

TABLE 1. Subject Characteristics at Enrollment

Characteristic	All (N = 50)	Wool First (n = 25)	Standard First (n = 25)	P
Race, n (%)				
White	29 (58)	14 (56)	15 (60)	0.57
African American	17 (34)	10 (40)	7 (28)	
Hawaiian	2 (4)	1 (4)	2 (8)	
Multiracial	2 (4)	0 (0)	1 (4)	
Male sex, n (%)	13 (26)	6 (24)	7 (28)	1.0
Age, y	26.7 (17.3)	26.8 (16.4)	26.6 (18.5)	0.76
Initial sIGA, n (%)				0.15
2	28 (56)	17 (68)	11 (44)	
3	22 (44)	8 (32)	14 (56)	
Initial EASI	4.9 (3.6)	4.5 (3.4)	5.4 (3.9)	0.51

P values are from Fisher exact test for categorical variables and Wilcoxon rank sum test for quantitative variables.

Abbreviations: EASI, Eczema Area and Severity Index; sIGA, static Investigator's Global Assessment.

quality of life in children and adults with atopic dermatitis aged 5 years and older.

MATERIALS AND METHODS

Subject and Enrollment Characteristics

Subjects entered the study between March 13, 2017, and December 28, 2017. The final study visit occurred on March 31, 2018. Fifty-six subjects were enrolled in the study, 50 of whom completed the study, 4 of whom were lost to follow-up and unresponsive to attempts at contact, and 2 of whom were terminated early because of adverse events (AEs; 1 asthma attack and 1 flare-up of dermatitis). The results presented in all subsequent sections refer to the 50 subjects who completed the study. Table 1 provides summary statistics for participant characteristics and comparisons between assignment groups. Most subjects were white and female and had static Investigator's Global Assessment (sIGA) score of 2. The average age was 26.7 years.

Although subjects obviously could not be blinded as to garment assignment, investigators were blinded when performing their assessments.

Design

Subjects were randomly allocated into 2 groups. They either wore their usual clothing for the first 6 weeks (standard first) and then switched to wool clothing for a further 6 weeks or wore the wool clothing first (wool first) followed by their usual clothing. The 2 cohorts were balanced with regard to demographic factors and initial atopic dermatitis condition. The following instructions were given to subjects:

- Wear an ensemble (a top and a bottom) of your choosing for at least 6 continuous hours each day.
- An ensemble may be worn as daytime wear or as nighttime wear.

- Wash ensembles using Martha Gardener Country Homestead Eucalyptus Wool Mix detergent, unless otherwise authorized to use your usual washing product.

Each subject undertook an initial visit to establish baseline condition, followed by regular 3-week visits until completion of the study. The mean (SD) duration between visits was 21.8 (4.1) days. Seventy-eight percent of all visit 2 to 5 assessments occurred within 21 ± 3 days (3 weeks) of the previous assessment. Sixty-four percent of all final assessments occurred within 84 ± 3 days (12 weeks) of the initial assessment, that is, within the design window.

Garments

Commercially sourced 100% Merino wool base layer garments with a mean fiber diameter less than or equal to $17.5 \mu\text{m}$ were the treatment used in this study. The garments were made from 1 fabric quality, the details of which are included in Table 2. In contrast to the Merino wool used in this study, other wool fabrics often contain fibers of a larger diameter. This difference can account for the perceived "itchiness" or "roughness" noted in the past with some wool garments.

Subjects were provided with a maximum of 4 different garment groups, as shown in Appendix 1.

No wool garments were included in the standard clothing.

Atopic Dermatitis and Quality-of-Life Assessment

At the initial and each subsequent visit, the following data were obtained: Eczema Area and Severity Index (EASI) score,¹² Dermatology Life Quality Index (DLQI),¹³ and sIGA. Skin hydration was assessed with a Courage + Khazaka Corneometer, Model MDD 4 (Multi Display Device), using a CM825 probe. The device was able to be calibrated and had an ambient condition sensor for room temperature and relative humidity.

Statistical Methods

Baseline demographic and clinical characteristics were summarized with counts and percentages for categorical variables and means, standard deviations, medians, and extrema for quantitative variables. Comparison of baseline characteristics was analyzed using Fisher exact test for categorical variables and the Wilcoxon rank sum test for quantitative variables.

TABLE 2. Details of the Wool Fabric Used in the Trial

Parameter	Value	Test Method
Fiber diameter		IWTO-12:2012
Mean, μm	17.5	
Percentage of fibers $\geq 25 \mu\text{m}$	2.1	
Mass, g^{-2}	157	AS 2001.2.13-1987
Thickness, mm	0.65	AS 2001.2.15-1989
Thermal resistance, $\text{m}^2 \text{kW}^{-1}$	0.03	ISO 11092-2014
Water vapor resistance, $\text{m}^2 \text{PaW}^{-1}$	2.96	ISO 11092-2014

TABLE 3. Results Associated With the Second Linear Mixed-Effects Model

• Initial clothing assignment (weeks 1–6)		
Baseline to week 3		
Standard		Significant decrease (P = 0.0004)
Merino wool		Significant decrease (P < 0.0001)
Standard vs wool		No difference (P = 0.65)
Weeks 3–6		
Standard		No change (P = 0.71)
Merino wool		No change (P = 0.18)
Standard vs wool		No difference (P = 0.49)
Baseline to week 6 (cumulative)		
Standard		Significant decrease (P = 0.0001)
Merino wool		Significant decrease (P < 0.0001)
Standard vs wool		No difference (P = 0.25)
• After clothing switch (weeks 7–12)		
Weeks 6–9		
Standard		No change (P = 0.79)
Merino wool		Significant decrease (P = 0.001)
Standard vs wool		Significant difference (P = 0.04)
Weeks 9–12		
Standard		No change (P = 0.42)
Merino wool		No change (P = 0.73)
Standard vs wool		No difference (P = 0.41)
Weeks 6–12 (cumulative)		
Standard		No change (P = 0.28)
Merino wool		Significant decrease (P = 0.004)
Standard vs wool		No difference (P = 0.20)

Assigned Cohort	Baseline	Week 3	Week 6	Week 9	Week 12
Standard First	5.4 (4.3, 6.5)	3.6 (2.5, 4.7)	3.4 (2.3, 4.5)	1.8 (0.6, 2.9)	1.9 (0.8, 3.0)
Wool First	4.5 (3.4, 5.6)	2.4 (1.3, 3.5)	1.7 (0.6, 2.8)	1.6 (0.5, 2.7)	1.2 (0.1, 2.3)

Values are means (95% confidence interval) for EASI scores at each visit for each cohort. Cells shaded in blue are baseline measurements, before clothing assignment; cells shaded in green represent groups wearing merino wool during the previous time interval; and cells shaded in pink represent those wearing regular clothing. The focus of hypothesis testing from this model was to compare visit-to-visit changes in Eczema Area and Severity Index scores within each assignment group and between assignment groups.

Two linear mixed-effects models were fitted for each of the EASI, DLQI, and skin hydration measurements:

- The first model included the following 3 fixed factors: (1) time period, parametrized as weeks 1 to 6 versus weeks 7 to 12; (2) assigned group, parameterized as wool first or standard first; and (3) clothing material, parameterized as wool or standard. The model included random intercepts per subject. Standard analysis of variance tests of each factor was conducted.
- The second model included 10 fixed factors—1 for each of the 5 visits for each of the 2 assigned groups—and no intercept. Tests comparing changes from visit to visit were conducted as appropriate linear contrasts applied to the fixed effects, for example, week 3 versus week 0 for the wool-first group. Random intercepts per subject were included in the model.

The EASI, DLQI, and skin hydration retention were summarized at baseline, week 6, and week 12 with means and standard

deviations. Means and 95% confidence intervals were derived at each visit for each assignment group from the second mixed-effects model. The sIGA scores were summarized at each visit in each group with counts and percentages. Visit-to-visit changes within each group were tested with the Wilcoxon signed rank test and compared between groups with the Wilcoxon rank sum test. All analyses were conducted in the open source R software environment (R: A language and environment for statistical computing, version 3.5.0; R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

Eczema Area and Severity Index Score and Investigator Assessment (sIGA)

Significant decreases in mean EASI scores from baseline to week 3 were seen in both groups, that is, those who wore regular clothing (standard first) and those who wore Merino wool (wool first). These

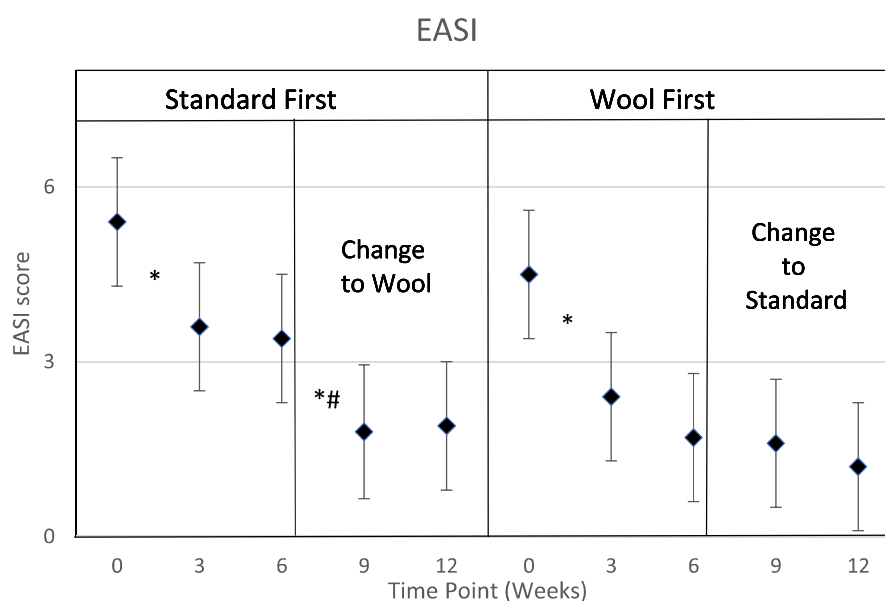


Figure 1. Mean EASI over time for the 2 study cohorts. The asterisk (*) indicates a significant reduction in EASI scores during the given interval. The dagger (#) indicates that the mean change in EASI scores was significantly different between the 2 cohorts. The results are associated with the second linear mixed-effects model.

decreases were sustained but did not further improved from week 3 to week 6. Those who switched to Merino wool at week 6 experienced a further significant decrease in EASI scores, in contrast to those who switched to regular clothing (Table 3, Fig. 1).

All subjects experienced decreases in sIGA in the initial study period from baseline to week 3 and cumulatively from baseline to week 6. Those wearing Merino wool experienced a significant decrease from week 3 to week 6. However, there were no differences in sIGA over the period from baseline to week 6. After the week 6 switch in clothing, the Merino wool group experienced significant decreases in sIGA from week 6 to week 9 and cumulatively from week 6 to week 12. Those wearing regular clothing did not exhibit any significant changes from week 6 to week 9 or to week 12. Those wearing Merino wool from week 6 to week 9 experienced significantly greater reductions in sIGA than those wearing regular clothing, but no other differences were significant, as shown in Table 4.

The factor of primary interest is the clothing type factor, which compares mean EASI when Merino wool is being worn with mean EASI when it is not being worn. This factor was significant ($P = 0.02$), because mean EASI was lower when Merino wool was being worn. In addition, mean EASI tended to decrease over time for all cohorts. The assignment group factor was not significant ($P = 0.13$), indicating that the order in which subjects wore Merino wool and regular clothing did not significantly impact mean EASI.

Quality of Life (DLQI)

Reduction in mean DLQI scores occurred only when Merino wool was worn, and these reductions occurred for the first 3 weeks of wearing Merino wool, that is, from baseline to week 3 in the wool-first cohort and from week 6 to week 9 in the standard clothing-first cohort, as shown in Table 5 and Figure 2.

The clothing type factor was significant ($P = 0.001$), indicating that mean DLQI scores were lower when Merino wool was worn. The time period factor was significant ($P < 0.0001$), indicating that mean DLQI tended to decrease over time. The assignment group factor was nonsignificant ($P = 0.06$), indicating that the order in which subjects wore Merino wool and regular clothing did not significantly impact mean DLQI.

Skin Hydration

Increases in mean skin hydration occurred for both clothing types for the first 6 weeks. These increases were not significantly improved upon after the first 6 weeks. No statistically significant differences between Merino wool and regular clothing were observed. However, in those who wore wool first, hydration tended to decline after switching to standard clothing, and in those who wore standard clothing first, hydration tended to improve when switching to wool, as shown in Table 6 and Figure 3.

Adverse Events

Fourteen AEs occurred involving 12 subjects, none of which was serious. One event was not resolved by the end of the study; all others were resolved. All AEs were single episode, except the unresolved AE that is continuous. Ten AEs were of moderate severity, and 4 were of mild severity. No AEs were related to clothing or to detergent use. Although all the AEs required medication, only 2 subjects required a prohibited concomitant medication and were discontinued from the study.

No AEs were related to clothing or detergent use; however, 5 events occurring in 4 subjects were of interest per protocol—that is, they occurred during or immediately after wearing the wool ensemble. Of these 4 subjects with AEs of interest, 2 were discontinued because of the need for a prohibited medication and therefore not included in

TABLE 4. Summary Statistics for sIGA Scores by Week and Cohort

• Initial clothing assignment (weeks 1–6)		
Baseline to week 3		
Standard		Significant decrease ($P = 0.0006$)
Merino wool		Significant decrease ($P < 0.04$)
Standard vs wool		No difference ($P = 0.93$)
Weeks 3–6		
Standard		No change ($P = 0.11$)
Merino wool		Significant decrease ($P < 0.02$)
Standard vs wool		No difference ($P = 0.37$)
Baseline to week 6 (cumulative)		
Standard		Significant decrease ($P = 0.0004$)
Merino wool		Significant decrease ($P < 0.0008$)
Standard vs wool		No difference ($P = 0.41$)
• After clothing switch (weeks 7–12)		
Weeks 6–9		
Standard		No change ($P = 0.53$)
Merino wool		Significant decrease ($P = 0.002$)
Standard vs wool		Significant difference ($P = 0.001$)
Weeks 9–12		
Standard		No change ($P = 0.06$)
Merino wool		No change ($P = 0.43$)
Standard vs wool		No difference ($P = 0.06$)
Weeks 6–12 (cumulative)		
Standard		No change ($P = 0.18$)
Merino wool		Significant decrease ($P = 0.006$)
Standard vs wool		No difference ($P = 0.22$)

Assigned Cohort	sIGA Score	Baseline	Week 3	Week 6	Week 9	Week 12
Standard First	0				4 (16%)	2 (8%)
	1		1 (4%)	4 (16%)	10 (40%)	12 (48%)
	2	11 (44%)	17 (68%)	16 (64%)	9 (36%)	8 (32%)
	3	14 (56%)	7 (28%)	5 (20%)	2 (8%)	3 (12%)
Wool First	0			2 (8%)	2 (8%)	5 (20%)
	1		5 (20%)	9 (36%)	9 (36%)	8 (32%)
	2	17 (68%)	16 (64%)	12 (48%)	10 (40%)	10 (40%)
	3	8 (32%)	4 (16%)	2 (8%)	4 (16%)	2 (8%)

Values are number (percentage) of subjects having each static Investigator's Global Assessment score. Cells shaded in blue are baseline measurements, before clothing assignment; cells shaded in green represent groups wearing merino wool during the previous time interval; and cells shaded in pink represent those wearing regular clothing.

the outcome measures. Adverse events of interest per the protocol and incidences in the study are listed hereinafter in parentheses.

The following AEs were recorded if they occurred during or immediately after wearing wool ensemble:

- Increased irritation of the skin (1 subject had atopic flare, not in area of clothing, discontinued)
- Increased skin dryness (none)
- Increased pruritus (none)
- Rash/allergic contact dermatitis (1 subject had poison ivy dermatitis on bilateral arms)

- Irritation of the respiratory tract (1 subject had asthma and pneumonia and was discontinued; 1 had an upper respiratory tract infection)
- Irritation of the eye (none)
- Irritation of the nose (none)
- Irritation of the gastrointestinal tract (none)

DISCUSSION

This study assessed atopic dermatitis severity using the EASI score and a static investigator's assessment. Both of these metrics showed

TABLE 5. Summary Statistics for DLQI Scores by Time Period and Cohort

Assigned Cohort	Baseline		Weeks 1-6		Weeks 7-12	
	Mean (SD)	Median [Min, Max]	Mean (SD)	Median [Min, Max]	Mean (SD)	Median [Min, Max]
Standard Clothing First	6.7 (4.8)	5.0 [1.0, 22.0]	6.2 (5.0)	5.0 [0.0, 16.0]	3.7 (3.5)	3.0 [0.0, 16.0]
Wool Clothing First	6.9 (5.2)	5.0 [1.0, 21.0]	3.4 (5.1)	2.0 [0.0, 15.0]	3.0 (3.3)	2.5 [0.0, 17.0]

Values are mean (SD) or median (min, max). Cells shaded in blue are baseline measurements, before clothing assignment; cells shaded in green represent groups wearing Merino wool during the previous time interval; and cells shaded in pink represent those wearing regular clothing

improvement after subjects wore the wool clothing as compared with their own usual clothing. Those who wore the wool clothing first showed improvement as soon as 3 weeks after starting the program. When they switched back to their regular clothing, their scores remained stable, perhaps as a reflection of the improvement made while wearing the wool clothing. Those who started the study by staying with their regular clothing showed some initial improvement by week 3, likely because they were taking better care of their skin because they were enrolled in a research project. When they switched to the wool clothing after 6 weeks, they showed more marked improvement, however.

Of the 25 subjects with “mild” (17) to “moderate” (8) eczema by sIGA who wore the wool clothing initially, 2 were rated “clear” and 9 were scored as “mild” by week 6. Only 2 of 8 with a rating of “moderate” at baseline were still rated “moderate” at week 6. Of the 25 subjects (11 by “mild” and 14 by “moderate”) who started the study by staying with their regular clothing, only 4 improved to a “mild” score and none improved to “clear” by week 6.

Most important to our patients is their own rating of the severity of their eczema and their comfort. As measured by the DLQI, their severity was significantly improved when wearing the wool clothing, a fact that was surprising to some of them. A decrease in the

symptoms of itchy, scratchy, and painful skin was the largest improvement, followed closely by a decrease in feelings of embarrassment and being self-conscious of skin appearance.

The only parameter we measured that did not demonstrate statistically significant improvement by wearing the fine-diameter Merino wool garments was skin hydration. However, the results of this measurement showed that there was a trend toward increased skin hydration when wearing wool, although it did not meet statistical significance. If a significant improvement in skin hydration is not the reason for improvement in atopic symptoms, it is uncertain why the improvement was seen. Perhaps, the improvement in hydration, although not meeting the definition of statistical significance, was enough to allow for symptom improvement. In addition, the Merino garments likely caused less frictional irritation than conventional clothing. Reduced cutaneous itch and pain were noted by our subjects, which also was likely to lead to improved EASI and sIGA scores for “the itch that rashes.”

Limitations

Although investigators were blinded as to clothing assignment when performing their assessments, subjects could not be when answering DLQI and adverse reaction questions.

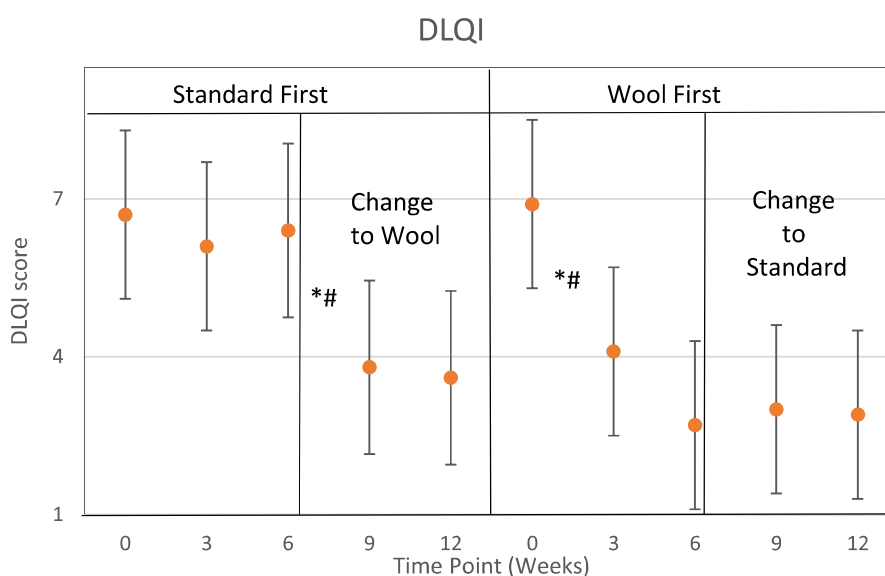


Figure 2. Mean DLQI over time for the 2 study cohorts. The asterisk (*) indicates a significant reduction in DLQI scores during the given interval. The dagger (†) indicates that the mean change in DLQI scores was significantly different between the 2 cohorts.

TABLE 6. F Statistics and P Values for Study Factors From Model of Skin Hydration Scores

Assigned Cohort	Baseline	Week 3	Week 6	Week 9	Week 12
Standard First	38.3 (32.9, 43.8)	41.8 (36.3, 47.2)	44.7 (39.2, 50.1)	48.5 (43.1, 54)	48.7 (43.2, 54.1)
Wool First	42.8 (37.3, 48.2)	46.9 (41.5, 52.4)	51.1 (45.7, 56.6)	50.4 (45, 55.9)	49.8 (44.3, 55.2)

Values are means (95% confidence interval) for skin hydration at each visit for each cohort. Cells shaded in blue are baseline measurements, before clothing assignment; cells shaded in green represent groups wearing Merino wool during the previous time interval; and cells shaded in pink represent those wearing regular clothing.

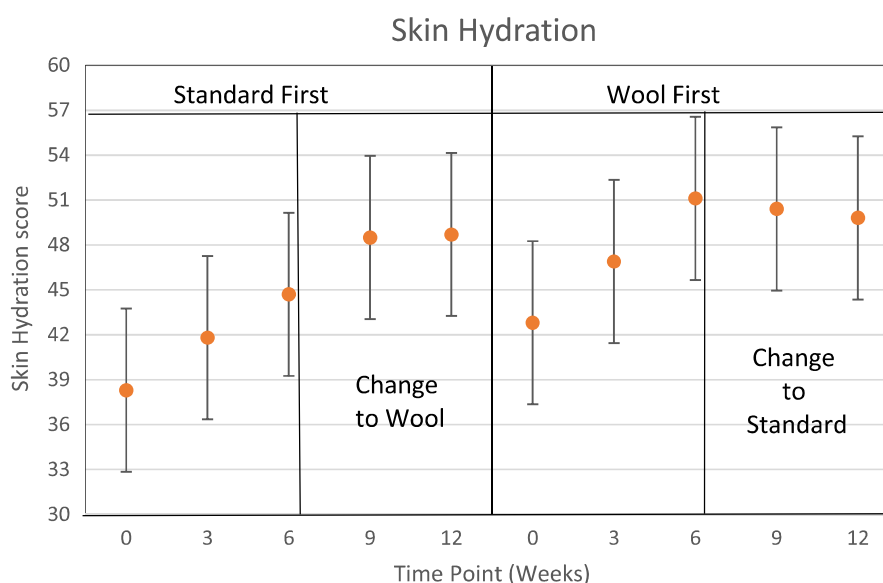


Figure 3. Mean skin hydration over time for the 2 study cohorts. No visit-to-visit comparisons were significant (only cumulative, 6-week comparisons).

CONCLUSIONS

The typical recommendation for clothing use by people with eczema has been to wear cotton or sometimes silk.¹⁴ It has been felt that these fibers offer superior softness and comfort compared with other types of fabrics. This study has demonstrated that wearing fine-diameter Merino wool garments may actually improve signs and symptoms in patients with mild to moderate atopic dermatitis. This is in contrast to the opinion of some patients and professionals¹⁵ who feel that wool clothing is necessarily scratchy and exacerbates irritation in individuals with sensitive skin. The Merino wool fiber used in the clothing for this study was all of fine diameter, which has been demonstrated to be comfortable to wear.¹⁰

Interestingly, a recent study of the use of silk clothing in individuals with moderate to severe atopic dermatitis showed no demonstrable benefit from wearing silk.¹⁶ This study and those of Su et al¹¹ and Spelman et al¹⁷ show that fine-diameter Merino wool clothing should be considered acceptable for people with eczema and seems to be therapeutic to patients with mild to moderate atopic dermatitis.

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Appendix 1

Plate 1. Illustration of the garment types used in the trial.

- Wear ensemble (a top and a bottom) of your choosing for at least 6 continuous hours.
- Ensemble may be worn as daytime wear or as nighttime wear.
- Wash ensembles using Martha Gardener Country Homestead Eucalyptus Wool Mix, unless otherwise authorized to use your usual washing product.