

## **Pharmacoeconomic evaluation of antimicrobial wound dressings in the treatment of venous leg ulcers**

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### **Abstract**

Venous leg ulcers (VLUs) account for most lower extremity wounds. Wound management include cleansing, debridement, infection control and applying wound dressing. There exist various types of dressings which can maintain adequate moisture, offer protection, and support the reepithelization of VLUs. The aim of this study is to evaluate the cost-effectiveness of the antimicrobial wound dressing containing ionic silver (Aquacel® Ag+Extra™) in the treatment of VLUs compared to conventional gauze dressing in Serbia. The data regarding the effectiveness and frequency of dressings for both the Aquacel® Ag+Extra™ and conventional dressing were obtained from literature sources. Only direct costs were considered, and values were taken from the published price list of health services or procurement procedures. Sensitivity analyses were performed.

The total cost per patient for Aquacel® Ag+Extra™ was 34,178.76 RSD, while the total cost for gauze was 82,800.90 RSD. Besides lower costs, antimicrobial wound dressing shows higher effectiveness than the gauze, implying that Aquacel® Ag+Extra™ is the dominant strategy. The sensitivity analysis supports the robustness of the results.

The use of antimicrobial wound dressing containing ionic silver is the preferred option for the treatment of VLUs due to lower costs and the higher curing rate of the wounds.

**Key words:** dressing, economic evaluation, venous leg ulcer, cost-effectiveness

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## **Introduction**

Venous leg ulcers (VLUs) account for most lower extremity wounds and are a subtype of vascular ulceration (1, 2). Venous ulcers occur as a consequence of prolonged venous insufficiency, where pathological conditions and poor blood flow occur due to elevated venous pressure.

The prevalence of the varicose veins, which is a risk factor for VLUs, varies between 10–40% in male population and 25–32% in female population (3). VLUs have an overall prevalence of 1% and increases with age. The prevalence of the active VLU is about 0.5% in the adult Western population (2). About half of VLUs heal within four months, but ulcers have high recurrence rate (up to 70%) within five years (4).

The clinical treatment of VLUs includes two approaches: compression therapy and wound management (4, 5). Wound management include cleansing, debridement, infection control and applying wound dressings (4, 6, 7). Dressings maintain adequate moisture, offer protection, and support the reepithelization of VLUs. The use of topical antibiotics in infected wounds is not recommended due to the lack of evidence of efficacy, possible toxicity or allergenic potential. Dressings containing ionic silver, on the other hand, show adequate effect and are recommended for infected wounds (4). For exudative wounds, moisture-retaining dressings with hydrocolloids are recommended (8). Although the use of gauze for these wounds is not recommended (4) and many studies have shown the superiority of wound dressings (9), gauze is still widely used in clinical practice in Serbia.

VLUs pose a significant social and economic burden on healthcare systems and society in general. For example, a study done in Germany concluded that the mean one-year cost per VLU patient is around 9,000 euros, with hospitalization and non-drug treatment costs, including wound dressing, as main cost drivers (10).

The aim of this study was to perform the economic evaluation of the antimicrobial wound dressing containing ionic silver and antibiofilm formulation (Aquacel® Ag+Extra™) in the treatment of VLUs compared to conventional gauze dressing in Serbia.

## **Methods**

### **Effectiveness**

Several literature sources were used to determine the rate of wound reduction over a defined period of time (effectiveness) and the frequency of dressings for both the Aquacel® Ag+Extra™ and conventional dressing (gauze). There are currently no published data on effectiveness for Aquacel® Ag+Extra™ dressing in the treatment of VLUs through randomized clinical trials.

A prospective randomized trial conducted in Sweden reported a 19% reduction in venous ulceration over a 6-week observation period with gauze, compared with a 51% reduction with a modern hydrocolloid dressing over the same period. The average

duration of gauze dressing on the wound was 0.56 days (with a dressing frequency of approximately 2 times per day) and 3.23 days with modern dressings (11). Another randomized clinical trial conducted in Croatia (12) reported a dressing frequency of one per day for gauze and one in two days for hydrocolloid dressing. The follow-up period was either until healing or until 10 dressings had been used. A randomized clinical trial that was conducted in the United Kingdom and examined the effects of a single-layer Aquacel® hydrofiber dressing (without antimicrobial agents) in the treatment of ulcers showed a mean dressing duration of 4.1 days and a 30.5% ulcer reduction. In this study, the use of a secondary dressing was considered, which probably did not affect the effectiveness of the primary but is a likely reason for the longer dressing duration on the wound (13). Finally, another study from the United Kingdom in patients with chronic VLUs (14) also considered the use of a single layer hydrofiber dressing with an average dressing retention time of 3.63 days.

The hydrocolloid dressing used in all of the above studies is comparable to the Aquacel® Ag+Extra™ dressing due to the similarity of the basic composition (15). Additionally, the Aquacel® Ag+Extra™ dressing has antimicrobial activity and a 36% greater retention capacity than a single layer hydrofiber dressing (16).

The literature data used for the effectiveness are summarized in Table I.

**Table I** Data on the effectiveness and frequency of dressings

**Tabela I** Podaci o efektivnosti i učestalosti previjanja

Study, country, reference	Study period	Dressings	Effectiveness – VLU reduction (%)	Duration of dressings (days)
Ohisson P, et al, Sweden (11)	6 weeks	Hydrocolloid	51%	3.23
		Gauze	19%	0.56
Greguric S, et al, Croatia (12)	Until healing or 10 dressings	Hydrocolloid	NA	2
		Gauze	NA	1
Armstrong SH, et al, UK (13)	6 weeks or until healing	Single layer hydrofiber	30.5%	NA
Harding HG, et al, UK (14)	12 weeks	Single layer hydrofiber	NA	3.63

VLU – venous leg ulcer; UK – United Kingdom; NA – not applicable

The effectiveness was presented as probabilities for the rate of VLU reduction. The effectiveness of 0.19 for gauze and 0.31 for Aquacel® TM Ag+ Extra™ were applied (11, 13). Since the studies and research used for the economic evaluation stated the average duration of dressing in days, the frequency of dressings per day was calculated. Based on the data and in accordance with clinical practice, dressing a wound

with two 10x10cm gauze compresses per day was compared to dressing with one 10x10cm Aquacel® Ag+Extra™ for 3.23 days (0.28 dressings per day) (11). The 10x10cm dressing size was chosen because it is the most common size used in the studies and clinical practice. The time period for analysis was six weeks (11, 12), since it was a sensitive interval to detect clinically relevant and economically meaningful differences in wound healing outcomes in patients with VLUs.

## Costs

Only direct costs were considered in the analysis. All costs are expressed in Serbian dinars (RSD, exchange rate 1 EUR = 117.085 RSD for the year 2024, according to the National Bank of Serbia). The cost data were taken from the official price list of health services and public procurement procedures provided by the Republic Institute for Health Insurance (17, 18). Table II shows the specific materials and services with prices that were included in the economic evaluation.

**Table II** Costs used in the economic evaluation

**Tabela II** Troškovi upotrebljeni u ekonomskoj evaluaciji

Material/service	Unit size or quantity	Unit price (RSD)	Quantity per one dressing
Aquacel® Ag+Extra™	10x10cm	1 020.00	1
Sterile gauze	10x10cm	18.10	2
Sterile solution 0.9% sodium chloride	0.5L	69.90	0.2L
Antiseptic solution with octenidine hydrochloride	1L	3 960.00	0.1L
Sterile gloves	1	42.40	1
Fixating bandage*	0.01x5m	47.95	1
Adhesive plaster*	0.025x1m	9.40	0.1m
Service		1 420.00	1

\* used only in case of gauze for fixating

The cost of dressing per day was calculated by multiplying the cost of one dressing by the frequency of dressings per day. The calculated values for both types of dressings are shown in Table III. The total cost for six weeks for both comparators was obtained by multiplying the cost of dressing per day by 42.

**Table III** Total cost per dressing and per day for both comparators (all values are in RSD)

**Tabela III** Ukupni troškovi po previjanju i po danu za obe poredbene strategije (sve vrednosti su u RSD)

Cost item	Gauze	Aquacel® Ag+Extra™
Wound dressing	36.20	1 020.00
Cleansing	466.36	466.36
Fixating	48.89	
Service	1 420.00	1 420.00
Total cost per dressing	1 971.45	2 906.36
No of dressing per day	1	0.28
Total cost per day	1 971.45	813.78

### Analysis

All calculations and analyses were performed using Microsoft Excel (Microsoft Corporation, USA, 2024). In cost-effectiveness analysis, the results are presented as cost per rate of reduction in VLUs (unit effect). An incremental cost-effectiveness analysis (ICER) was also performed. To assess the robustness of the model, a one-way sensitivity analysis was performed. The following variables were tested in the sensitivity analysis: an amount of gauze per dressing, the frequency of dressing and the effectiveness of Aquacel® Ag+Extra™.

### Results

The results of the cost-effectiveness analysis are presented in Table IV. The total cost per patient using antimicrobial wound dressing containing ionic silver and antibiofilm formulation was 34,178.76 RSD, while the total cost with conventional gauze was 82,800.90 RSD. Considering the effectiveness, rate of wound reduction over a defined period of time, contemporary antimicrobial wound dressing shows higher effectiveness than gauze dressing – 31% and 19%, respectively. Due to these findings, the cost-effectiveness analysis shows that Aquacel® Ag+Extra™ is dominant compared to gauze, i.e. it is a strategy with lower costs and higher effectiveness.

**Table IV** Cost-effectiveness results**Tabela IV** Rezultati ekonomske evaluacije

Strategy	Total cost (RSD)	Effectiveness – probability for VLE reduction	Cost/effect (RSD/patient with VLE reduction)	ICER (RSD/patient with VLE reduction)
Aquacel® Ag+Extra™	34 178.76	0.31	110 254.06	
Conventional gauze	82 800.90	0.19	435 794.21	dominated

ICER – Incremental Cost-Effectiveness Ratio

One-way sensitivity analyses were performed for three variables: an amount of gauze per dressing, the frequency of dressing and the effectiveness of Aquacel® Ag+Extra™ for  $\pm 20\%$ . The results were not sensitive to any of the variables, confirming the results of the base-case analysis.

## Discussion

As already mentioned, the number of wounds and expenditures related to these are significant and constantly growing due to the aging population and difficult management of chronic wounds. VLU have a large recurrence rate, almost one third of treated VLU patients have 4 or more episodes after wound closure (19, 20).

All data on the effectiveness of contemporary antimicrobial wound dressing containing ionic silver and antibiofilm formulation used for this analysis indicate significantly better outcomes in relation to conventional gauze dressing that remains dominantly present in clinical practice. Also, contemporary wound dressing shows significantly less frequency of dressing change in relation to gauze given the far greater capacity of absorption and detention of wound exudate. Less frequent changes of Aquacel® Ag+Extra™ dressing explain the major cost difference identified in this analysis, and consequently its dominant position in the economic evaluation.

A similar study from Germany concluded that the use of superabsorbent wound dressing in patients with exuding VLUs leads to higher benefits with fewer costs compared to the standard of care. The authors showed that the cost savings were 771 EUR per patient over the period of 6 months. At the same time, 34.3% of the patients had wound closure when treated with superabsorbent wound dressing, compared to 31.7% treated with the standard of care (21).

From the UK National Health Care perspective, treatment with dressing containing ionic silver during the initial four weeks provided a total cost saving of 141.57 pounds compared with treatment with non-silver dressings. This was linked to a higher healing rate (7.6% compared with 3.4%, respectively) and a shorter time to wound closure (13.8 weeks compared with 16.7 weeks, respectively) (22).

In addition, the use of modern dressing has a significant impact on the patient's quality of life promoting faster effects, shortening the period of treatment, and diminishing the negative consequences of the chronic wound on the patient's daily life (23). Also worthwhile is the pain reduction during the dressing change using the contemporary dressings compared to conventional gauze (11), as well as a significant reduction in pain that persists in the wound (24).

This analysis was conducted using a literature data for different parameters and several assumptions that may affect the result and therefore act as limitations of the study. Due to the absence of randomized controlled trials specifically evaluating Aquacel® Ag+Extra™ in the treatment of VLU, we relied on the effectiveness estimates extrapolated from the studies involving similar, though not identical, wound care products and indications. While these products share comparable mechanisms of action, such as antimicrobial properties and moisture retention, their clinical performance in VLUs may differ due to the variations in wound type, patient populations, and study designs. This extrapolation introduces considerable uncertainty into the effectiveness assumptions used in our analysis. Therefore, the results should be interpreted with caution, and future research specifically targeting the use of Aquacel® Ag+Extra™ in VLU populations is warranted to validate these findings. We used the sterile gauze for the purpose of analysis, but the sterilization can also be done in the hospital. Since, the cost data for this type of gauze doesn't exist, it was not possible to include it in the analysis. Additionally, only one-way sensitivity analysis was performed which may underestimate the uncertainty of the results (25). Furthermore, the cost of compression was not included in the analysis, despite the fact that it is a complementary approach to wound management (4).

The results of this analysis show that the use of Aquacel® Ag+Extra™ dressing can have a relevant impact on clinical and economic benefits when treating VLUs. Even with much higher unit cost compared to conventional gauze dressing, the use of antimicrobial wound dressing containing ionic silver is a preferred option due to lower costs associated with less frequent dressing change and higher curing rate of the wounds.

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### **Declaration of Competing Interest**

The authors have no conflicts of interest to declare.

### **Author contributions**

DD: Conceptualization, Data curation, Formal analysis, Writing – original draft. NBS: Conceptualization, Formal analysis, Writing – review & editing. DK: Formal

analysis, Writing – review & editing. DL: Resources, Validation, Writing – original draft, review & editing.

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# **Farmakoekonomska evaluacija antimikrobnih obloga za rane u tretmanu venskih ulceracija**

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## **Kratak sadržaj**

Venski ulkusi su najčešći tip rane na donjim ekstremitetima. Zbrinjavanje venskog ulkusa uključuje čišćenje, obradu tj. pripremu rane, kontrolu infekcije i nanošenje obloga za rane. Postoje različite vrste obloga koje pružaju adekvatnu vlažnost, zaštitu i podržavaju reepitelizaciju venskih ulkusa. Cilj analize je procena troškovne isplativosti antimikrobne obloge za rane koji sadrži jonsko srebro (Aquacel® Ag+Extra™) u lečenju venskih ulkusa u poređenju sa konvencionalnim previjanjem gazom u Republici Srbiji. Podaci o efikasnosti i učestalosti previjanja za obe strategije dobijeni su iz literature. Uzeti su u obzir samo direktni troškovi, a vrednosti su preuzete iz objavljenog cenovnika zdravstvenih usluga ili postupaka javne nabavke. Sprovedena je analiza osetljivosti.

Ukupni troškovi po pacijentu za Aquacel® Ag+Extra™ iznosili su 34.178,76 dinara, dok su ukupni troškovi primenom gaze iznosili 82.800,90 dinara. Pored nižih troškova, antimikrobna obloga za rane pokazuje veću efikasnost od gaze, što implicira da je Aquacel® Ag+Extra™ dominantna strategija. Analiza osetljivosti podržava robusnost rezultata.

Upotreba antimikrobne obloge za rane koja sadrži jonsko srebro je željena opcija za lečenje venskog ulkusa zbog nižih troškova i veće stope zarastanja rana.

**Ključne reči:** obloge za rane, ekonomska evaluacija, venske ulceracije, troškovna isplativost

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