Exactech
Surgeon focused. Patient driven.™

GLOBAL HEADQUARTERS
2320 NW 66TH COURT
GAINESVILLE, FL 32653 USA
+1 352.377.1140
+1 352.378.2617

*****URGENT DEAR HEALTHCARE PROFESSIONAL COMMUNICATION*****

28 June 2021

To: Surgeons, Hospitals, Health care professionals
Description: Exactech Connexion GXL acetabular polyethylene liners

Section 1- Introduction

Dear Surgeon:

The purpose of this letter is to inform you of recent observations made by Exactech regarding the clinical performance of the Connexion GXL acetabular liner. This communication relates to all Exactech Connexion GXL liners. The product specific information is listed in Table 1 below.

It is the practice of Exactech to perform detailed analysis and inform our surgeon customers and patients as soon as possible when such observations are made.

- During the past ~24 months, Exactech has observed that in a small percentage of patients (.118%) who are between 3-6 years from index total hip arthroplasty, the Connexion GXL liner exhibits early linear and volumetric wear.
- In some of these patients, wear has led to proximal femoral and acetabular osteolysis.
- This phenomenon appears to occur when the relative implant position of the acetabular and femoral components in either/both the coronal plane and the sagittal plane results in edge loading of the femoral head on the liner.
- This phenomenon appears to be more common in direct anterior (DA) hip approaches.
- This phenomenon appears to be more common in patients with higher activity levels[1].
- The phenomenon appears to be more common and more pronounced in patients who have been implanted with larger femoral heads (e.g. 36mm), and in which the thinnest available acetabular liner was used (e.g., a 36mm CoCr head used in 52mm acetabular socket).
- In patients where the femoral head is articulating orthogonally to the acetabular component in the functional pelvic position (i.e. edge loading is not occurring), this wear phenomenon does not appear to occur.

Exactech's recommendation for surgeons is that Connexion GXL patients who are less than six (6) years from index surgery and who have not been seen in over 12 months return to the office/clinic for a routine clinical exam and x-rays, including standing AP pelvis, cross-table lateral, and sitting/functional lateral. These x-rays will assess the relative alignment of the acetabular and femoral components and should identify edge loading. For patients with edge loading components, early asymmetric polyethylene wear, and early signs of lysis, the surgeon should consider revising the Connexion GXL liner to Exactech's latest generation HXLPE, Vitamin E liner, if possible.

Actions to be Taken:

- **Review this communication thoroughly.**
- **Contact your local Exactech Representative** if you have any questions regarding this communication.
- **Complete and sign** the ***"Dear Healthcare Profession Letter Response Form"*** on the last page of this communication and return to Exactech via the form instructions **within 10 business days of receipt.**

GLOBAL HEADQUARTERS
2320 NW 66TH COURT
GAINESVILLE, FL 32653 USA
+1 352.377.1140
+1 352.378.2617

Table 1: Product Information:

Catalog Number	Description	Catalog Number	Description
104-28-XX	MCS +5GXL LINER 5/15 DEG	**132-36-XX**	Acumatch GXL 15 Degree Liner, 36mm
	MCS GXL LINER 5/15 DEG		Novation GXL Liner, Lipped Ant, 36mm
104-32-XX	MCS +5GXL LINER 5/15 DEG		Novation GXL Liner, Lipped, 36mm
	MCS GXL LINER 5/15 DEG	**132-40-XX**	Novation GXL Liner, Lipped Ant, 40mm
104-36-XX	MCS +5GXL LINER 5/15 DEG		Novation GXL Liner, Lipped, 40mm
	MCS GXL LINER 5/15 DEG	**134-28-XX**	Acumatch GXL, Ext Cov Liner, 28mm
130-22-XX	Novation GXL Neutral Liner, G00, 22mm ID	**136-22-XX**	Novation GXL Liner, +5mm Lateralized, G00, 22mm ID
130-28-XX	Acumatch GXL 0 Degree Liner, 28mm	**136-28-XX**	Novation GXL Liner, +5mm Lateralized, 28mm
	Novation GXL Liner, Neutral, 28mm		Novation GXL Liner, +5mm Lateralized, G0, 22mm ID
	Novation GXL Neutral Liner, G0, 28mm ID	**136-32-XX**	Novation GXL Liner, +5mm Lateralized, 32mm
130-32-XX	Acumatch GXL 0 Degree Liner, 32mm	**136-36-XX**	Novation GXL Liner, +5mm Lateralized, 36mm
	Novation GXL Liner, Neutral, 32mm	**136-40-XX**	Novation GXL Liner, +5mm Lateralized, 40mm
130-36-XX	Acumatch GXL 0 Degree Liner, 36mm	**138-22-XX**	Novation GXL 10 deg Liner, G00, 22mm ID
	Novation GXL Liner, Neutral, 36mm	**138-28-XX**	Acumatch GXL 15 Degree, +5 Lat Liner, 28mm
130-40-XX	Novation GXL Liner, Neutral, 40mm		Novation GXL 10 Deg Liner, G0, 28mm ID
132-22-XX	Novation GXL Liner, G00, 22mm ID		Novation GXL Liner, 10 Deg Face, 28mm
	Novation GXL Liner, Lipped Ant, 28mm	**138-32-XX**	Novation GXL Liner, 10 Deg Face, 32mm
132-28-XX	Acumatch GXL 15 Degree Liner, 28mm	[redacted]	
	Novation GXL Liner, G0, 28mm ID		
	Novation GXL Liner, Lipped Ant, 28mm		
	Novation GXL Liner, Lipped, 28mm		
132-32-XX	Acumatch GXL 15 Degree Liner, 32mm		
	Novation GXL Liner, Lipped Ant, 32mm		
	Novation GXL Liner, Lipped, 31mm		

GLOBAL HEADQUARTERS
2320 NW 66TH COURT
GAINESVILLE, FL 32653 USA
+1 352.377.1140
+1 352.378.2617

Catalog Number	Description	Catalog Number	Description
	Novation GXL Liner, Lipped, 32mm	[redacted]	

Our first concern is for the health and safety of patients and the users of our products. Actions of this type are collaborative efforts and require your participation to be effective.

Sincerely,

Sharat Kusuma (Jun 29, 2021 14:16 EDT)

Sharat Kusuma, MD
Chief Medical Officer
Exactech, Inc.
2320 NW 66th Court
Gainesville, FL 32653
800.392.2832

GLOBAL HEADQUARTERS
2320 NW 66TH COURT
GAINESVILLE, FL 32653 USA
+1 352.377.1140
+1 352.378.2617

Section 2 - Synthesis of worldwide clinical data regarding Exactech Connexion GXL

Since 2008, 89,050 Connexion GXL liners have been implanted worldwide (as of April 2021). Exactech has maintained and monitored several data sources to document the clinical track record of the Connexion GXL liner. A review of all available data sources as of May 3rd, 2021, reveals 105 total complaints related to liner wear (overall complaint rate of 0.118% since 2008). Within this group of 105 complaints, there have been 90 worldwide known revisions for wear-related issues (wear-related revision rate of 0.101%). Kaplan-Meier survivorship analysis suggests that ~ 1% of liners will fail at eight years due to polyethylene wear.

The most common implant characteristics associated with increased risk of wear-related revision include:

1. A lateralized (+5mm) or face-changing liner – **this group has a ~2.5x increased risk of revision**
2. Use of the thinnest liner (i.e., the largest available femoral head is used with the implanted acetabular shell) – **this group has ~2.0x increased risk of revision**
3. When these implant factors are combined with an edge loading environment, the risk of premature wear further increases.

It is relevant that complaint rates of the Connexion GXL liner vary significantly between institutions and even within countries. For example, both the United States (0.521%) and Germany (0.828%) have higher complaint rates than the overall complaint rate. Additionally, some institutions have reported failure rates as high as 3.2% [1], with others reporting rates as low as 0.1% for wear-related issues [Exactech clinical data]. In those series with the highest revision rates, 78% of revised cases have used the thinnest available liner (#2 above).

It is also important to note that since 2007, Exactech has conducted an ongoing, large scale clinical study of the Connexion GXL liner that includes 1,394 patients. This post-market clinical follow-up (PMCF) study comprises 22 surgeons from 12 different sites. This actively and regularly monitored patient group has demonstrated a total of three revisions (0.21%) for liner wear issues.

In summary, the overall currently known, wear-related failure rate for ~90,000 implanted devices is 0.115%. The survivorship rate of the Connexion GXL liner is within registry standards for safe devices. Exactech's regularly monitored PMCF database of 1,394 patients demonstrates a 0.21% revision rate for polyethylene wear and lysis.

Section 3 – Synthesis, conclusions, and Exactech recommendations and support for surgeons

1. Like all implant companies, Exactech is constantly innovating and improving implants.
2. The Connexion GXL resulted from the careful analysis of the state-of-the-art THA bearing technology when it was developed in ~2007.
3. Moderate crosslinking was considered safe at that time and is protective against liner fracture.
4. Connexion GXL has robust wear resistance and fracture resistance properties as evidenced by bench testing and large long-term clinical follow-up series.
5. Individual institutional series have demonstrated that a small percentage of patients have significant lysis and wear with Connexion GXL liner; the highest reported single institution wear-related failure rate is 3.2%
6. Cup position on AP x-rays is not predictive of wear.
7. The phenomenon of significant wear and lysis is multifactorial in those patients who exhibit it.
8. The Connexion GXL liner is inherently susceptible to edge loading differently than HXLPE. Connexion GXL tends to exhibit accelerated linear and volumetric wear when edge loaded (as opposed to breaking or dissociating).

GLOBAL HEADQUARTERS
2320 NW 66TH COURT
GAINESVILLE, FL 32653 USA
+1 352.377.1140
+1 352.378.2617

9. When the combined anteversion and/or combined abduction of the acetabular and femoral components is high, edge loading and accelerated wear can present
10. Individual patient biologic, immunologic response is also an important determinant of osteolysis
11. Exactech recommends regular follow-up on patients with Connexion GXL liners who are < 6 years from index THA.
12. For patients < 6 yrs. from index THA who have not been seen in > 12 months, recommend follow-up:
    a. AP pelvis x-ray
    b. Cross-table lateral x-ray
    c. Functional sitting and standing x-rays, if possible
13. For patients with x-ray signs of either:
    a. Edge loading (by x-ray)
    b. Early lysis
    c. Exactech recommends either repeat follow-up in 6-12 months, CT scan imaging (if considered clinically necessary to assess lytic lesions), and potentially revision to the next generation Exactech Vitamin E, HXLPE if possible, based on the surgeon's judgment.
14. Finally, Exactech encourages surgeons who receive this letter to inform Exactech as soon as possible if they are aware of Connexion GXL failures in their own personal series that have not been previously reported.

Appendix:

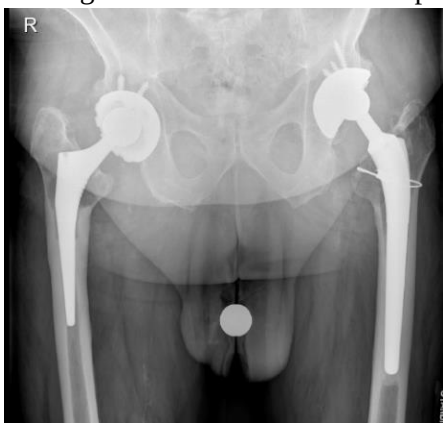
X-ray image examples of Connexion GXL liner cases exhibiting early failure:

1. Significant combined anteversion with anterior edge loading of the femoral head on the acetabular liner

2. Osteolysis, radiolucencies, and/or asymmetric wear

GLOBAL HEADQUARTERS
2320 NW 66TH COURT
GAINESVILLE, FL 32653 USA
+1 352.377.1140
+1 352.378.2617

3. Significant vertical/abduction positioning of the acetabular component



Background/history of UHMWPE and XLPE in hip/knee arthroplasty and design rationale of Exactech Connexion GXL acetabular liner

The R&D work that led to the development of the Exactech Connexion GXL liner was completed between 2005-2008. The Connexion GXL liner was first released for broad commercialization in 2008.

Between the years of ~1999-2005, HXLPE was first introduced to the market by several companies. During these early years of HXLPE usage, numerous reports of HXLPE mechanical failures were reported (Zimmer Longevity HXLPE acetabular liner, the Zimmer Prolong knee polyethylene, and the DePuy Pinnacle HXLPE liner) [2]–[8]. It was not as clear in the early 2000's as it is today that HXLPE and Vitamin E antioxidant infused liners would be safe and would exhibit sufficient fracture resistance[9], [10].

Therefore, Exactech (similar to other companies), conducted extensive research and development activity to produce the "moderately" crosslinked Connexion GXL liner that attempts to optimize mechanical properties of fracture resistance with the crosslinking benefits of reduced polyethylene wear. Hip simulation studies have long shown that gamma radiation in the range of 50-100kGy can reduce abrasive wear in polyethylene[10], [11].

This type of data was used to develop the Connexion GXL manufacturing process, in which compression molded UHMWPE undergoes two precision split-doses of 25kGy irradiation for a total of 50kGy. Bench testing demonstrated that the Connexion GXL liner exhibits a 59% reduction in wear and excellent performance in three-point bending testing (i.e. fracture resistance). As of April 2021, nearly 90,000 Connexion GXL liners have been implanted globally, and Exactech has not had any reports of liner fracture and/or catastrophic liner dissociation.
It is important to note that similar to other moderately crosslinked liners, recent bench testing of the Connexion GXL liner has substantiated our clinical experience by demonstrating that it can wear at a faster rate when placed in an environment of anterior edge loading and posterior impingement (as is often seen with anterior approaches). In many reported cases of Connexion GXL liner wear and osteolysis, it is noted that either the combined anteversion or combined abduction of the components results in edge loading of the Connexion GXL liner. In cases where edge loading is not occurring, accelerated wear does not appear to occur.

Therefore, like every implant company, Exactech is constantly in the process of improving its products. The field of hip arthroplasty has evolved over the past decade – 15-year global clinical HXLPE experience is now widely available and demonstrates its high performance in THA. Concurrent with this global experience, Exactech has taken care to evolve its liners from the moderately crosslinked Connexion GXL to our next generation of

GLOBAL HEADQUARTERS
2320 NW 66TH COURT
GAINESVILLE, FL 32653 USA
+1 352.377.1140
+1 352.378.2617

polyethylene highly crosslinked Vitamin E liners, which were introduced in 2018. Bench testing reveals that Exactech's new HXLPE does outperform the Connexion GXL liner in both volumetric wear and edge loading assessments.

Synthesis of recent peer-reviewed published data regarding Exactech Connexion GXL acetabular liner

Since 2019, three peer-reviewed publications have been produced regarding early wear and osteolysis with the Connexion GXL liner. These publications have helped Exactech elucidate which Connexion GXL patients are at risk for early failures[1], [12], [13].

These articles have identified a total of 19 patients that experienced of medium-term failure of Connexion GXL liners. The failure rates of the Connexion GXL liner in these series range from 1%-3.2% at ~ 5 years. The articles propose that surveillance of Connexion GXL patients is warranted. The average time to revision in these three papers was ~ 5 years. In addition, Exactech's deeper analysis of these 19 cases has revealed what has been described above – the highest risk patients for wear-related failure are those with the thinnest polyethylene liners.
Additionally, in these series was a tendency for early and accelerated wear to be demonstrated in patients who had cup positions toward cups at upper ends of Lewinnek abduction/anteversion, and a tendency towards younger, (<70 yrs.) more active patients. Of note, these papers did not measure the functional pelvic position of the acetabular components. These papers used the Lewinnek safe zone concept on static x-rays to determine the relative appropriateness of cup position[1], [12], [13].

It is well understood that Lewinnek safe zones have relatively limited clinical utility. Rather, a patient's sitting and standing functional pelvic position is more predictive of hip stability and edge loading [14]–[17].
It is also noted that the index THA in many of the patients in these series was performed through a direct anterior approach. It has been reported that the direct anterior approach to the hip can lead to supranormal combined anteversion of the acetabular and femoral components with subsequent anterior edge loading[16], [18], [19].

Finally, it is also important to note that the immunologic response to wear debris is highly variable between patients [20], [21]. Therefore, it is likely that a subset of patients who have significant biologic and immunologic response to wear debris are at greater risk for early osteolysis.

In summary, these published articles have helped identify risk factors early wear and lysis in patients who have been implanted with a Connexion GXL liner. [18], [19].

References

[1] C. A. Kahlenberg, L. Menken, A. S. Ranawat, and J. A. Rodriguez, "Early failure of a modern moderately cross-linked polyethylene acetabular liner," *Arthroplasty Today*, vol. 6, no. 2, pp. 224–226, Jun. 2020, doi: 10.1016/j.artd.2020.02.002.
[2] M. P. Ast, T. K. John, A. Labbisiere, N. Robador, and A. G. D. Valle, "Fractures of a single design of highly cross-linked polyethylene acetabular liners: an analysis of voluntary reports to the United States Food and Drug Administration," *J. Arthroplasty*, vol. 29, no. 6, pp. 1231–1235, Jun. 2014, doi: 10.1016/j.arth.2013.12.022.
[3] J. Furmanski, M. J. Kraay, and C. M. Rimnac, "Crack Initiation in Retrieved Cross-Linked Highly Cross-Linked Ultrahigh-Molecular-Weight Polyethylene Acetabular Liners: An Investigation of 9 Cases," *J. Arthroplasty*, vol. 26, no. 5, pp. 796–801, Aug. 2011, doi: 10.1016/j.arth.2010.07.016.
[4] W. Waewsawangwong and S. B. Goodman, "Unexpected failure of highly cross-linked polyethylene acetabular liner," *J. Arthroplasty*, vol. 27, no. 2, p. 323.e1–4, Feb. 2012, doi: 10.1016/j.arth.2011.04.010.

GLOBAL HEADQUARTERS
2320 NW 66TH COURT
GAINESVILLE, FL 32653 USA
+1 352.377.1140
+1 352.378.2617

[5] A. Yun *et al.*, "Polyethylene Liner Dissociation Is a Complication of the DePuy Pinnacle Cup: A Report of 23 Cases," *Clin. Orthop.*, vol. 474, no. 2, pp. 441–446, Feb. 2016, doi: 10.1007/s11999-015-4396-5.

[6] O. J. Diamond, L. Howard, and B. Masri, "Five cases of tibial post fracture in posterior stabilized total knee arthroplasty using Prolong highly cross-linked polyethylene," *The Knee*, vol. 25, no. 4, pp. 657–662, Aug. 2018, doi: 10.1016/j.knee.2018.05.005.

[7] D. Hara *et al.*, "Late failure of annealed highly cross-linked polyethylene acetabular liner," *J. Mech. Behav. Biomed. Mater.*, vol. 28, pp. 206–212, Dec. 2013, doi: 10.1016/j.jmbbm.2013.08.003.

[8] M. A. Yee, T. J. O'Keefe, and S. Winter, "Incarcerated fracture fragments of Longevity polyethylene liners after total hip arthroplasty," *Arthroplasty Today*, vol. 2, no. 1, pp. 6–10, Mar. 2016, doi: 10.1016/j.artd.2015.12.006.

[9] D. T. Schroder, N. H. Kelly, T. M. Wright, and M. L. Parks, "Retrieved highly crosslinked UHMWPE acetabular liners have similar wear damage as conventional UHMWPE," *Clin. Orthop.*, vol. 469, no. 2, pp. 387–394, Feb. 2011, doi: 10.1007/s11999-010-1552-9.

[10] J. A. D'Antonio, "CORR Insights®: Wear and Osteolysis of Highly Crosslinked Polyethylene at 10 to 14 Years: The Effect of Femoral Head Size," *Clin. Orthop.*, vol. 474, no. 2, pp. 372–373, Feb. 2016, doi: 10.1007/s11999-015-4365-z.

[11] O. K. Muratoglu, C. R. Bragdon, D. O. O'Connor, M. Jasty, and W. H. Harris, "A novel method of cross-linking ultra-high-molecular-weight polyethylene to improve wear, reduce oxidation, and retain mechanical properties. Recipient of the 1999 HAP Paul Award," *J. Arthroplasty*, vol. 16, no. 2, pp. 149–160, Feb. 2001, doi: 10.1054/arth.2001.20540.

[12] W. C. Thomas, H. K. Parvataneni, R. G. Vlasak, and C. F. Gray, "Early Polyethylene Failure in a Modern Total Hip Prosthesis: A Note of Caution," *J. Arthroplasty*, vol. 35, no. 5, pp. 1297–1302, May 2020, doi: 10.1016/j.arth.2019.12.043.

[13] R. Yakkanti *et al.*, "Unexpected Wear of a Moderately Crosslinked Polyethylene in Total Hip Arthroplasty," *Artic. Press*, 2021.

[14] T. Tezuka, N. D. Heckmann, R. J. Bodner, and L. D. Dorr, "Functional Safe Zone Is Superior to the Lewinnek Safe Zone for Total Hip Arthroplasty: Why the Lewinnek Safe Zone Is Not Always Predictive of Stability," *J. Arthroplasty*, vol. 34, no. 1, pp. 3–8, Jan. 2019, doi: 10.1016/j.arth.2018.10.034.

[15] M. P. Abdel, P. von Roth, M. T. Jennings, A. D. Hanssen, and M. W. Pagnano, "What Safe Zone? The Vast Majority of Dislocated THAs Are Within the Lewinnek Safe Zone for Acetabular Component Position," *Clin. Orthop.*, vol. 474, no. 2, pp. 386–391, Feb. 2016, doi: 10.1007/s11999-015-4432-5.

[16] W. S. Murphy, H. H. Yun, B. Hayden, J. H. Kowal, and S. B. Murphy, "The Safe Zone Range for Cup Anteversion Is Narrower Than for Inclination in THA," *Clin. Orthop.*, vol. 476, no. 2, pp. 325–335, Feb. 2018, doi: 10.1007/s11999.0000000000000051.

[17] J. M. Elkins, J. J. Callaghan, and T. D. Brown, "The 2014 Frank Stinchfield Award: The 'landing zone' for wear and stability in total hip arthroplasty is smaller than we thought: a computational analysis," *Clin. Orthop.*, vol. 473, no. 2, pp. 441–452, Feb. 2015, doi: 10.1007/s11999-014-3818-0.

[18] B. F. Mayeda, J. G. Haw, A. K. Battenberg, and T. P. Schmalzried, "Femoral-Acetabular Mating: The Effect of Femoral and Combined Anteversion on Cross-Linked Polyethylene Wear," *J. Arthroplasty*, vol. 33, no. 10, pp. 3320–3324, Oct. 2018, doi: 10.1016/j.arth.2018.06.003.

[19] K. Watanabe, K. Mitsui, Y. Usuda, and K. Nemoto, "An increase in the risk of excessive femoral anteversion for relatively younger age and types of femoral morphology in total hip arthroplasty with direct anterior approach," *J. Orthop. Surg. Hong Kong*, vol. 27, no. 2, p. 2309499019836816, Aug. 2019, doi: 10.1177/2309499019836816.

[20] P. E. Purdue, P. Koulouvaris, H. G. Potter, B. J. Nestor, and T. P. Sculco, "The cellular and molecular biology of periprosthetic osteolysis," *Clin. Orthop.*, vol. 454, pp. 251–261, Jan. 2007, doi: 10.1097/01.blo.0000238813.95035.1b.

GLOBAL HEADQUARTERS
2320 NW 66TH COURT
GAINESVILLE, FL 32653 USA
+1 352.377.1140
+1 352.378.2617

[21] C. A. Engh, H. Ho, C. C. Powers, C. Huynh, S. E. Beykirch, and R. H. Hopper, "Osteolysis propensity among bilateral total hip arthroplasty patients," *J. Arthroplasty*, vol. 26, no. 4, pp. 555–561, Jun. 2011, doi: 10.1016/j.arth.2010.05.014.