to be the variable having the most important effect. An ACD below 3.3 mm has been observed in 4 cases of explantations due to endothelial cell loss over 5. e(ACD is not available in the 6th case of explantation due to cell loss). - Mean ACD in the sub-population explanted due to endothelial cell loss was 3.1 +/- 0.1 mm. - Mean ACD in the overall population, excluding the explanted patients is 3.4 +/- 0.3 mm. However, one case of explantation due to endothelial cell loss has an ACD of 3.4 mm that excludes the conclusion that tightness of anterior chamber lead is the single factor leading to dramatic corneal decompensation. These materiovigilance cases may be of multifactor origins. Due to the design of the study, no data is available concerning the way of life of the patients (sport …). However, extrapolation curves based on the data available so far shows a potential 40-50% cell loss after 60 month implantation. Regular and rigorous survey of corneal endothelium of implanted patients using periodic specular microscopy remains the mean of choice to detect any dramatic corneal decompensation.