KARO HEALTHCARE CLAIMS DOCUMENT	
JOB NAME	GC CSS Lamisil 1% Cream – Terbinafine Hydrochloride 1% Cream
JOB NUMBER	GCCSS-SKH-0058.003 (in ZINC: GCSH/CHLAM/0003/17(2))

HISTORY			
ACTION	**FULL APPROVAL**		**DATE**
	YES	**NO**	
Version 001: New GC CSS based on list of globally approved claims from legacy Novartis documentation	☒	☐	**10. April 2017**
Version 002: Claims 5, 6 and 16: Disclaimer deleted. New Claim 8.a) added. Claim 16: Added new claim wording. Claims 3.a), 5.a), 7.a): Clarified claim substantiation of claims.	☒	☐	**8. November 2017**
Version 003: Changes made to previous version: • Notes For Guidance updated • Context clarified: Claim 15 • Claim substantiation of claim clarified: Claim 4 • Expert claim wording added: Claims 1, 5.a), 5.b), 6, 12, 13.a), 13.b) and 14 • New shortened Triple Action and Dual Action claims added: Claim 17 and 18	☐	☒	**24. April 2018**
Version 004: Changes made to previous version: • Change of wording to claims 5, 13, 15, 16.a), 16.b), 17.a), 17.b) • Dual action claim added - Claim 19	☒	☒	**25. March 2019**

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Notes For Guidance:

1) **Restrictions on usage of the claim section must be strictly adhered to. Claims are grouped into claim territories. The respective claim territory is indicated in the first row each time. An index of all claim territories can be found under 4) below.**

2) **There are two treatment schedules for Athlete's Foot that are covered by this CSS a) single daily application for 7 days and b) twice daily application for 7 days. These two treatment schedules are supported by different clinical data, please ensure that you check which treatment schedule is applicable to your market and only include supporting materials and claims for that treatment schedule in your local version of this CSS.**

3) **Legend:**
   - **Language in (round brackets) – Optional and can be left out when in need of a short claim.**
   - **Language in [squared brackets] – Only optional if claim context makes clear that you are specifically talking about context specified in these brackets.**
   - **Language separated by slash mark – Only one of the options separated by a slash mark must be selected.**

4) **Index of claim territories**
   1. **Fungicidal Action**
   2. **Fungicidal vs Fungistatic Action**
   3. **Efficacy in Athlete's Foot**
   4. **Efficacy in Ringworm and Jock Itch**
   5. **Mycological Cure in Athlete's Foot**
   6. **Mycological Cure in Ringworm and Jock Itch**
   7. **Efficacy of Symptoms Reduction in Athlete's Foot**
   8. **Efficacy of Itch Reduction in Athlete's Foot**
   9. **Efficacy of Burning/Stinging Reduction in Athlete's Foot**

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10. Efficacy of Symptoms Reduction in Ringworm and Jock Itch
11. Efficacy of Itch Reduction in Ringworm and Jock Itch
12. Keeps Working
13. Protection from Recurrence in Athlete's Foot
14. 7 Day Treatment
15. 4 x Shorter/Faster Treatment
16. Triple Action Formula for Athlete's Foot
17. Shortened Triple Action Formula for Athlete's Foot
18. Dual Action Formula for Athlete's Foot, Ringworm and Jock Itch
19. Dual Action Kills Foot Fungus and Prevents recurrence

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BRAND DESIGNATION	**GLOBAL PRODUCT**			☒	**LOCAL PRODUCT**			☐
	POWER BRAND	**SENSODYNE**	**PANADOL**	**VOLTAREN**	**POLIDENT**	**OTRIVIN**	**THERAFLU**	**PARODONTAX**
		☐	☐	☐	☐	☐	☐	☐
	SUB-BRAND							
	CORE BRAND	**FENISTIL**	**FLONASE**	**HORLICKS**	**ABREVA**	**ZOVIRAX**	**EXCEDRIN**	
		☐	☐	☐	☐	☐	☐	
		PHYSIOGEL	**LAMISIL**	**ENO**	**FENBID**	**CONTAC**	**BIOTÈNE**	
		☐	☒	☐	☐	☐	☐	
	SUB-BRAND							

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PRODUCT REGULATORY CLASSIFICATION	**PRESCRIPTION MEDICINE**	☐	**NON-PRESCRIPTION MEDICINE**	☒	**DIETARY SUPPLEMENT**	☐
	NON-PRESCRIPTION DEVICE	☐	**COSMETIC**	☐	**NUTRITIONAL**	☐
	FOOD	☐	**OTHER (SPECIFY)**			
PRODUCT FORMAT	**AEROSOL**	☐	**ADHESIVE STRIP**	☐	**CAPSULE**	☐
	CHEWING GUM	☐	**CREAM**	☒	**LOZENGE**	☐
	OINTMENT	☐	**ORAL POWDER**	☐	**ORAL RINSE**	☐
	PASTE	☐	**PLASTER**	☐	**SYRUP**	☐
	TABLET/CAPLET	☐	**TOOTHBRUSH**	☐	**TOPICAL GEL**	☐
	OTHER (SPECIFY)					

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SPECIFIED ACITIVE(S) or SIGNIFICANT INGREDIENTS/PRODUCTS/DOSAGES/PACK TYPE/MFC	**MFCs: F.100 Cream, T321800SY.03U** [18] **ACTIVE INGREDIENT:** Terbinafine Hydrochloride 1% (10mg/g) **EXCIPIENTS:** Purified water, Sodium hydroxide, Benzyl alcohol, Sorbitan stearate, Cetyl palmitate, Cetyl alcohol, Stearyl alcohol, Polysorbate 60, Isopropyl myristate **DOSAGE:** For indications interdigitale type tinea pedis: Apply once or twice a day for one week (depending on local product information) For indications tinea cruris and tinea corporis: Apply once a day for one week. **PACK TYPE:** Tube in different sizes (7.5g, 10g, 12g, 15g, 30g)

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Fungicidal Action		
Wording and contextual use of the claim	**Substantiation of the Claim**	**Restrictions on usage of the claim**
1. CLAIM: Fungicidal Kills the fungus Kills skin fungus Kills body skin fungus Kills foot fungus Kills the fungi that cause tinea pedis, tinea corporis and tinea cruris Kills dermatophytes Kills the fungus over 7 days* * Treat with Lamisil for 7 days as directed by Usage Instructions **CONTEXT:**	Terbinafine, the active ingredient in Lamisil 1% Cream, is an allylamine and has fungicidal action against many types of fungi i.e. it kills these fungi [1, 2]. In vitro susceptibility tests have shown that terbinafine has primarily fungicidal activity against dermatophytes, Aspergillus species, Scopulariopsis brevicaulis, Blastomyces dermatitidis, Histoplasma capsulatum and Candida parapsilosis, but only fungistatic activity against Candida albicans [3]. Tinea pedis is most commonly caused by the dermatophytes Trichophyton rubrum and Trichophyton interdigitale (formerly T. mentagrophytes var. interdigitale). Tinea cruris is most commonly caused by the dermatophytes Trichophyton rubrum, Trichophyton interdigitale and Epidermophyton floccosum. Tinea corporis is most commonly caused by of the genera Trichophyton and Microsporum [4]. Ergosterol is an essential component of virtually all fungal cells as it is required for membrane integrity and also for growth. Most antifungal agents interfere with ergosterol either by directly inhibiting its biosynthesis (allylamines, azoles, morpholines, thiocarbamates) or by interacting with it in the cell membrane (polyenes) [1]. Terbinafine, like other allylamines, specifically inhibits fungal ergosterol biosynthesis at the point of squalene epoxidation.	**VERBATIM USE ONLY** ☐ **Claim can be used for the following;** **CONSUMERS** ☐ **HCPS** ☐ **SPECIFY HCPs:** **BOTH** ☒ **CANNOT BE USED FOR THE FOLLOWING:** - **OTHER RESTRICTIONS**: Terbinafine does not kill all existing types of fungi so it is NOT correct to state or imply that this product kills all types of fungi or similar.

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This claim wording must only be used in the context of interdigitale type tinea pedis, tinea corporis and/or tinea cruris.	As a result, treated fungal cells rapidly accumulate the intermediate squalene and become deficient in the end-product of the pathway, ergosterol. The gradual onset of fungal cell death is believed to be primarily due to accumulation of high levels of intracellular squalene, probably in combination with ergosterol deficiency [1].	

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Fungicidal vs Fungistatic Action		
Wording and contextual use of the claim	**Substantiation of the Claim**	**Restrictions on usage of the claim**
2. CLAIM: Works to kill the fungus, not just inhibit its growth **CONTEXT:** This claim is to be used when comparing mode of action of Lamisil 1% Cream to Azole containing products This claim wording must only be used in the context of interdigitale type tinea pedis, tinea corporis and/or tinea cruris.	See 1. claim substantiation - Terbinafine is an allylamine with fungicidal action against many types of fungi i.e. it acts to kill these fungi [1, 2]. Most topical treatments for fungal skin infections contain an *azole* active ingredient like for example clotrimazole, miconazole or ketoconazole. Azoles inhibit the production of ergosterol further down the synthesis pathway than terbinafine and do not result in the build-up of high levels of squalene. Azoles inhibit the biosynthesis of ergosterol reducing bioavailability and slowing down reproduction therefore inhibiting growth. Azoles therefore are fungistatic [2].	**VERBATIM USE ONLY** ☐ **Claim can be used for the following;** **CONSUMERS** ☐ **HCPS** ☐ **SPECIFY HCPs:** **BOTH** ☒ **CANNOT BE USED FOR THE FOLLOWING:** **-** **OTHER RESTRICTIONS:** This claim MUST not be used when the comparison is made to another allylamine containing product with for example naftifine. Terbinafine does not kill all existing types of fungi so it is NOT correct to state or imply that this product kills all types of fungi or similar.

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Efficacy in Athlete's Foot		
Wording and contextual use of the claim	**Substantiation of the Claim**	**Restrictions on usage of the claim**
3.a) CLAIM: Effectively treats athlete's foot Effective/clinically proven treatment for athlete's foot **CONTEXT:** **This claim wording must only be used in countries in which Lamisil 1% Cream is approved to treat interdigitale type tinea pedis with <u>once a day</u> for one week treatment schedule.**	Lamisil 1% Cream is used for the topical treatment of interdigitale type tinea pedis (athlete's foot) with a once a day for one week treatment schedule [5]. A multicentre, randomized, double-blind, placebo-controlled clinical trial with Lamisil 1% Cream was conducted in in total 100 adult subjects with interdigitale type tinea pedis [6]. Subjects were instructed to use the Cream once daily in the evening for 7 days on affected areas. On day 8, 14, 42 and 56, subjects were evaluated for clinical response. The primary efficacy endpoint was *mycological cure* (negative microscopy and culture) at the end of the study, defined as the last non-missing, post-baseline observation during the study. Secondary efficacy endpoints included *total clinical signs and symptoms score* and *clinical response*. The severity of seven clinical signs and symptoms (erythema, scaling, vesiculation, pruritus, pustules, exudation and crusting) was recorded on a 4-point scale. Total signs and symptoms score was the sum of the individual scores (i.e. between 0 and 21). Clinical response was categorized as either effective or ineffective treatment. Effective treatment was defined as mycological cure with mild or no residual erythema and/or scaling and/or pruritus (total signs and symptoms score ≤2), and no other clinical signs.	**VERBATIM USE ONLY** ☐ **Claim can be used for the following;** **CONSUMERS** ☐ **HCPS** ☐ **SPECIFY HCPs:** **BOTH** ☒ **CANNOT BE USED FOR THE FOLLOWING:** Must NOT be used in countries in which Lamisil 1% Cream is approved to treat interdigitale type tinea pedis with any other treatment schedule than once a day for one week. **OTHER RESTRICTIONS**: -

	Mycological cure: Lamisil 1% cream was significantly more effective than vehicle in both achieving and maintaining mycological cure. At end of study, 91.4% of subjects (32/35) in the Lamisil 1% Cream group had mycological cure, compared to 37.1% of subjects (13/35) in the vehicle group ($p<0.001$). The number of subjects with mycological cure was significantly greater in the Lamisil 1% Cream group than in the vehicle group from the third visit (day 14) onwards ($p<0.001$) [6]. *Total clinical signs and symptoms score*: At baseline, mean total signs and symptoms score were 7.2 and 7.3 in the Lamisil 1% Cream group and the vehicle group respectively. From visit 4 (day 42) onwards a statistically significant difference in total signs and symptoms score in favour of Lamisil 1% Cream was established ($p\leq0.001$). The total signs and symptoms scores at the final visit were 1.5 in Lamisil 1% Cream group and 3.7 in vehicle group ($p<0.001$) [6]. *Clinical response*: By visit 4 (day 42), Lamisil 1% Cream group displayed a statistically significant higher rate of effective treatment response than vehicle group ($p<0.001$). At the end of the study, 74.3% of subjects (26/35) in the Lamisil 1% Cream group had effective treatment, compared to 25.7% of subjects (9/35) in the vehicle group ($p<0.001$) [6].	

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Efficacy in Athlete's Foot		
Wording and contextual use of the claim	**Substantiation of the Claim**	**Restrictions on usage of the claim**
3.b) CLAIM: Effectively treats athlete's foot Effective/clinically proven treatment for athlete's foot **CONTEXT:** **This claim wording must only be used in countries in which Lamisil 1% Cream is approved to treat interdigitale type tinea pedis with twice a day for one week treatment schedule.**	Lamisil 1% Cream is used for the topical treatment of interdigitale type tinea pedis (athlete's foot) with a twice a day for one week treatment schedule [7]. Several multicentre, randomized, double-blind and either placebo-controlled or active-controlled (clotrimazole 1% cream) clinical trials with Lamisil 1% Cream provide evidence for effectively treating interdigitale type tinea pedis with a twice a day for one week treatment schedule [8-10]. A multicentre, randomized, double-blind, placebo-controlled clinical trial with Lamisil 1% Cream was conducted in in total 159 adult subjects with interdigitale type tinea pedis [9]. Subjects were instructed to use the cream twice daily, morning and evening, for 7 days on affected areas. After 1, 2, 4, and 6 weeks, subjects were evaluated for clinical response. Efficacy endpoint were *mycological cure* (negative microscopy and culture) of target lesion and *clinical signs and symptoms* of target lesion, among others. The severity of eight clinical signs and symptoms (fissuring, erythema, maceration, vesicles, desquamation, exudation, pruritus, burning/stinging) of the target lesion was rated on a 4-point scale. *Mycological cure*: Lamisil 1% Cream was significantly more effective than vehicle in achieving mycological cure of target lesion (p=0.003	**VERBATIM USE ONLY** ☐ **Claim can be used for the following;** **CONSUMERS** ☐ **HCPS** ☐ **SPECIFY HCPs:** **BOTH** ☒ **CANNOT BE USED FOR THE FOLLOWING:** Must NOT be used in countries in which Lamisil 1% Cream is approved to treat interdigitale type tinea pedis with any other treatment schedule than twice a day for one week. **OTHER RESTRICTIONS**: -

	at week 1; p<0.001 at weeks 2, 4, and 6). Mycological cure was observed in 51% of subject at week 1 and in 88% of subject at week 6 in the Lamisil 1% Cream group, compared to 27% and 23% of subjects in the vehicle group, respectively. *Clinical signs and symptoms*: At baseline, mean sum of target lesion severity scores for clinical signs and symptoms were 9.9 in both groups. In the Lamisil 1% Cream group, this score declined to 5.2 after week 1 and to 2.1 after week 6, resulting in a 79% reduction from baseline (p<0.001 vs vehicle). In the vehicle group, this score declined to 6.0 after week 1 and to 5.5 after week 6. The two clinical symptoms, pruritus and burning/stinging, were also examined separately. At week 1, pruritus was reduced compared to baseline values by 70% and burning/stinging by 78% in the Lamisil 1% Cream group. In the vehicle cream group, pruritus was reduced by 60% and burning/stinging by 62.5% at week 1 [9]. Furthermore, a multicentre, randomized, double-blind, active-controlled clinical trial with Lamisil 1% Cream vs. clotrimazole 1% cream was conducted in total 193 adult subjects with interdigitale type tinea pedis for a 1- or 4-week course of treatment with each [8]. Subjects were instructed to use product twice daily on affected areas. After 1, 2, 4, 6, 9 and 12 weeks, subjects were evaluated for clinical response. Efficacy endpoint were *mycological cure* (negative microscopy and culture) of target lesion and *clinical signs and symptoms* of target lesion, among others. The severity of eight clinical signs and symptoms (fissuring, erythema, maceration,	

	vesicles, desquamation, exudation, pruritus, burning/stinging) of the target lesion was rated on a 4-point scale. *Mycological cure*: Lamisil 1% Cream for 1 week course of treatment group achieved mycological cure rate of 81% at last study visit. Clotrimazole 1% cream achieved mycological cure rates of 30% and 68% at last study visit for 1 week course of treatment group and 4 week course of treatment group, respectively. Only 9.3% of mycologically cured subjects in the Lamisil 1% Cream for 1 week course of treatment group experienced a relapse/reinfection (evidenced by reversion to positive culture) on or before the 12-week assessment, in comparison to 47% and 30% of mycologically cured subjects in the clotrimazole 1% cream for 1 week course of treatment group and 4 week course of treatment group, respectively [8]. *Clinical signs and symptoms*: At baseline, mean sum of target lesion severity scores for clinical signs and symptoms were 12.1, 11.4 and 11.1 for the Lamisil 1% Cream for 1 week course of treatment group, and the clotrimazole 1% cream for 1 week and 4 week course of treatment groups, respectively. At last study visit, both the Lamisil 1% Cream for 1 week course of treatment group and the clotrimazole 1% cream for 4 week course of treatment group achieved about 80% reduction from baseline, compared to about 60% reduction from baseline for the clotrimazole 1% cream for 1 week course of treatment group [8].	

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Efficacy in Ringworm and Jock Itch		
Wording and contextual use of the claim	**Substantiation of the Claim**	**Restrictions on usage of the claim**
4. CLAIM: Effectively treats tinea corporis Effectively treats tinea cruris Effective/clinically proven treatment for tinea corporis Effective/clinically proven treatment for tinea cruris **CONTEXT:**	Lamisil 1% Cream is used for the topical treatment of tinea corporis (ringworm of the trunk, arms, legs) and tinea cruris (jock itch or dhobie itch) with a once a day for one week treatment schedule [5]. A multicentre, randomized, double-blind, placebo-controlled clinical trial with Lamisil 1% Cream was conducted in in total 120 adult subjects with tinea corporis and cruris [11]. Subjects were instructed to use the cream once daily in the evening for 7 days on affected areas. On day 8, 14, 42 and 56, subjects were evaluated for clinical response. The primary efficacy endpoint was *mycological cure* and secondary efficacy endpoints included *total clinical signs and symptoms score* and *clinical response* (see 3. claim substantiation about study [6] for definition of these endpoints) *Mycological cure*: Lamisil 1% Cream was significantly more effective than vehicle in both achieving and maintaining mycological cure. At end of study, 84.2% of subjects in the Lamisil 1% Cream group had mycological cure, compared to 23.3% of subjects in the vehicle group ($p<0.001$). The number of subjects with mycological cure was significantly greater in the Lamisil 1% Cream group than in the vehicle group from the second visit (day 8) onwards ($p<0.001$) [11]. *Total clinical signs and symptoms score*: At baseline, mean total signs and symptoms score were 6.9 and 7.0 in the Lamisil 1% Cream group and the vehicle group respectively. By visit 2 (day 8) a statistically	**VERBATIM USE ONLY** ☐ **Claim can be used for the following;** **CONSUMERS** ☐ **HCPS** ☐ **SPECIFY HCPs:** **BOTH** ☒ **CANNOT BE USED FOR THE FOLLOWING:** **-** **OTHER RESTRICTIONS: -**

	significant difference in total signs and symptoms score in favour of Lamisil 1% Cream was established (p<0.001) [11]. *Clinical response*: By visit 2 (day 8), Lamisil 1% Cream group displayed a statistically significant higher rate of effective treatment response than vehicle group (p<0.001). At the end of the study, 84.2% of subjects in the Lamisil 1% Cream group had effective treatment, compared to 21.7% of subjects in the vehicle group (p<0.001) [11]. Furthermore, a multicentre, randomized, double-blind, active-controlled clinical trial with Lamisil 1% Cream vs. bifonazole 1% cream was conducted in in total 185 adult subjects with tinea cruris [12]. Subjects were instructed to use either Lamisil 1% Cream once daily for 7 days on affected areas followed by 2 weeks of placebo or bifonazole 1% once daily for 3 weeks. At week 1, 2, 3 and 8, subjects were evaluated for clinical response. The primary efficacy endpoint was *mycological cure* (negative microscopy and culture). Further efficacy endpoints included *global evaluation of clinical efficacy*. The severity of four clinical signs and symptoms (erythema, scales, pruritus, and papule) was recorded on a 3-point scale. Global evaluation of clinical efficacy was the sum of the individual scores (i.e. between 0 and 8; 0 = cured, 1-3 = mild, 4-8 = severe) *Mycological cure*: The rate of mycological cure was 72.88% in the bifonazole group and 77.78% in the Lamisil 1% Cream group at week 1 and 97.51% and 97.75% at week 3 respectively. At week 8, the relapse rates were 20.42% for the bifonazole group and 11.76% for	

	the Lamisil 1% Cream. These differences were not statistically significant different (p>0.05) [12]. *Global evaluation of clinical efficacy*: The rate of clinical response (cured and mild) was 88.04% in the bifonazole group and 93.33% in the Lamisil 1% Cream group at week 1. These became 98.89% and 100% at week 2 and 98.84% and 100% at week 3. These differences were not statistically significant different (p>0.05) [12].	

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Mycological Cure in Athlete's Foot		
Wording and contextual use of the claim	**Substantiation of the Claim**	**Restrictions on usage of the claim**
5.a) CLAIM: Clinically proven to cure most athlete's foot High mycological cure rate [in athlete's foot] Proven to cure athlete's foot Proven to cure athletes foot with 7 days treatment. **CONTEXT:** **This claim wording must only be used in countries in which Lamisil 1% Cream is approved to treat interdigitale type tinea pedis with <u>once a day</u> for one week treatment schedule.**	See 3.a) claim substantiation - A multicentre, randomized, double-blind, placebo-controlled clinical trial with Lamisil 1% Cream was conducted in in total 100 adult subjects with interdigitale type tinea pedis [6]. Subjects were instructed to use the cream once daily in the evening for 7 days on affected areas. On day 8, 14, 42 and 56, subjects were evaluated for clinical response. *Mycological cure* (negative microscopy and culture) was assessed as the primary efficacy endpoint at the end of the study, defined as the last non-missing, post-baseline observation during the study. Lamisil 1% Cream was significantly more effective than vehicle in both achieving and maintaining mycological cure. At end of study, 91.4% of subjects (32/35) in the Lamisil 1% Cream group had mycological cure, compared to 37.1% of subjects (13/35) in the vehicle group ($p<0.001$). The number of subjects with mycological cure was significantly greater in the Lamisil 1% Cream group than in the vehicle group from the third visit (day 14) onwards ($p<0.001$) [6]. A mycological cure rate of 91.4% at end of study is considered as high.	**VERBATIM USE ONLY** ☐ **Claim can be used for the following;** **CONSUMERS** ☐ **HCPS** ☐ **SPECIFY HCPs:** **BOTH** ☒ **CANNOT BE USED FOR THE FOLLOWING:** Must NOT be used in countries in which Lamisil 1% Cream is approved to treat interdigitale type tinea pedis with any other treatment schedule than once a day for one week. **OTHER RESTRICTIONS: -**

Wording in brackets is optional if claim context makes clear that you are specifically talking about interdigitale type tinea pedis and not any other disease.		
Mycological Cure in Athlete's Foot		
Wording and contextual use of the claim	**Substantiation of the Claim**	**Restrictions on usage of the claim**
5.b) CLAIM: Clinically proven to cure most athlete's foot High mycological cure rate [in athlete's foot] Proven to cure athlete's foot Proven to cure athletes foot with 7 days treatment.	See 3.b) claim substantiation - A multicentre, randomized, double-blind, placebo-controlled clinical trial with Lamisil 1% Cream was conducted in in total 159 adult subjects with interdigitale type tinea pedis [9]. Subjects were instructed to use the cream twice daily, morning and evening, for 7 days on affected areas. *Mycological cure*: Lamisil 1% Cream was significantly more effective than vehicle in achieving mycological cure of target lesion (p=0.003 at week 1; p<0.001 at weeks 2, 4, and 6). Mycological cure was observed in 51% of subject at week 1 and in 88% of subject at week 6 in the Lamisil 1% Cream group, compared to 27% and 23% of subjects in the vehicle group, respectively [9]. A mycological cure rate of 88% at week 6 is considered as high.	**VERBATIM USE ONLY** ☐ **Claim can be used for the following;** **CONSUMERS** ☐ **HCPS** ☐ **SPECIFY HCPs:** **BOTH** ☒ **CANNOT BE USED FOR THE FOLLOWING:** Must NOT be used in countries in which Lamisil 1% Cream is approved to treat interdigitale type tinea pedis with any

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CONTEXT: **This claim wording must only be used in countries in which Lamisil 1% Cream is approved to treat interdigitale type tinea pedis with twice a day for one week treatment schedule.** Wording in brackets is optional if claim context makes clear that you are specifically talking about interdigitale type tinea pedis and not any other disease.		other treatment schedule than twice a day for one week. **OTHER RESTRICTIONS: -**
Mycological Cure in Ringworm and Jock Itch		
Wording and contextual use of the claim	**Substantiation of the Claim**	**Restrictions on usage of the claim**

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JOB NAME	GC CSS Lamisil 1% Cream – Terbinafine Hydrochloride 1% Cream
JOB NUMBER	GCCSS-SKH-0058.003 (in ZINC: GCSH/CHLAM/0003/17(2))

6. CLAIM: Clinically proven to cure most tinea corporis Clinically proven to cure most tinea cruris High mycological cure rate [in tinea corporis] High mycological cure rate [in tinea cruris] **CONTEXT:** Wording in brackets is optional if claim context makes clear that you are specifically talking about tinea corporis and/or tinea cruris but not any other disease.	See 4. claim substantiation - A multicentre, randomized, double-blind, placebo-controlled clinical trial with Lamisil 1% Cream was conducted in in total 120 adult subjects with tinea corporis and cruris [11]. Subjects were instructed to use the cream once daily in the evening for 7 days on affected areas. On day 8, 14, 42 and 56, subjects were evaluated for clinical response. *Mycological cure* (negative microscopy and culture) was assessed as the primary efficacy endpoint at the end of the study, defined as the last non-missing, post-baseline observation during the study. Lamisil 1% Cream was significantly more effective than vehicle in both achieving and maintaining mycological cure. At end of study, 84.2% of subjects in the Lamisil 1% Cream group had mycological cure, compared to 23.3% of subjects in the vehicle group ($p<0.001$). The number of subjects with mycological cure was significantly greater in the Lamisil 1% Cream group than in the vehicle group from the second visit (day 8) onwards ($p<0.001$) [11]. A mycological cure rate of 84.2% at end of study is considered as high.	**VERBATIM USE ONLY** ☐ **Claim can be used for the following;** **CONSUMERS** ☐ **HCPS** ☐ **SPECIFY HCPs:** **BOTH** ☒ **CANNOT BE USED FOR THE FOLLOWING:** - **OTHER RESTRICTIONS: -**

KARO HEALTHCARE CLAIMS DOCUMENT	
JOB NAME	GC CSS Lamisil 1% Cream – Terbinafine Hydrochloride 1% Cream
JOB NUMBER	GCCSS-SKH-0058.003 (in ZINC: GCSH/CHLAM/0003/17(2))

Efficacy of Symptoms Reduction in Athlete's Foot		
Wording and contextual use of the claim	**Substantiation of the Claim**	**Restrictions on usage of the claim**
7.a) CLAIM: Clinically proven to ease/reduce/relieve symptoms (redness, itching, scaling, blistering, pustules, exudation and crusting) [of athlete's foot] **CONTEXT:** **This claim wording must only be used in countries in which Lamisil 1% Cream is approved to treat interdigitale type tinea pedis with once a day for one week treatment schedule.** Wording in brackets is optional if claim context makes clear that you are specifically talking about interdigitale type tinea pedis and not any other disease.	See 3.a) claim substantiation - A multicentre, randomized, double-blind, placebo-controlled clinical trial with Lamisil 1% Cream was conducted in in total 100 adult subjects with interdigitale type tinea pedis [6]. Subjects were instructed to use the cream once daily in the evening for 7 days on affected areas. On day 8, 14, 42 and 56, subjects were evaluated for clinical response. *Total clinical signs and symptoms score* was assessed as a secondary efficacy endpoint. The severity of seven clinical signs and symptoms (erythema, scaling, vesiculation, pruritus, pustules, exudation and crusting) was recorded on a 4-point scale. Total signs and symptoms score was the sum of the individual scores (i.e. between 0 and 21). At baseline, mean total signs and symptoms score were 7.2 and 7.3 in the Lamisil 1% Cream group and the vehicle group respectively. From visit 4 (day 42) onwards a statistically significant difference in total signs and symptoms score in favour of Lamisil 1% Cream was established ($p \leq 0.001$). The total signs and symptoms scores at the final visit were 1.5 in Lamisil 1% Cream group and 3.7 in vehicle group ($p<0.001$) [6].	**VERBATIM USE ONLY** ☐ **Claim can be used for the following;** **CONSUMERS** ☐ **HCPS** ☐ **SPECIFY HCPs:** **BOTH** ☒ **CANNOT BE USED FOR THE FOLLOWING:** Must NOT be used in countries in which Lamisil 1% Cream is approved to treat interdigitale type tinea pedis with any other treatment schedule than once a day for one week. Must not be used for any other indication than interdigitale type tinea pedis. **OTHER RESTRICTIONS: -**

KARO HEALTHCARE CLAIMS DOCUMENT	
JOB NAME	GC CSS Lamisil 1% Cream – Terbinafine Hydrochloride 1% Cream
JOB NUMBER	GCCSS-SKH-0058.003 (in ZINC: GCSH/CHLAM/0003/17(2))

Wording in round brackets is optional and can be left out when in need of a short claim.		

KARO HEALTHCARE CLAIMS DOCUMENT	
JOB NAME	GC CSS Lamisil 1% Cream – Terbinafine Hydrochloride 1% Cream
JOB NUMBER	GCCSS-SKH-0058.003 (in ZINC: GCSH/CHLAM/0003/17(2))

Efficacy of Symptoms Reduction in Athlete's Foot		
Wording and contextual use of the claim	**Substantiation of the Claim**	**Restrictions on usage of the claim**
7.b) CLAIM: Clinically proven to ease/reduce/relieve symptoms (itching, burning/stinging, redness, cracking, maceration, blistering, desquamation, exudation) [of athlete's foot] **CONTEXT:** **This claim wording must only be used in countries in which Lamisil 1% Cream is approved to treat interdigitale type tinea pedis with twice a day for one week treatment schedule.** Wording in brackets is optional if claim context makes clear that you are specifically talking about interdigitale type tinea pedis and not any other disease.	See 3.b) claim substantiation - A multicentre, randomized, double-blind, placebo-controlled clinical trial with Lamisil 1% Cream was conducted in in total 159 adult subjects with interdigitale type tinea pedis [9]. Subjects were instructed to use the cream twice daily, morning and evening, for 7 days on affected areas. *Clinical signs and symptoms* of target lesion were assessed as an efficacy endpoint. The severity of eight clinical signs and symptoms (fissuring, erythema, maceration, vesicles, desquamation, exudation, pruritus, burning/stinging) of the target lesion was rated on a 4-point scale. *Clinical signs and symptoms*: At baseline, mean sum of target lesion severity scores for clinical signs and symptoms were 9.9 in both groups. In the Lamisil 1% Cream group, this score declined to 5.2 after week 1 and to 2.1 after week 6, resulting in a 79% reduction from baseline ($p<0.001$ vs vehicle). In the vehicle group, this score declined to 6.0 after week 1 and to 5.5 after week 6. The two clinical symptoms, pruritus and burning/stinging, were also examined separately. At week 1, pruritus was reduced compared to baseline values by 70% and burning/stinging by 78% in the Lamisil 1% Cream group. In the vehicle cream group, pruritus was reduced by 60% and burning/stinging by 62.5% at week 1 [9].	**VERBATIM USE ONLY** ☐ **Claim can be used for the following;** **CONSUMERS** ☐ **HCPS** ☐ **SPECIFY HCPs:** **BOTH** ☒ **CANNOT BE USED FOR THE FOLLOWING:** Must NOT be used in countries in which Lamisil 1% Cream is approved to treat interdigitale type tinea pedis with any other treatment schedule than twice a day for one week. Must not be used for any other indication than interdigitale type tinea pedis. **OTHER RESTRICTIONS: -**

KARO HEALTHCARE CLAIMS DOCUMENT	
JOB NAME	GC CSS Lamisil 1% Cream – Terbinafine Hydrochloride 1% Cream
JOB NUMBER	GCCSS-SKH-0058.003 (in ZINC: GCSH/CHLAM/0003/17(2))

Wording in round brackets is optional and can be left out when in need of a short claim.		

KARO HEALTHCARE CLAIMS DOCUMENT	
JOB NAME	GC CSS Lamisil 1% Cream – Terbinafine Hydrochloride 1% Cream
JOB NUMBER	GCCSS-SKH-0058.003 (in ZINC: GCSH/CHLAM/0003/17(2))

Efficacy of Itch Reduction in Athlete's Foot		
Wording and contextual use of the claim	**Substantiation of the Claim**	**Restrictions on usage of the claim**
8.a) CLAIM: Clinically proven to ease/reduce/relieve/soothe itch [in athlete's foot] **CONTEXT:** **This claim wording must only be used in countries in which Lamisil 1% Cream is approved to treat interdigitale type tinea pedis with <u>once a day</u> for one week treatment schedule.** Wording in brackets is optional if claim context makes clear that you are specifically talking about interdigitale type tinea pedis and not any other disease.	See 3.a) claim substantiation - A multicentre, randomized, double-blind, placebo-controlled clinical trial with Lamisil 1% Cream was conducted in in total 100 adult subjects with interdigitale type tinea pedis [6]. Subjects were instructed to use the cream once daily in the evening for 7 days on affected areas. On day 8, 14, 42 and 56, subjects were evaluated for clinical response. *Total clinical signs and symptoms score* was assessed as a secondary efficacy endpoint. The severity of seven clinical signs and symptoms (erythema, scaling, vesiculation, pruritus, pustules, exudation and crusting) was recorded on a 4-point scale. Total signs and symptoms score was the sum of the individual scores (i.e. between 0 and 21). At baseline, mean total signs and symptoms score were 7.2 and 7.3 in the Lamisil 1% Cream group and the vehicle group respectively. From visit 4 (day 42) onwards a statistically significant difference in total signs and symptoms score in favour of Lamisil 1% Cream was established ($p \leq 0.001$). The total signs and symptoms scores at the final visit were 1.5 in Lamisil 1% Cream group and 3.7 in vehicle group ($p<0.001$) [6]. The corresponding Clinical Study Report [19] of this study [6] also examined individual signs and symptoms including pruritus. At end of study, significant better results for Lamisil 1% Cream group than vehicle group were achieved for erythema (p=0.004), scaling (0.002), exudation (p=0.014) and pruritus (p=0.009) [19].	**VERBATIM USE ONLY** ☐ **Claim can be used for the following;** **CONSUMERS** ☐ **HCPS** ☐ **SPECIFY HCPs:** **BOTH** ☒ **CANNOT BE USED FOR THE FOLLOWING:** Must NOT be used in countries in which Lamisil 1% Cream is approved to treat interdigitale type tinea pedis with any other treatment schedule than once a day for one week. Must not be used for any other indication than interdigitale type tinea pedis. **OTHER RESTRICTIONS: -**

KARO HEALTHCARE CLAIMS DOCUMENT	
JOB NAME	GC CSS Lamisil 1% Cream – Terbinafine Hydrochloride 1% Cream
JOB NUMBER	GCCSS-SKH-0058.003 (in ZINC: GCSH/CHLAM/0003/17(2))

Efficacy of Itch Reduction in Athlete's Foot		
Wording and contextual use of the claim	**Substantiation of the Claim**	**Restrictions on usage of the claim**
8.b) CLAIM: Clinically proven to ease/reduce/relieve/soothe itch [in athlete's foot] **CONTEXT:** **This claim wording must only be used in countries in which Lamisil 1% Cream is approved to treat interdigitale type tinea pedis with twice a day for one week treatment schedule.** Wording in brackets is optional if claim context makes clear that you are specifically talking about interdigitale type tinea pedis and not any other disease.	See 3.b) claim substantiation - A multicentre, randomized, double-blind, placebo-controlled clinical trial with Lamisil 1% Cream was conducted in in total 159 adult subjects with interdigitale type tinea pedis [9]. Subjects were instructed to use the cream twice daily, morning and evening, for 7 days on affected areas. At week 1, pruritus was reduced compared to baseline values by 70% in the Lamisil 1% Cream group. In the vehicle cream group, pruritus was reduced by 60% at week 1 [9]. Itch reduction is further confirmed in a multicentre, randomized, double blind, placebo controlled clinical trial to investigate the efficacy and safety of Lamisil 1% Cream when applied twice daily for three days, five days or seven days compared to clotrimazole cream 1% or placebo vehicle applied twice daily for 7 days in in total 322 adult subjects with interdigitale type tinea pedis [13]. Itch was scored in subject diaries and assessed at each of days 1-7 and at the end of weeks 2, 3, 4, 5 and 6. There was significantly less itching in all three Lamisil 1% Cream treatment groups than in the placebo vehicle group over Weeks 2-6 ($p<0.01$). There was also significantly less itching in the Lamisil 1% Cream 7 day treatment group than in the placebo vehicle group at Day 7 ($p=0.05$) [13].	**VERBATIM USE ONLY** ☐ **Claim can be used for the following;** **CONSUMERS** ☐ **HCPS** ☐ **SPECIFY HCPs:** **BOTH** ☒ **CANNOT BE USED FOR THE FOLLOWING:** Must NOT be used in countries in which Lamisil 1% Cream is approved to treat interdigitale type tinea pedis with any other treatment schedule than twice a day for one week. Must not be used for any other indication than interdigitale type tinea pedis. **OTHER RESTRICTIONS: -**

KARO HEALTHCARE CLAIMS DOCUMENT	
JOB NAME	GC CSS Lamisil 1% Cream – Terbinafine Hydrochloride 1% Cream
JOB NUMBER	GCCSS-SKH-0058.003 (in ZINC: GCSH/CHLAM/0003/17(2))

Efficacy of Burning/Stinging Reduction in Athlete's Foot		
Wording and contextual use of the claim	**Substantiation of the Claim**	**Restrictions on usage of the claim**
9.b) CLAIM: Clinically proven to ease/reduce/relieve/soothe burning/stinging [in athlete's foot] **CONTEXT:** **This claim wording must only be used in countries in which Lamisil 1% Cream is approved to treat interdigitale type tinea pedis with twice a day for one week treatment schedule.** Wording in brackets is optional if claim context makes clear that you are specifically talking about interdigitale type tinea pedis and not any other disease.	See 3.b) claim substantiation - A multicentre, randomized, double-blind, placebo-controlled clinical trial with Lamisil 1% Cream was conducted in in total 159 adult subjects with interdigitale type tinea pedis [9]. Subjects were instructed to use the cream twice daily, morning and evening, for 7 days on affected areas. At week 1, burning/stinging was reduced compared to baseline values by 78% in the Lamisil 1% Cream group. In the vehicle cream group, burning/stinging was reduced by 62.5% at week 1. Of the Lamisil 1% Cream treated subjects who had moderate/severe burning/stinging at baseline, 91% were reduced to absent/mild by Day 7 compared to 75% in the vehicle cream group [9]. Burning/stinging reduction is further confirmed in a multicentre, randomized, double blind, placebo controlled clinical trial to investigate the efficacy and safety of Lamisil 1% Cream when applied twice daily for three days, five days or seven days compared to clotrimazole cream 1% or placebo vehicle applied twice daily for 7 days in in total 322 adult subjects with interdigitale type tinea pedis [13]. Burning/stinging was scored in subject diaries and assessed at each of days 1-7 and at the end of weeks 2, 3, 4, 5 and 6. There was significantly less burning/stinging in the Lamisil 1% Cream 7 day and 5 day treatment groups compared to the placebo vehicle group at week 4 ($p=0.02$ for 7 day treatment group vs placebo and $p<0.01$ for	**VERBATIM USE ONLY** ☐ **Claim can be used for the following;** **CONSUMERS** ☐ **HCPS** ☐ **SPECIFY HCPs:** **BOTH** ☒ **CANNOT BE USED FOR THE FOLLOWING:** Must NOT be used in countries in which Lamisil 1% Cream is approved to treat interdigitale type tinea pedis with any other treatment schedule than twice a day for one week. Must not be used for any other indication than interdigitale type tinea pedis. **OTHER RESTRICTIONS: -**

	5 day treatment vs placebo), week 5 (p≤.0.01) and week 6 (p≤.0.01) [13].	

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JOB NAME	GC CSS Lamisil 1% Cream – Terbinafine Hydrochloride 1% Cream
JOB NUMBER	GCCSS-SKH-0058.003 (in ZINC: GCSH/CHLAM/0003/17(2))

Efficacy of Symptoms Reduction in Ringworm and Jock Itch		
Wording and contextual use of the claim	**Substantiation of the Claim**	**Restrictions on usage of the claim**
10. CLAIM: Clinically proven to ease/reduce/relieve symptoms (redness, itching, scaling, blistering, pustules, exudation and crusting) [of tinea corporis] Clinically proven to ease/reduce/relieve symptoms (redness, itching, scaling, blistering, pustules, exudation and crusting) [of tinea cruris] **CONTEXT:** Wording in brackets is optional if claim context makes clear that you are specifically talking about tinea corporis and/or tinea cruris but not any other disease.	See 4. claim substantiations - A multicentre, randomized, double-blind, placebo-controlled clinical trial with Lamisil 1% Cream was conducted in in total 120 adult subjects with tinea corporis and cruris [11]. Subjects were instructed to use the cream once daily in the evening for 7 days on affected areas. On day 8, 14, 42 and 56, subjects were evaluated for clinical response. *Total clinical signs and symptoms score* was assessed as a secondary efficacy endpoint. At baseline, mean total signs and symptoms score were 6.9 and 7.0 in the Lamisil 1% Cream group and the vehicle group respectively. By visit 2 (day 8) a statistically significant difference in total signs and symptoms score in favour of Lamisil 1% Cream was established ($p<0.001$) [11].	**VERBATIM USE ONLY** ☐ **Claim can be used for the following;** **CONSUMERS** ☐ **HCPS** ☐ **SPECIFY HCPs:** **BOTH** ☒ **CANNOT BE USED FOR THE FOLLOWING:** Must not be used for indications other than tinea corporis and tinea cruris **OTHER RESTRICTIONS: -**

KARO HEALTHCARE CLAIMS DOCUMENT	
JOB NAME	GC CSS Lamisil 1% Cream – Terbinafine Hydrochloride 1% Cream
JOB NUMBER	GCCSS-SKH-0058.003 (in ZINC: GCSH/CHLAM/0003/17(2))

Wording in round brackets is optional and can be left out when in need of a short claim.		

KARO HEALTHCARE CLAIMS DOCUMENT	
JOB NAME	GC CSS Lamisil 1% Cream – Terbinafine Hydrochloride 1% Cream
JOB NUMBER	GCCSS-SKH-0058.003 (in ZINC: GCSH/CHLAM/0003/17(2))

Efficacy of Itch Reduction in Ringworm and Jock Itch		
Wording and contextual use of the claim	**Substantiation of the Claim**	**Restrictions on usage of the claim**
11. CLAIM: Clinically proven to ease/reduce/relieve/sooth itch [in tinea corporis] Clinically proven to ease/reduce/relieve/sooth itch [in tinea cruris] **CONTEXT:** Wording in brackets is optional if claim context makes clear that you are specifically talking about tinea corporis and/or tinea cruris but not any other disease.	See 4. and 8. claim substantiations - A multicentre, randomized, double-blind, placebo-controlled clinical trial with Lamisil 1% Cream was conducted in in total 120 adult subjects with tinea corporis and cruris [11]. Subjects were instructed to use the cream once daily in the evening for 7 days on affected areas. On day 8, 14, 42 and 56, subjects were evaluated for clinical response. *Total clinical signs and symptoms score* was assessed as a secondary efficacy endpoint. At baseline, mean total signs and symptoms score were 6.9 and 7.0 in the Lamisil 1% Cream group and the vehicle group respectively. By visit 2 (day 8) a statistically significant difference in total signs and symptoms score in favour of Lamisil 1% Cream was established ($p<0.001$) [11]. In the Clinical Study report [14] of this study [11], each individual sign and symptom score was analysed at each visit. The results for the following signs and symptoms showed a significantly better result for the Lamisil 1% Cream group than the vehicle group: erythema ($p<0.001$), scaling ($p<0.001$), crusting ($p<0.001$) and pruritus ($p<0.001$) all at end of study [14].	**VERBATIM USE ONLY** ☐ **Claim can be used for the following;** **CONSUMERS** ☐ **HCPS** ☐ **SPECIFY HCPs:** **BOTH** ☒ **CANNOT BE USED FOR THE FOLLOWING:** Must not be used for indications other than tinea corporis and tinea cruris **OTHER RESTRICTIONS: -**

KARO HEALTHCARE CLAIMS DOCUMENT	
JOB NAME	GC CSS Lamisil 1% Cream – Terbinafine Hydrochloride 1% Cream
JOB NUMBER	GCCSS-SKH-0058.003 (in ZINC: GCSH/CHLAM/0003/17(2))

Keeps Working		
Wording and contextual use of the claim	**Substantiation of the Claim**	**Restrictions on usage of the claim**
12. CLAIM: Keeps working even after you finish treatment* Continues to work beyond the 7 days of treatment* Continues to work up to 7 days after end of treatment* Forms a reservoir of terbinafine at fungicidal levels in the skin that is maintained up to 7 days after end of treatment Terbinafine binds to keratin/corneocytes in the skin *Fungicidal levels measured in skin up to 7 days after end of treatment	Pharmacokinetics of Lamisil 1% Cream were assessed in 20 healthy adults randomized to receive once daily application of Lamisil 1% Cream for 1, 3, 5 or 7 consecutive days, respectively, on their backs [15]. Skin tape strips taken from stratum corneum at various time points up to 7 days after last application of Lamisil 1% Cream were analysed by high performance liquid chromatography for terbinafine amounts. The terbinafine level measured 7 days after cessation of 7 days' treatment (0.33 ng/cm^2) are considered to still exceed the *in vitro* minimum fungicidal concentration (MFC) of most relevant dermatophyte strains by about 100 times. In contrast, terbinafine levels weren't' detectable 7 days after cessation of 1, 3, or 5 days' treatments, respectively [15]. The reason why terbinafine remains in the stratum corneum for such a long time is because it's highly lipophilic and attaches to corneocytes [20]. The stratum corneum acts as a reservoir for terbinafine administered topically. Although terbinafine absorbs to keratin at a relatively high rate, it is easily released without losing its activity [21]. A more recent pharmacokinetic study too showed a fungicidal reservoir effect of terbinafine from Lamisil 1% Cream and Lamisil 1% Film Forming Solution (FFS) in human skin [16]. Lamisil 1% Cream or Lamisil 1% FFS was applied to areas of the backs in 18 healthy	**VERBATIM USE ONLY** ☐ **Claim can be used for the following;** **CONSUMERS** ☐ **HCPS** ☐ **SPECIFY HCPs:** **BOTH** ☒ **CANNOT BE USED FOR THE FOLLOWING:** Must not be used for indications other than interdigitale type tinea pedis, tinea corporis and tinea cruris **OTHER RESTRICTIONS:** This claims is supported by measured presence of terbinafine levels in skin. Appropriateness of such pharmacokinetic data for local claim substantiation must be assessed locally.

CONTEXT: This claim wording must only be used in the context of interdigitale type tinea pedis, tinea corporis and/or tinea cruris.	subjects once daily for 7 days or for a single application, respectively. Skin tape strips taken from stratum corneum at various time points up to 312 hours after first application were analysed by liquid chromatography/mass spectrometry for terbinafine amounts. The terbinafine level measured 7 days after cessation of 7 days' Lamisil 1% cream treatment (46 ng/cm^2) are considered to still exceed the *in vitro* minimum fungicidal concentration (MFC) of most relevant dermatophyte strains. Terbinafine levels measured 13 days after single application of Lamisil 1% FFS (24 ng/ cm^2) were close and also considered to still exceed the *in vitro* minimum fungicidal concentration (MFC) of most relevant dermatophyte strains [16]. Both pharmacokinetic studies [15,16] also provide support for these claims for countries in which Lamisil 1% Cream is approved for twice daily application for 1 week to treat interdigitale type tinea pedis. It is expected that twice daily application of Lamisil 1% Cream will deliver at least as much active ingredient into the skin than once daily application for 7 days, presumably even more.	

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JOB NUMBER	GCCSS-SKH-0058.003 (in ZINC: GCSH/CHLAM/0003/17(2))

Protection from Recurrence in Athlete's Foot		
Wording and contextual use of the claim	**Substantiation of the Claim**	**Restrictions on usage of the claim**
13.a) CLAIM: Protects from recurrence* [of athlete's foot] Prevents recurrence* [of athlete's foot] Low recurrence rate* [of athlete's foot] *Up to 3 months **CONTEXT:** **This claim wording must only be used in countries in which Lamisil 1% Cream is approved to treat interdigitale type tinea pedis with <u>once a day</u> for one week treatment schedule.** Wording in brackets is optional if claim context makes clear that you	A multicentre, randomized, double-blind, parallel group clinical trial with Lamisil 1% cream was conducted to investigate the minimum duration of treatment [17]. In this trial, 78 adult subjects with interdigitale type tinea pedis were randomized to receive once-daily treatment for 1 day, 3 days, 5 days or 7 days with Lamisil 1% Cream (followed by 6, 4, 2 or 0 days of vehicle cream base, respectively, to maintain double-blinding). On day 8, 14, 28 and 84, subjects were evaluated for clinical response. The key trial endpoint was day 28. The day 84 assessment was included to investigate whether there was a significant incidence of relapse following such short durations of treatment. The efficacy endpoints were *mycological cure* (negative microscopy and culture), *total clinical signs and symptoms score* and *clinical response*. At day 28, 83% (10 out of 12) of subjects in the 7 day treatment group had mycological cure, compared to 78%, 83% and 82% in the 1, 3, and 5 day treatment groups, respectively. In the 7 day treatment group, mycological cure improved between Days 28 and 84 to 92% (11 out of 12) without any recurrence of infection. Also in the 1 and 5 day treatment groups mycological cure improved between Days 28 and 84, to 94% and 88% respectively. In the 3 day treatment group 3 of the 15 subjects mycologically cured at day 28 had mycological evidence of a recurrence of infection, resulting in a 67% mycological cure rate at Day 84 [17].	**VERBATIM USE ONLY** ☐ **Claim can be used for the following;** **CONSUMERS** ☐ **HCPS** ☐ **SPECIFY HCPs:** **BOTH** ☒ **CANNOT BE USED FOR THE FOLLOWING:** Must NOT be used in countries in which Lamisil 1% Cream is approved to treat interdigitale type tinea pedis with any other treatment schedule than once a day for one week. Must not be used for any other indication than interdigitale type tinea pedis. **OTHER RESTRICTIONS: -**

are specifically talking about interdigitale type tinea pedis and not any other disease.	A low recurrence rate is supported since no recurrence was observed in the 7 day treatment group.	

KARO HEALTHCARE CLAIMS DOCUMENT	
JOB NAME	GC CSS Lamisil 1% Cream – Terbinafine Hydrochloride 1% Cream
JOB NUMBER	GCCSS-SKH-0058.003 (in ZINC: GCSH/CHLAM/0003/17(2))

Protection from Recurrence in Athlete's Foot		
Wording and contextual use of the claim	**Substantiation of the Claim**	**Restrictions on usage of the claim**
13.b) CLAIM: Protects from recurrence* [of athlete's foot] Prevents recurrence* [of athlete's foot] Low recurrence rate* [of athlete's foot] *Up to 3 months **CONTEXT:** **This claim wording must only be used in countries in which Lamisil 1% Cream is approved to treat interdigitale type tinea pedis with <u>twice a day</u> for one week treatment schedule.** Wording in brackets is optional if claim context makes clear that you	See 3.b) claim substantiation – A multicentre, randomized, double-blind, active-controlled clinical trial with Lamisil 1% Cream vs. clotrimazole 1% cream was conducted in total 193 adult subjects with interdigitale type tinea pedis for a 1- or 4-week course of treatment with each [8]. Subjects were instructed to use product twice daily on affected areas. After 1, 2, 4, 6, 9 and 12 weeks, subjects were evaluated for clinical response *Mycological cure*: Only 9.3% of mycologically cured subjects in the Lamisil 1% Cream for 1 week course of treatment group experienced a relapse/reinfection (evidenced by reversion to positive culture) on or before the 12-week assessment, in comparison to 47% and 30% of mycologically cured subjects in the clotrimazole 1% cream for 1 week course of treatment group and 4 week course of treatment group, respectively [8]. A recurrence rate of 9.3% is considered as low.	**VERBATIM USE ONLY** ☐ **Claim can be used for the following;** **CONSUMERS** ☐ **HCPS** ☐ **SPECIFY HCPs:** **BOTH** ☒ **CANNOT BE USED FOR THE FOLLOWING:** Must NOT be used in countries in which Lamisil 1% Cream is approved to treat interdigitale type tinea pedis with any other treatment schedule than twice a day for one week. Must not be used for any other indication than interdigitale type tinea pedis. **OTHER RESTRICTIONS: -**

are specifically talking about interdigitale type tinea pedis and not any other disease.		

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JOB NUMBER	GCCSS-SKH-0058.003 (in ZINC: GCSH/CHLAM/0003/17(2))

7 Day Treatment		
Wording and contextual use of the claim	**Substantiation of the Claim**	**Restrictions on usage of the claim**
14. CLAIM: Only 7 days of treatment Needs only 1 week of treatment Short treatment course **CONTEXT:** The claim wording must only be used in the context of interdigitale type tinea pedis, tinea corporis and/or tinea cruris. Treatment time must NOT be confused with healing time.	See 3.a)/3.b) and 4. claim substantiations – Lamisil 1% Cream was effective in treating interdigitale type tinea pedis, tinea corporis and tinea cruris in clinical trials with one week treatment schedule [6,9,11]. 1 week is considered a short treatment course.	**VERBATIM USE ONLY** ☐ **Claim can be used for the following;** **CONSUMERS** ☐ **HCPS** ☐ **SPECIFY HCPs:** **BOTH** ☒ **CANNOT BE USED FOR THE FOLLOWING:** Must not be used for indications other than interdigitale type tinea pedis, tinea corporis and tinea cruris. **OTHER RESTRICTIONS: -**

KARO HEALTHCARE CLAIMS DOCUMENT	
JOB NAME	GC CSS Lamisil 1% Cream – Terbinafine Hydrochloride 1% Cream
JOB NUMBER	GCCSS-SKH-0058.003 (in ZINC: GCSH/CHLAM/0003/17(2))

Shorter/Faster Treatment		
Wording and contextual use of the claim	**Substantiation of the Claim**	**Restrictions on usage of the claim**
15. CLAIM: Up to 4 times shorter treatment* Up to 4 times faster treatment* *than azole containing products with 3 to 4 weeks of treatment duration **CONTEXT:** This claim wording must only be used in the context of interdigitale type tinea pedis, tinea corporis and/or tinea cruris. Local product information of relevant azole containing products need to be checked to ensure claim is appropriate and accurate. If not, claim wording and disclaimer must be amended to be in line with local	See 3.a)/3.b) and 4. claim substantiations – Lamisil 1% Cream was effective in treating interdigitale type tinea pedis, tinea corporis and tinea cruris in clinical trials with one week treatment schedule [6,9,11]. Topical antifungal treatments with an azole as active ingredient (for example clotrimazole, miconazole or ketoconazole) indicated for the treatment of interdigitale type tinea pedis, tinea corporis and tinea cruris recommend a treatment duration of typically up to 4 weeks. Please check local labels of relevant azole containing products to ensure claim is appropriate locally.	**VERBATIM USE ONLY** ☐ **Claim can be used for the following;** **CONSUMERS** ☐ **HCPS** ☐ **SPECIFY HCPs:** **BOTH** ☒ **CANNOT BE USED FOR THE FOLLOWING:** Must not be used for indications other than interdigitale type tinea pedis, tinea corporis and tinea cruris. **OTHER RESTRICTIONS:** This claim may not be permitted in all markets; please check with LOC Regulatory and Legal in your market. Local labels of relevant azole containing products need to be checked to ensure claim is appropriate locally.

product information of relevant azole containing products. Treatment time must NOT be confused with healing time.		

KARO HEALTHCARE CLAIMS DOCUMENT	
JOB NAME	GC CSS Lamisil 1% Cream – Terbinafine Hydrochloride 1% Cream
JOB NUMBER	GCCSS-SKH-0058.003 (in ZINC: GCSH/CHLAM/0003/17(2))

Triple Action Formula for Athlete's Foot		
Wording and contextual use of the claim	**Substantiation of the Claim**	**Restrictions on usage of the claim**
16.a) CLAIM: Triple-action formula: • Relieves symptoms (redness, itching, scaling, blistering, pustules, exudation and crusting) • Cures athlete's foot with 7 days of treatment • Protects from recurrence* Triple-action formula: • Relieves itching [in athlete's foot] • Kills the fungus • Protects from recurrence* [of athlete's foot]	See 1., 3.a), 5.a), 7.a), 8.a), 13.a) and 14. claim substantiations	**VERBATIM USE ONLY** ☐ **Claim can be used for the following;** **CONSUMERS** ☐ **HCPS** ☐ **SPECIFY HCPs:** **BOTH** ☒ **CANNOT BE USED FOR THE FOLLOWING:** Must NOT be used in countries in which Lamisil 1% Cream is approved to treat interdigitale type tinea pedis with any other treatment schedule than once a day for one week. Must not be used for any other indication than interdigitale type tinea pedis. **OTHER RESTRICTIONS: -**

KARO HEALTHCARE CLAIMS DOCUMENT	
JOB NAME	GC CSS Lamisil 1% Cream – Terbinafine Hydrochloride 1% Cream
JOB NUMBER	GCCSS-SKH-0058.003 (in ZINC: GCSH/CHLAM/0003/17(2))

*Up to 3 months **CONTEXT:** **This claim wording must only be used in countries in which Lamisil 1% Cream is approved to treat interdigitale type tinea pedis with <u>once a day</u> for one week treatment schedule.** Wording in brackets is optional if claim context makes clear that you are specifically talking about interdigitale type tinea pedis and not any other disease. Wording in round brackets is optional and can be left out when in need of a short claim. Treatment time must NOT be confused with healing time.		
Triple Action Formula for Athlete's Foot		
Wording and contextual use of the claim	**Substantiation of the Claim**	**Restrictions on usage of the claim**

KARO HEALTHCARE CLAIMS DOCUMENT	
JOB NAME	GC CSS Lamisil 1% Cream – Terbinafine Hydrochloride 1% Cream
JOB NUMBER	GCCSS-SKH-0058.003 (in ZINC: GCSH/CHLAM/0003/17(2))

16.b) CLAIM: Triple-action formula: • Relieves symptoms (itching, burning/stinging, redness, cracking, maceration, blistering, desquamation, exudation) • Cures athlete's foot with 7 days of treatment • Protects from recurrence* Triple-action formula: • Relieves itching [in athlete's foot] • Kills the fungus • Protects from recurrence* [of athlete's foot] *Up to 3 months **CONTEXT:**	See 1., 3.b), 5.b), 7.b), 8.b), 13.b) and 14. claim substantiations	**VERBATIM USE ONLY** ☐ **Claim can be used for the following;** **CONSUMERS** ☐ **HCPS** ☐ **SPECIFY HCPs:** **BOTH** ☒ **CANNOT BE USED FOR THE FOLLOWING:** Must NOT be used in countries in which Lamisil 1% Cream is approved to treat interdigitale type tinea pedis with any other treatment schedule than twice a day for one week. Must not be used for any other indication than interdigitale type tinea pedis. **OTHER RESTRICTIONS: -**

KARO HEALTHCARE CLAIMS DOCUMENT	
JOB NAME	GC CSS Lamisil 1% Cream – Terbinafine Hydrochloride 1% Cream
JOB NUMBER	GCCSS-SKH-0058.003 (in ZINC: GCSH/CHLAM/0003/17(2))

This claim wording must only be used in countries in which Lamisil 1% Cream is approved to treat interdigitale type tinea pedis with twice a day for one week treatment schedule. Wording in brackets is optional if claim context makes clear that you are specifically talking about interdigitale type tinea pedis and not any other disease. Wording in round brackets is optional and can be left out when in need of a short claim. Treatment time must NOT be confused with healing time.		
Shortened Triple Action Formula for Athlete's Foot		
Wording and contextual use of the claim	**Substantiation of the Claim**	**Restrictions on usage of the claim**
17.a) CLAIM:	See 1., 3.a), 7.a), 8.a) and 13.a) claim substantiations	**VERBATIM USE ONLY** ☐ **Claim can be used for the following;**

KARO HEALTHCARE CLAIMS DOCUMENT	
JOB NAME	GC CSS Lamisil 1% Cream – Terbinafine Hydrochloride 1% Cream
JOB NUMBER	GCCSS-SKH-0058.003 (in ZINC: GCSH/CHLAM/0003/17(2))

Athlete's foot. Stop it.* Kill it.^ Keep it away.§ * Relieves symptoms/itching ^ Kills the fungus § Protects from recurrence up to 3 months **CONTEXT:** **This claim wording must only be used in countries in which Lamisil 1% Cream is approved to treat interdigitale type tinea pedis with <u>once a day</u> for one week treatment schedule.** Only one of the options separated by a slash mark must be selected.		**CONSUMERS** ☐ **HCPS** ☐ **SPECIFY HCPs:** **BOTH** ☒ **CANNOT BE USED FOR THE FOLLOWING:** Must NOT be used in countries in which Lamisil 1% Cream is approved to treat interdigitale type tinea pedis with any other treatment schedule than once a day for one week. Must not be used for any other indication than interdigitale type tinea pedis. **OTHER RESTRICTIONS: -**

Shortened Triple Action Formula for Athlete's Foot		
Wording and contextual use of the claim	**Substantiation of the Claim**	**Restrictions on usage of the claim**
17.b) CLAIM:	See 1., 3.b), 7.b), 8.b) and 13.b) claim substantiations	**VERBATIM USE ONLY** ☐

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JOB NUMBER	GCCSS-SKH-0058.003 (in ZINC: GCSH/CHLAM/0003/17(2))

Athlete's foot. Stop it.* Kill it.^ Keep it away.§ * Relieves symptoms/itching ^ Kills the fungus § Protects from recurrence up to 3 months **CONTEXT:** **This claim wording must only be used in countries in which Lamisil 1% Cream is approved to treat interdigitale type tinea pedis with twice a day for one week treatment schedule.** Only one of the options separated by a slash mark must be selected.		**Claim can be used for the following;** **CONSUMERS** ☐ **HCPS** ☐ **SPECIFY HCPs:** **BOTH** ☒ **CANNOT BE USED FOR THE FOLLOWING:** Must NOT be used in countries in which Lamisil 1% Cream is approved to treat interdigitale type tinea pedis with any other treatment schedule than twice a day for one week. Must not be used for any other indication than interdigitale type tinea pedis. **OTHER RESTRICTIONS: -**

Dual Action Formula for Athlete's Foot, Ringworm and Jock Itch		
Wording and contextual use of the claim	**Substantiation of the Claim**	**Restrictions on usage of the claim**
18.a) CLAIM:	See 1., 3.a), 4., 7.a) and 10 claim substantiations	**VERBATIM USE ONLY** ☐

KARO HEALTHCARE CLAIMS DOCUMENT	
JOB NAME	GC CSS Lamisil 1% Cream – Terbinafine Hydrochloride 1% Cream
JOB NUMBER	GCCSS-SKH-0058.003 (in ZINC: GCSH/CHLAM/0003/17(2))

Fungal skin infection.* Stop it.^ Kill it. § * Athlete's foot, ringworm and jock itch only ^ Relieves symptoms § Kills the fungus **CONTEXT:** **This claim wording must only be used in countries in which Lamisil 1% Cream is approved to treat interdigitale type tinea pedis with <u>once a day</u> for one week treatment schedule.**		**Claim can be used for the following;** **CONSUMERS** ☐ **HCPS** ☐ **SPECIFY HCPs:** **BOTH** ☒ **CANNOT BE USED FOR THE FOLLOWING:** Must NOT be used in countries in which Lamisil 1% Cream is approved to treat interdigitale type tinea pedis with any other treatment schedule than once a day for one week. Must not be used for any other indication than interdigitale type tinea pedis, tinea corporis and tinea cruris. **OTHER RESTRICTIONS: -**
Dual Action Formula for Athlete's Foot, Ringworm and Jock Itch		
Wording and contextual use of the claim	**Substantiation of the Claim**	**Restrictions on usage of the claim**
18.b) CLAIM:	See 1., 3.b), 4., 7.b) and 10 claim substantiations	**VERBATIM USE ONLY** ☐

KARO HEALTHCARE CLAIMS DOCUMENT	
JOB NAME	GC CSS Lamisil 1% Cream – Terbinafine Hydrochloride 1% Cream
JOB NUMBER	GCCSS-SKH-0058.003 (in ZINC: GCSH/CHLAM/0003/17(2))

Fungal skin infection.* Stop it.^ Kill it. § * Athlete's foot, ringworm and jock itch only ^ Relieves symptoms § Kills the fungus **CONTEXT:** **This claim wording must only be used in countries in which Lamisil 1% Cream is approved to treat interdigitale type tinea pedis with twice a day for one week treatment schedule.**		**Claim can be used for the following;** **CONSUMERS** ☐ **HCPS** ☐ **SPECIFY HCPs:** **BOTH** ☒ **CANNOT BE USED FOR THE FOLLOWING:** Must NOT be used in countries in which Lamisil 1% Cream is approved to treat interdigitale type tinea pedis with any other treatment schedule than twice a day for one week. Must not be used for any other indication than interdigitale type tinea pedis, tinea corporis and tinea cruris. **OTHER RESTRICTIONS: -**

KARO HEALTHCARE CLAIMS DOCUMENT	
JOB NAME	GC CSS Lamisil 1% Cream – Terbinafine Hydrochloride 1% Cream
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Dual Action Kills Foot Fungus and Prevents recurrence		
Wording and contextual use of the claim	**Substantiation of the Claim**	**Restrictions on usage of the claim**
19. CLAIM: **Kills Foot Fungus over 7 days* and prevents recurrence^** *** Treat with Lamisil for 7 days as directed in Usage Instructions** **^ For up to 3 months** **CONTEXT:** **This claim wording can be used in countries in which Lamisil 1% Cream is approved to treat interdigital type tinea pedis with once a day or twice a day for one week treatment schedule**	See 1., 3.b), 4., 7.b) 10 and 13 claim substantiations	**VERBATIM USE ONLY** ☐ **Claim can be used for the following;** **CONSUMERS** ☐ **HCPS** ☐ **SPECIFY HCPs:** **BOTH** ☒ **CANNOT BE USED FOR THE FOLLOWING:** **OTHER RESTRICTIONS: -**

KARO HEALTHCARE CLAIMS DOCUMENT	
JOB NAME	GC CSS Lamisil 1% Cream – Terbinafine Hydrochloride 1% Cream
JOB NUMBER	GCCSS-SKH-0058.003 (in ZINC: GCSH/CHLAM/0003/17(2))

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