Summary of Clinical Data on Safety, Performance and Efficacy of the

Bactiguard® Noble Metal Alloy Coating

This document summarizes the clinical data on safety, performance and efficacy of the Bactiguard noble metal alloy coating on urinary catheters (BIP Foley catheters/Bardex I.C/Lubri-Sil I.C), central venous catheters (BIP CVC) and endotracheal tubes (BIP ETT/BIP ETT Evac). It is based on a comprehensive analysis of available pre- and post-market clinical data relevant to the intended use* of the noble metal coating present on these devices and any adverse events or safety issues discovered/reported for these devices[1].

Pre- and Post-Market Clinical Data

Overall, 35 relevant articles have been found and reviewed regarding urinary catheters (28 articles), central venous catheters (4 articles) and endotracheal tubes (3 articles) with Bactiguard Technology[1]. These studies covered approximately ~20,000 patients with coated devices. If including all patients (i.e. control patients and patients with coated devices), and also other published studies that are not retrieved in the literature reviews and post market reports, approximately 100,000 patients are covered, in total[1].

Selected key clinical studies of devices with Bactiguard Technology (see Table 1) demonstrate a:

- 35% reduction of symptomatic catheter associated urinary tract infections (CAUTI) when using Bactiguard coated urinary catheters compared to uncoated control catheters[1].
- 49% reduction of catheter related infections when using Bactiguard coated CVCs compared to uncoated control catheters[1].
- Trend of 67% reduction of ventilator associated infections when using Bactiguard coated ETTs compared to uncoated control ETTs[1].

Product Complaints and Adverse Event Reports

No adverse events or safety issues concerning the Bactiguard coating of BIP Foley catheters, BIP CVCs and BIP ETTs have been discovered in any of the complaints handled by Bactiguard (post market data until 2020-12-31)[1] or in the adverse event reports in the databases MAUDE and/or MHRA (pre-and post-market data until 2020-12-31)[1].

Conclusion

Based on pre-and post-market data, complaints handled by Bactiguard, and adverse events retrieved from MAUDE and MHRA, it can be interpreted that the clinical use of Bactiguard Technology on BIP Foley Catheter, BIP CVC and BIP ETT/BIP ETT Evac is safe. Their performance has demonstrated to be in agreement with their intended use, and they show a 30-70% reduction of device related, no socomial infections. No risks related to the use of the Bactiguard coating has been identified over 20 years the Bactiguard products have been on the market[1].

Table 1. Summary of key clinical studies of Bactiguard coated Urinary Catheters, Bactiguard coated CVCs and Bactiguard coated ETTs showing efficacy data. RCT: Randomized Controlled Trial; ICU: Intensive Care Unit; CAUTI: Catheter Associated Urinary Tract Infections; CRBSI: Catheter Related Bloodstream Infection; VAP: Ventilator Associated Pneumonia. *Data for patients catheterised ≤2 days were excluded from this calculation, following the CDC CAUTI definition. **Not included in mean reduction calculations (reason for exclusion reported in italics).

Type of Device	Author (year)	Type of Study	No. Patients	Site	Time Catheterized/ intubated	Incidence-reduction infection (p value)
Bactiguard coated urinary catheters	Kai-Larsen (2021)[2]	RCT	1,000	Urology, surgery and ICU, India	11 days (mean)	69% (p<0.001)
	Banaszek (2020)[3]	Before-after	302	Spine surgery, Canada	27-28 days (median)	59% (p<0.05)
	Chung (2017)[4]	Before-after	306	Rehabilitation units Kawloon Hospital, Hong Kong	9.3 days (conventional Foley) and 48 days (BIP Foley)	31% (p=0.095)
	Aljohi (2016)[5]	RCT	60	ICU, Saudi Arabia	3 days	90% (p=0.006)
	Stenzelius (2016)[6]	Ward-Randomized Cross-over	322	High risk ICU patients, Sweden	9 days (mean)	-13.2% (p=0.79) (Higher rate of infection in the study group, not significant)
	Hidalgo Fabrellas (2015)[7] (Article in Spanish)	RCT	116	Cardiology, Spain	4 days (mean)	38% (p=0.037)

*The review of the clinical data was performed under responsibility of Bactiguard, from whom Zimmer Biomet license the technology for orthopedic devices.

Table 1. *Continued*

Type of Device	Author (year)	Type of Study	No. Patients	Site	Time Catheterized/ intubated	Incidence-reduction infection (p value)
Bactiguard coated urinary catheters *Continued*	Lederer (2014)[8]	Before-after	853	7 hospitals, hospital-wide, USA	7-9 days (mean)	58% (p<0.0001)
	Pickard (2012)[9-11]	RCT	1,224*	24 hospitals, surgical care, UK	3-10 days*	17%* (p=0.157)
	Stenzelius (2011)[12]	RCT	439	Surgical, Sweden	2 days (median)	73% (p=0.027)** *Bacteriuria. CAUTI not an endpoint.*
	Seymour (2006)[13]	Before-after	117	One acute general hospital, UK	>2 days	71% (p=0.14)
	Gentry (2005)[14]	Before-after	133	Medical and surgical wards, UK	7-10 days (mean)	34% (p=0.72)
	Rupp (2004)[15]	Before-after	Not given (48,662 catheter days in total)	10 units (transplants, ICUs, burn, rehab), USA	Not given (48,662 catheter days in total)	57%** (p=0.002) *Number of patients or number of catheters not provided.*
	Newton (2002)[16]	Retrospective before-after	1,757	Burn unit ICU, USA	7-8 days	32% (p=0.029)
	Karchmer (2000)[17]	Ward Randomized Cross-over	Not given (11,032 catheters used)	Hospital wide, USA	Not given	32 % (p=0.001)
	In total, mean reduction (weighed against study population size) for Bactiguard coated Urinary Catheters:					**35% reduction of CAUTI**
Bactiguard coated CVCs	Ardehali (2019)[18] (letter to editor)	RCT	138	ICU, Iran	Not given	CRBSI: 43% reduction (Not significant).
	Björling (2018)[19]	Randomized clinical pilot study	33	Karolinska University Hospital, Sweden	9-13 days (mean)	CRBSI: 1 case in the control group vs 0 cases in the BIP CVC group)** *Patient cohort too small.*
	Harter (2002)[20]	RCT	233	University of Heidelberg, Internal Medicine, Germany	10.25 days (median)	Thrombosis prevalence: 3 cases in the control group vs 1 case in the BIP CVC group. CRBSI: 52% reduction (p=0.011).**
	In total, mean reduction (weighed against study population size) for Bactiguard coated CVCs:					**49% reduction of CRBSI**
Bactiguard coated ETTs	Thorarinsdottir (2020)[21]	Before-after (different periods with different types of ETT)	76	ICU, Sweden	3-4 days (median)	36% reduction of high grade biofilm formation on ETTs (multivariable analysis: OR 0.34, p=0.036)** *Biofilm formation. Infection not an endpoint.*
	Björling (2015)[22]	Prospective, controlled, randomized	29	Karolinska University Hospital, Sweden	3-8 hours	Fewer and milder adverse events in BIP ETT group (no difference in rate and severity between BIP and control group).** *Short term intubation – Infection rates not recorded.*
	Tincu (2015)[23] (Poster)	Prospective, controlled, randomized	100	Bucharest Clinical Emergency Hospital, Romania	5 days	VAP: BIP ETT: 4% Standard group: 12% (p=0.14) Relative reduction: 67%
	In total, for Bactiguard coated ETTs:					**Reduction of VAP (for BIP ETT): 67% (based on Tincu et al.[23]).**

References

1. Data on file at Bactiguard (REP-03324-5.0, Review of the clinical safety of Bactiguard coated products, 2021).
2. Kai-Larsen *et al.* Foley catheter with noble metal alloy coating for preventing catheter-associated urinary tract infections: a large, multi-center clinical trial. Antimicrobial Resistance and Infection Control. 2021 10(1):40, doi: 10.1186/s13756-021-00907-w.
3. Banaszek *et al.* Effectiveness of silver alloy-coated silicone urinary catheters in patients with acute traumatic cervical spinal cord injury: Results of a quality improvement initiative. *Journal of Clinical Neuroscience.* 2020 78: 135-138.
4. Chung *et al.* A prospective interventional study to examine the effect of a silver alloy and hydrogel-coated catheter on the incidence of catheter-associated urinary tract infection. *Hong Kong Medical Journal.* 2017 23(3): 239-245.
5. Aljohi *et al.* The efficacy of noble metal alloy urinary catheters in reducing catheter-associated urinary tract infection. Urology Annals. 2016 8(4): 423-429, doi: 10.4103/0974-7796.192099.
6. Stenzelius *et al.* Catheter-associated urinary tract infections and other infections in patients hospitalized for acute stroke: A prospective cohort study of two different silicone catheters. *Scandinavian Journal of Urology.* 2016 50(6): 483-488.
7. Hidalgo Fabrellas *et al.* Incidencia de la infección urinaria en pacientes postoperados de cirugía cardiaca: estudio comparative según el dispositivo de sondaje. Enfermería Intensiva. 2015 26(2): 54-62.
8. Lederer *et al.* Multicenter Cohort Study to Assess the Impact of a Silver-Alloy and Hydrogel-Coated Urinary Catheter on Symptomatic Catheter-Associated Urinary Tract Infections. *Journal of Wound Ostomy & Continence Nursing.* 2014 41(5): 1-8.
9. Pickard *et al.* Antimicrobial catheters for reduction of symptomatic urinary tract infection in adults requiring short-term catheterisation in hospital: a multicentre randomised controlled trial. The Lancet. 2012 380: 1927-1935, doi: 10.1016/S0140-6736(12)61380-4.
10. Data on file at Bactiguard (Reanalyses of data from the Lancet - Statistical Analysis Report - Bactiguard, 2012).
11. Data on file at Bactiguard (Bactiguard Meta-Analysis Report, 2019).
12. Stenzelius *et al.* Noble metal alloy-coated latex versus silicone Foley catheter in short-term catheterization: A randomized controlled study. *Scandinavian Journal of Urology and Nephrology.* 2011 45: 258-264.
13. Seymour. Audit of catheter-associated UTI using silver alloy-coated Foley catheters. *British Journal of Nursing.* 2006 15(11): 598-603.
14. Gentry and Cope. Using silver to reduce catheter-associated urinary tract infections. Nursing Standard. 2005 19(50): 51-54.
15. Rupp *et al.* Effect of silver-coated urinary catheters: Efficacy, cost-effectiveness, and antimicrobial resistance. American Journal of Infection Control, 2004 32(8): 445-450.
16. Newton *et al.* A Comparison of the Effect of Early Insertion of Standard Latex and Silver-Impregnated Latex Foley Catheters on Urinary Tract Infections in Burn Patients. Infection Control and Hospital Epidemiology. 2002 23(4): 217-218.
17. Karchmer *et al.* A Randomized Crossover Study of Silver-Coated Urinary Catheters in Hospitalized Patients. Archives of Internal Medicine. 2000 160: 3294-3298.
18. Ardehali *et al.* The Rate of Catheter-Related Infections using Metal Coated Central Venous Catheters; a Letter to Editor. Archives of Academic Emergency Medicine. 2019 7(1): e33.
19. Björling *et al.* Evaluation of central venous catheters coated with a noble metal alloy – A randomized clinical pilot study of coating durability, performance and tolerability. *Journal of Biomedical Materials Research Part B: Applied Biomaterials.* 2018 160(6): 2337-2344.
20. Harter *et al.* Catheter-Related Infection and Thrombosis of the Internal Jugular Vein in Hematologic-Oncologic Patients Undergoing Chemotherapy – A Prospective Comparison of Silver-Coated and Uncoated Catheters. Cancer. 2002 94(1): 245-251.
21. Thorarinsdottir *et al.* Biofilm formation on three different endotracheal tubes: a prospective clinical trial. Critical Care. 2020 24: 382, doi:10.1186/s13054-020-03092-1.
22. Björling *et al.* Tolerability and performance of BIP endotracheal tubes with noble metal alloy coating – a randomized clinical evaluation study. BMC Anesthesiology. 2015 15: 174, doi: 10.1186/s12871-015-0156-z, PMID: 26625869; PMCID: PMC4667467.
23. Tincu *et al.* Ventilator associated pneumonia: do silver-coated endotracheal tubes really work? [poster]. Euroanesthesia, Berlin 30th May – 2nd June 2015.

*Bactiguard-coated ZNN nails are intended to reduce device related infections, but are not indicated for the treatment of established infections. Use of this product does not replace existing standard practice for infection prevention such as the use of prophylactic antibiotics.

Bactiguard® is a registered trademark of Bactiguard AB.

Laboratory testing is not necessarily indicative of clinical performance.

This material is intended for health care professionals. Distribution to any other recipient is prohibited.

For indications, contraindications, warnings, precautions, potential adverse effects and patient counselling information,
see the package insert or contact your local representative;
visit www.zimmerbiomet.com for additional product information.

ZIMMER BIOMET
Your progress. Our promise.®

3581.1-EMEA-en-Issue Date-2021-08-18