doi:10.36849/JDD.9457R1

 ORIGINAL ARTICLE Journal of Drugs in Dermatology

Evaluating the Safety and Efficacy of Sirolimus Topical Gel 0.2% to Treat Acanthosis Nigricans

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ABSTRACT

Background: There are currently no FDA-approved pharmacologic treatments for acanthosis nigricans (AN), a common dermatologic condition characterized by hyperpigmented, velvety plaques. AN disproportionately affects individuals with skin of color and is often associated with insulin resistance and obesity. There is a need for effective, safe, and well-tolerated treatments for AN.

Objective: To evaluate the safety and efficacy of sirolimus gel 0.2% in improving pigmentation, skin texture, and quality of life in patients with AN.

Methods: In this investigator-initiated, single-center, 12-week phase 2 pilot study, five adults with AN on the posterior neck applied sirolimus gel 0.2% twice daily. Assessments were conducted at baseline and weeks 4, 8, and 12. Efficacy was evaluated using a narrowband reflectance spectrophotometer and colorimeter to assess Melanin Index (M-index), Acanthosis Nigricans Scoring Chart (ANSC), Dermatology Life Quality Index (DLQI), Patient and Investigator Global Evaluations (PGE and IGE), and Treatment Satisfaction Questionnaire for Medication (TSQM). Safety and tolerability were monitored.

Results: At week 12, participants demonstrated a significant reduction in pigmentation, with a 19.7% ± 4.9% decrease in M-index (P=0.0037) and a 30.2% reduction in ANSC scores (P=0.0011). Improvements were observed as early as week 4. DLQI scores improved significantly from baseline (P=0.0086). No serious adverse events occurred; mild application-site dryness and erythema were the only reported side effects.

Conclusion: Sirolimus gel 0.2% was safe and effective for AN, producing early improvements in pigmentation, texture, and patient-reported outcomes. Larger randomized controlled trials are warranted to validate these findings.

J Drugs Dermatol. 2026;25(7):615-620. doi:10.36849/JDD.9457R1

INTRODUCTION

Acanthosis nigricans (AN) is a common cutaneous disorder characterized by hyperpigmented, velvety plaques, typically in flexural areas such as the neck, axillae, and groin. In the United States, its prevalence may be as high as 19.4% and disproportionately impacts individuals with skin of color, with African Americans 25 times more likely to be diagnosed with AN than Caucasians.[1-4] Extrapolating these findings to a global population that now exceeds 8 billion, it is estimated that over 155 million individuals could be impacted by AN. Beyond its prevalence, AN underscores a significant healthcare concern as well as a potential health equity issue. Individuals with AN often report substantial decreases in self-esteem and concomitant increases in depression and anxiety, underscoring the need for effective, readily accessible treatments that improve both the physical and psychosocial aspects of the condition.[1,5,6] Despite the global rise in AN prevalence, there are currently no FDA-approved pharmacotherapies available for its treatment.[7]

In addition to its association with insulin resistance and obesity, AN can serve as a paraneoplastic marker and has been linked to various endocrine disorders, further emphasizing the multifaceted etiology and clinical importance of this condition.[8,9] Large-scale studies have reinforced its strong correlation with hyperinsulinemia, type 2 diabetes, and metabolic syndrome, highlighting the necessity for both dermatologic and systemic evaluation.[10,11] The American Diabetes Association thus recommends thorough metabolic screening when AN is diagnosed, given its role as a clinical marker of potential insulin resistance and cardiovascular risk.[10]

The pathogenesis of AN is closely tied to dysregulated activity of the mammalian target of rapamycin (mTOR), driven by hyperactivation of several tyrosine kinase receptors—insulin-like growth factor receptor (IGFR), endothelial growth factor receptor (EGFR), and fibroblast growth factor receptor 3 (FGFR3).[12,13] These receptors can become overactive in insulin resistance, malignancies, and skeletal dysplasia syndromes, respectively, each leading to upregulated mTOR signaling.[13,14] The resulting mTOR overactivity drives excessive epidermal keratinocyte differentiation, proliferation, and stratification—hallmarks of AN that are consistently observed histologically.[14,15] While lifestyle modifications and treatments targeting underlying conditions like insulin resistance can reduce mTOR activity in non-lesional skin, they often fail to adequately address the persistent mTOR hyperactivation within AN lesions, limiting clinical improvements.[16] Such findings underscore the rationale for topical therapeutic strategies that can directly modulate mTOR activity in lesional skin.

Herein, we report the findings of an investigator developed phase 2 clinical trial investigating the safety and efficacy of sirolimus topical gel 0.2% in patients with AN. This study aimed to determine whether local inhibition of epidermal mTOR activity can lead to clinically significant improvements in AN severity, along with concomitant benefits to patient-reported quality of life.

Study Design

This single-center, prospective, single-arm, uncontrolled 12-week phase 2 pilot study was conducted at New York Harbor Veterans Affairs Brooklyn Campus between March and July 2025. The protocol was approved by the New York Harbor VA Brooklyn Campus Institutional Review Board. The study was conducted in accordance with the Declaration of Helsinki and Good Clinical Practice. All participants provided written informed consent prior to undergoing enrollment.

Patients

Eligible participants were adults, 18 years or older, with a clinical diagnosis of AN with stable AN lesions on the posterior neck who had not used topical or systemic treatments for their AN in the past 30 days. Detailed inclusion and exclusion criteria are listed in Table 1.

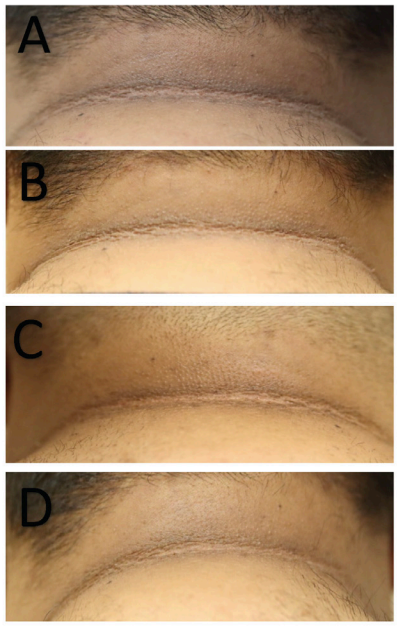
Study Products

Sirolimus topical gel 0.2%, a potent inhibitor of the mammalian target of rapamycin (mTOR) pathway, was applied at an approximate dose of 125 mg per 50 cm^2, with a maximum daily dose of 800 mg. The study medication was transported by participants using cold packs within an insulated bag and stored under refrigeration at home to maintain stability. Sirolimus topical gel 0.2% is FDA-approved for the treatment of facial angiofibromas associated with tuberous sclerosis complex (TSC) in adults and pediatric patients aged 6 years and older.

TABLE 1.

Eligibility Criteria	
Inclusion Criteria	**Exclusion Criteria**
• Men and women ages 18+. • Clinical diagnosis of acanthosis nigricans. • Available and willing to comply with study instructions and attend all study visits. • Able and willing to provide written and verbal informed consent.	• Subject has any skin pathology or condition that could interfere with the evaluation of the test products or requires the use of interfering topical or systemic therapy. • Subject has any condition which, in the investigator's opinion, would make it unsafe for the subject to participate in this research study. • Pregnant, lactating, or is planning to become pregnant during the study. • Subject is currently enrolled in an investigational drug or device study. • Subject has received an investigational drug or has been treated with an investigational device within 30 days prior to the initiation of treatment (baseline). • Subject is unable to communicate or cooperate with the investigator due to language problems, poor mental development, or impaired cerebral function. • Subject has known hypersensitivity or previous allergic reaction to any of the active or inactive components of the test articles. • Subject has the need or plans to be exposed to artificial tanning devices or excessive sunlight during the trial. • Erosions, ulcers, or other skin lesions within or closely neighboring the AN lesion application site. • Hypersensitivity reactions such as anaphylaxis or angioedema to siroli-mus or any component of sirolimus 0.2% topical gel (HYFTOR). • Dyslipidemia (cholesterol level >300mg/dL or >7.75mmol/L, triglyceride level >300 mg/dL or >3.42 mmol/L). • Subject cannot agree to take appropriate contraception for the duration of the study and 12 weeks after the final dose. • Exclusions apply to those who have used the following topical treatments to treat AN: retinoids, hydroquinone, corticosteroids, or other depigment-ing agents within one month prior to the study, or oral retinoids within six months prior to the study, or medications with mTOR inhibitory ac-tion within 12 months prior to the first visit. • Subjects with a malignant tumor.

FIGURE 1A-1D. Clinical improvement in AN lesions over 12 weeks of treatment. Standardized photographs of a participant at baseline (A), week 4 (B), week 8 (C), and week 12 (D).



Treatment

At the first study visit, a board-certified dermatologist evaluated each participant for AN severity. Study participants were instructed to apply sirolimus topical gel 0.2% twice daily (morning and before bedtime) to AN lesions at an approximate dose of 125 mg per 50 cm^2 with a maximum daily dose of 800 mg while avoiding contact with eyes, mouth, and mucous membranes for 12 weeks. Subsequently, participants were seen in the clinic at 4, 8, and 12 weeks after the initiation of treatment for clinical assessments and monitoring of adverse effects.

Efficacy Assessments

Given that changes in the Melanin index (M-index) reflect objective pigmentation shifts, with measurable improvements expected by week 12, assessments were conducted at baseline and at weeks 4, 8, and 12 to evaluate treatment efficacy. The primary endpoint was the change in the M-index from baseline to week 12, measured using the Mexameter MX18 (Courage + Khazaka, Cologne, Germany), a validated narrowband reflectance spectrophotometer. The SkinColorCatch (Delfin Technologies, Kuopio, Finland), a colorimeter-based instrument, was used concurrently to confirm M-index values. Secondary outcome measures included Acanthosis Nigricans Scoring Chart (ANSC) and Investigator Global Evaluation (IGE) scores, assessing pigmentation and textural changes, as well as Patient Global Evaluation (PGE) and Dermatology Life Quality Index (DLQI), which captured patient-reported perceptions of skin appearance and quality of life. Additionally, the Treatment Satisfaction Questionnaire for Medication (TSQM) was administered to evaluate treatment satisfaction, including ease of use and perceived effectiveness.

At each study visit, standardized digital photographs documented clinical progression. Photographs were taken using the TwinFlash RL Clinical camera (Canfield Scientific, Parsippany, NJ). Safety assessments were performed throughout the study, with adverse events recorded at each visit.

Statistical Analysis

Statistical analyses were performed using Microsoft Excel (Microsoft Corporation, Redmond, WA). Data, including quantitative secondary outcomes measures, were analyzed using paired t-tests, comparing baseline and post-treatment values. A *P*-value < 0.05 was considered to be statistically significant.

Adverse Events

Throughout the study, participants were monitored for the occurrence of adverse events (AEs). Participants were advised to document any AEs in a diary and notify the research team of treatment-emergent concerns.

RESULTS

Participants

Five participants were enrolled and received sirolimus topical gel 0.2% to apply at home twice daily for 12 weeks. 60% of patients were female, mostly African American (80%), Hispanic or Latino (20%) and the mean age was 44 years old (range of 33 to 59 years old) (Table 2). Five (100%) participants completed the four study visits per protocol.

Safety and Tolerability

No severe AEs were reported. Mild treatment-related AEs occurred in 1 participant (20%) following initial application of sirolimus topical gel 0.2%. Reported symptoms included application site erythema and dryness. All events resolved without intervention or sequelae.

TABLE 2.

Baseline Demographics of Participants	
Characteristic	**Total (n = 5)**
Age in years, mean ± SD	44.4 ± 10.1
Sex, n (%)	
Female	3 (60%)
Male	2 (40%)
Race and ethnicity, n (%)	
Black or African Ameri-can	4 (80%)
Hispanic or Latino	1 (20%)
Fitzpatrick Skin Types, n (%)	
Type V	3 (60%)
Type VI	2 (40%)

Efficacy

Primary Outcome

Improvement in hyperpigmentation in AN lesions: At 12 weeks following initiation of sirolimus topical gel 0.2%, participants demonstrated a statistically significant reduction in pigmentation of AN lesions. This improvement was objectively measured using the Mexameter device, which showed an average 19.7% ± 4.9% decrease in the M-index from baseline (P=0.0037). Refer to Tables 3–7 for quantitative comparisons across baseline, week 4, week 8, and week 12. Representative photographs demonstrating clinical improvement are shown in Figures 1a-d.

Secondary Outcomes

Improvement in hyperpigmentation and skin texture: Post-treatment improvement in ANSC scores, which evaluates hyperpigmentation and skin texture in AN lesions, demonstrated measurable clinical benefit. From baseline (day 0) to the final visit (week 12), there was a 30.2% mean reduction in ANSC scores (P=0.0011), reflecting a significant improvement in skin quality. Improvement was observed as early as Week 4, with a 19.3% mean reduction compared to baseline. ANSC scores continued to improve from visit 2 (week 4) to visit 3 (week 8), and from visit 3 (week 8) to visit 4 (week 12), with statistically significant differences across timepoints (Table 7).

Investigator Assessed improvement in AN (Investigator Global Evaluation): Investigator-reported outcomes using the Global Evaluation scale demonstrated early and sustained perceived clinical improvement. At week 4, 80% of participants were graded as mild or 25% improvement, while 1 participant (20%) showed no improvement. By week 8, all participants (100%) were at least mild or 25% improvement. These scores were maintained through week 12, with no patients reporting worsening or lack of improvement, indicating consistent subjective benefit throughout the treatment course.

Patient self-reported improvement in AN (Patient Global Evaluation): Patient-reported outcomes demonstrated gradual and consistent perceived clinical improvement. At week 4,

TABLE 3.

Visit 1 (Day 0): Measurements of Melanin and Erythema Using the Mexameter and SkinColorCatch Devices, Including Individual Typology Angle (ITA°) and Acanthosis Nigricans Scoring Chart (ANSC) Scores For All Study Participants

Patient ID	M Index ($\bar{x}$) (Mexameter)	Erythema ($\bar{x}$) (Mexameter)	M Index ($\bar{x}$) (SkinColorCatch)	Erythema ($\bar{x}$) (SkinColorCatch)	ITA°($\bar{x}$) (SkinColorCatch)	ANSC
001	876.0	548.2	871.7	432.3	-46.3	10
002	652.0	485.1	831.0	454.67	-27.0	11
003	641.6	484.0	844.7	432.7	-34.0	9
004	1113.8	395.9	901.7	393.7	-64.3	13
005	1201.9	345.2	940	356	-84	14

TABLE 4.

Visit 2 (Week 4): Measurements of Melanin and Erythema Using the Mexameter and SkinColorCatch Devices, Including Individual Typology Angle (ITA°) and Acanthosis Nigricans Scoring Chart (ANSC) Scores For All Study Participants

Patient ID	M Index ($\bar{x}$) (Mexameter)	Erythema ($\bar{x}$) (Mexameter)	M Index ($\bar{x}$) (SkinColorCatch)	Erythema ($\bar{x}$) (SkinColorCatch)	ITA°($\bar{x}$) (SkinColorCatch)	ANSC
001	771.0	564.6	865.3	438.7	-40.6	7
002	563.0	470.3	806.7	458.3	-27.0	9
003	640.0	529.6	824.67	442.3	-34.7	8
004	938.1	382.0	900.0	395.7	-65.0	10
005	1121.6	344.6	929.3	364.6	-72.6	12

TABLE 5.

Visit 3 (Week 8): Measurements of melanin and Erythema Using The Mexameter and SkinColorCatch Devices, Including Individual Typology Angle (ITA°) and Acanthosis Nigricans Scoring Chart (ANSC) Scores For All Study Participants

Patient ID	M Index ($\bar{x}$) (Mexameter)	Erythema ($\bar{x}$) (Mexameter)	M Index ($\bar{x}$) (SkinColorCatch)	Erythema ($\bar{x}$) (SkinColorCatch)	ITA°($\bar{x}$) (SkinColorCatch)	ANSC
001	767.4	520.1	848.6	450.0	-37.6	6
002	500.3	401.6	803.0	467.6	-27.6	8
003	536.1	523.8	825.0	462.0	-34.0	7
004	864.9	445.7	873.0	422.0	-46.6	9
005	1129.3	392.4	922.6	363.6	-69.6	11

TABLE 6.

Visit 4 (Week 12): Measurements of Melanin and Erythema Using The Mexameter and SkinColorCatch Devices, Including Individual Typology Angle (ITA°) and Acanthosis Nigricans Scoring Chart (ANSC) Scores For All Study Participants						
Patient ID	M Index ($\bar{x}$) (Mexameter)	Erythema ($\bar{x}$) (Mexameter)	M Index ($\bar{x}$) (SkinColorCatch)	Erythema ($\bar{x}$) (SkinColorCatch)	ITA°($\bar{x}$) (SkinColorCatch)	ANSC
001	760.3	470.8	834.6	449.6	-38.3	6
002	485.3	391.9	793.6	465.0	-26.6	7
003	516.0	490.6	818.0	454.3	-36.3	7
004	838.2	440.9	871.6	430.3	-45.0	9
005	1017.2	400.2	913.3	363.3	-68.6	11

TABLE 7.

Aggregate Clinical Outcomes by Timepoint						
Week	M Index ($\bar{x}$) (Mexameter)	Erythema ($\bar{x}$) (Mexameter)	M Index ($\bar{x}$) (SkinColorCatch)	Erythema ($\bar{x}$) (SkinColorCatch)	ITA°($\bar{x}$) (SkinColorCatch)	ANSC
0	897.1	451.7	877.8	413.9	–51.1	11.4
4	806.7*	458.2	865.2*	419.9*	–48.0	9.2*
8	759.6*	456.7	854.4*	433.0*	–43.1	8.2*
12	723.4*	438.9	846.2*	432.5*	–43.0	8.0*

An asterisk (*) denotes statistically significant differences from Week 0 (baseline) based on two-tailed Student's t-tests at $P< 0.05$
Abbreviations: *M Index* = Melanin Index; *ITA°* = Individual Typology Angle (skin color lightness); *ANSC* = Acanthosis Nigricans Scoring Chart

80% of participants reported mild or 25% improvement, while one participant (20%) reported no improvement. By week 8, all participants (100%) reported at least mild or 25% improvement. At week 12, 60% of patients reported moderate or 50% improvement, and 40% maintained mild improvement. No patients reported worsening or lack of improvement at week 12.

Dermatology Life Quality Index score: Significant improvements in quality of life were observed following treatment, as measured by the DLQI. The mean DLQI score decreased from 3.8 ± 2.6 at baseline to 2.0 ± 2.7 post-treatment, indicating a meaningful reduction in the impact of skin disease on daily functioning (P=0.0086). Notably, 60% of participants reported a final DLQI score of 0, reflecting no negative impact of their skin condition on quality of life after completing treatment.

Treatment Satisfaction with Medication: Treatment satisfaction was consistently high among participants. 60% of patients reported being very satisfied with the medication's ability to prevent or treat their AN, and 80% were very or extremely satisfied with the relief of their symptoms. Regarding onset of action, 40% were satisfied and 60% were very or extremely satisfied with how quickly the medication began working. All participants found the medication extremely easy to use, with 100% reporting it was easy, very easy, or extremely easy to apply each time. Similarly, all patients rated the medication as very or extremely convenient to use as instructed. Confidence in the medication was also high, with 80% feeling very confident and 20% extremely confident that it was a good treatment for them. Overall satisfaction was positive, with all patients reporting being satisfied (20%), very satisfied (40%), or extremely satisfied (40%) with the treatment.

DISCUSSION

Our findings demonstrate that sirolimus topical gel 0.2% significantly improves hyperpigmentation and textural changes in AN, supporting its therapeutic potential in a condition with no FDA-approved pharmacologic treatments to date. Sirolimus acts via inhibition of the mammalian target of rapamycin (mTOR) pathway, which regulates keratinocyte proliferation and differentiation, processes that are central to the pathogenesis of AN.[12] The observed efficacy is consistent with prior reports of sirolimus use in related hyperproliferative dermatologic conditions. Topical sirolimus has demonstrated clinical benefit in confluent and reticulated papillomatosis and in epidermal nevi associated with FGFR3 mutations, both of which exhibit pathophysiologic and histologic similarities to AN.[13,17] In patients with facial angiofibromas, a condition characterized by elevated mTOR activity, various concentrations of topical sirolimus have produced significant improvements, with the 0.2% formulation showing the greatest therapeutic effect.[18] Additionally, sirolimus topical gel 0.2% has been successfully used off-label to treat keratosis pilaris rubra faciei, a follicular disorder marked by keratotic papules and erythema. In one case, a 15-year-old patient experienced substantial and sustained improvement following treatment with commercially available sirolimus topical gel 0.2%.[19] These findings are aligned with the outcomes of our study and suggest that topical sirolimus may have broader applicability in treating a spectrum of hyperproliferative and inflammatory dermatoses, including AN.

This investigator developed pilot study is the first clinical trial to assess the safety and efficacy of topical sirolimus for AN. There are currently no published cellular or animal model studies, nor controlled human trials, evaluating this approach. The absence of foundational research further underscores the novelty of this investigation. Our findings represent an important step forward, offering data that can inform the design and powering of future studies.

Participants experienced statistically significant improvement in pigmentation, with a mean 19.7% ± 4.9% reduction in melanin index (M-index) at week 12, as objectively measured using a narrowband spectrophotometer (Mexameter) and a narrowband reflectance colorimeter (SkinColorCatch). Improvements in pigmentation were evident as early as week 4 and continued through week 12. Similarly, the ANSC scores improved by an average of 30.2%, reflecting both pigmentary and textural improvement. These objective findings were reported by both investigator and patient global evaluations, which showed early and sustained improvement throughout the treatment period. Quality of life outcomes were also favorable. The mean DLQI score decreased from 3.8 ± 2.6 at baseline to 2.0 ± 2.7 post-treatment (P=0.0086), and 60% of participants reported a final DLQI score of 0, indicating that the condition no longer had any negative impact on their quality of life after completing treatment. Patient-reported satisfaction was high across all domains of the TSQM, with all participants finding the medication convenient and easy to use, and the majority expressing high levels of satisfaction with its effectiveness and onset of action.

No serious adverse events were reported, and the treatment was well-tolerated. Mild and transient side effects such as dryness and erythema at the application site were observed but resolved without intervention. This favorable safety profile further supports the feasibility of sirolimus topical gel 0.2% as a long-term topical therapy for AN. A major strength of this study is its innovative nature. Conducted in an academic medical center, this trial serves as the first clinical framework for evaluating a targeted, mechanistically driven topical treatment for AN. Limitations include the small sample size and lack of a comparator arm, which restricts generalizability. Additionally, the study was conducted during the late spring and summer months, when increased sun exposure may have influenced pigmentation outcomes despite the use of sunscreen, potentially confounding results. Nonetheless, the consistency of improvement across multiple validated measures, including spectrophotometry, clinical scoring, global assessments, and PROs provides strong evidence of therapeutic effect.

CONCLUSION

Sirolimus topical gel 0.2% demonstrated a favorable safety and efficacy profile in the treatment of AN, with statistically and clinically significant improvements in pigmentation, skin texture, and patient-reported quality of life. Objective biometrics and validated global assessments confirmed early and sustained therapeutic benefit. In the absence of FDA-approved pharmacologic therapies for AN, these findings support the potential utility of topical sirolimus as a targeted intervention. This investigator developed pilot study provides foundational data to inform the design of future randomized controlled trials and phase 3 placebo controlled trials to further characterize its role in evidence-based management of AN.

DISCLOSURES

Kayla Zafar BA, Margaret Kabakova BS, and David Bitterman MD do not have any relevant conflict of interests. Jared Jagdeo MD, MS is the investigator for this investigator-initiated study. SUNY Downstate Medical Center was the recipient of the grant funding.

Funding sources: Nobelpharma America, LLC

REFERENCES

1. Kong AS, Williams RL, Smith M, et al. Acanthosis nigricans and diabetes risk factors: prevalence in young persons seen in southwestern US primary care practices. *Ann Fam Med.* 2007;5(3):202-208. doi:10.1370/afm.678
2. Patel NU, Roach C, Alinia H, et al. Current treatment options for acanthosis nigricans. *Clin Cosmet Investig Dermatol.* 2018;11:407-413. doi:10.2147/ccid.S137527
3. Stuart CA, Gilkison CR, Smith MM, et al. Acanthosis nigricans as a risk factor for non-insulin dependent diabetes mellitus. *Clin Pediatr (Phila).* 1998;37(2):73-79. doi:10.1177/000992289803700203
4. Kong AS, Williams RL, Rhyne R, et al. Acanthosis nigricans: high prevalence and association with diabetes in a prac-tice-based research network consortium--a PRImary care Multi-Ethnic network (PRIME Net) study. *J Am Board Fam Med.* 2010;23(4):476-485. doi:10.3122/jabfm.2010.04.090221
5. Pirgon Ö, Sandal G, Gökçen C, et al. Social anxiety, depression and self-esteem in obese adolescent girls with acan-thosis nigricans. *J Clin Res Pediatr Endocrinol.* 2015;7(1):63-68. doi:10.4274/jcrpe.1515
6. Huang Y, Chen J, Yang J, et al. Evaluation of depressive symptoms in obese patients with or without acanthosis nigri-cans. *Hormones (Athens).* 2015;14(3):417-424. doi:10.14310/horm.2002.1575
7. Quinonez R, Woolery-Lloyd H, Williams K. The obesity epidemic and the rise of acanthosis nigricans: a case for life-style medicine. *J Drugs Dermatol.* 2020;19(7).
8. Arellano J, Iglesias P, Suarez C, et al. Malignant acanthosis nigricans as a paraneoplastic manifestation of metastatic breast cancer. *Int J Womens Dermatol.* 2019;5(3):183-186. doi:10.1016/j.ijwd.2019.03.002
9. Hughes EK, Rawla P. Acanthosis nigricans. In: *StatPearls.* StatPearls Publishing; 2025. Accessed March 26, 2025. https://www.ncbi.nlm.nih.gov/books/NBK431057/
10. ElSayed NA, Aleppo G, Aroda VR, et al. Classification and diagnosis of diabetes: standards of care in diabetes—2023. *Diabetes Care.* 2022;46(Supplement_1):S19-S40. doi:10.2337/dc23-S002
11. Phiske MM. An approach to acanthosis nigricans. *Indian Dermatol Online J.* 2014;5(3):239-249. doi:10.4103/2229-5178.137765
12. Eggiman E, Feldman SR. The underlying pathogenesis of obesity-associated acanthosis nigricans: a literature review. *Discov Med.* 2024;1(1):19. doi:10.1007/s44337-024-00017-7
13. Dodds M, Maguiness S. Topical sirolimus therapy for epidermal nevus with features of acanthosis nigricans. *Pediatr Dermatol.* 2019;36(4):554-555. doi:10.1111/pde.13833
14. Karagianni F, Pavlidis A, Malakou LS, et al. Predominant role of mtor signaling in skin diseases with therapeutic po-tential. *Int J Mol Sci.* 2022;23(3). doi:10.3390/ijms23031693
15. Ding X, Bloch W, Iden S, et al. mTORC1 and mTORC2 regulate skin morphogenesis and epidermal barrier formation. *Nat Commun.* 2016;7:13226. doi:10.1038/ncomms13226
16. Romo A, Benavides S. Treatment options in insulin resistance obesity-related acanthosis nigricans. *Ann Pharma-cother.* 2008;42(7):1090-1094. doi:10.1345/aph.1K446
17. Kurtyka DJ, Burke KT, DeKlotz CMC. Use of topical sirolimus (rapamycin) for treating confluent and reticulated pap-illomatosis. *JAMA Dermatol.* 2021;157(1):121-123. doi:10.1001/jamadermatol.2020.4083
18. Wataya-Kaneda M, Nakamura A, Tanaka M, et al. Efficacy and safety of topical sirolimus therapy for facial angiofi-bromas in the tuberous sclerosis complex: a randomized clinical trial. *JAMA Dermatol.* 2017;153(1):39-48. doi:10.1001/jamadermatol.2016.3545
19. Snow KP, Ong SK, Siegfried E. Off-label use of commercially available topical sirolimus for keratosis pilaris rubra fa-ciei. *JAAD Case Rep.* 2025;57:31-33. doi:10.1016/j.jdcr.2024.10.031

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