

Drug Policy:

Topical and Intralesional Therapies Use in Non-Melanoma Skin Cancers (NMSC) and Primary Cutaneous Lymphomas

POLICY NUMBER UM ONC_1445	SUBJECT Topical and Intralesional Therapies Use in Non-Melanoma Skin Cancers (NMSC) and Primary Cutaneous Lymphomas		DEPT/PROGRAM UM Dept	PAGE 1 of 10
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PRIMARY BUSINESS OWNER: UM		COMMITTEE/BOARD APPROVAL Utilization Management Committee		
NCQA STANDARDS UM 2		ADDITIONAL AREAS OF IMPACT		
CMS REQUIREMENTS	STATE/FEDERAL REQUIREMENTS		APPLICABLE LINES OF BUSINESS Commercial, Exchange, Medicaid	

I. PURPOSE

To define and describe the accepted indications for topical and intralesional therapies usage in the treatment of early stage NMSC and primary cutaneous lymphomas, including FDA approved indications, and off-label indications.

Evolent is responsible for processing all medication requests from network ordering providers. Medications not authorized by Evolent may be deemed as not approvable and therefore not reimbursable.

The use of these drugs must be supported by one of the following: FDA approved product labeling, CMS-approved compendia, National Comprehensive Cancer Network (NCCN), American Academy of Dermatology, American Society for Dermatologic Surgery Association, American Society for Moh's Surgery, or peer-reviewed literature that meets the requirements of the CMS Medicare Benefit Policy Manual Chapter 15.

II. DEFINITIONS

- A. Non-Melanoma Skin Cancers (NMSC):** refers to all the types of cancer that occur in the skin that are not melanoma with the most common types being basal cell carcinoma and squamous cell carcinoma.
- B. Non-Cancerous Skin Lesions:** may include primary cutaneous B-cell or T-cell lymphoma, a type of skin lymphoma that may result in skin lesions, are slow growing, limited, and localized. Although the skin is involved, primary cutaneous lymphomas can spread to the lymph nodes,

blood, or other organs such as the spleen, liver, or lungs. Skin directed therapies for the treatment of primary cutaneous lymphomas include topical therapy, local radiation, and phototherapy.

- C. Basal cell carcinomas (BCC):** is a common type of skin cancer arising from the basal layer of the epidermis which may occur on the face or the trunk. BCC is usually slow-growing and rarely metastasize (< 1%), but they do cause localized tissue destruction, compromised function, and cosmetic disfigurement if left untreated. The most common histologic forms of BCC are nodular, superficial, and morpheaform subtypes. Topical therapies are more effective in the treatment superficial BCC, a less aggressive type of BCC than nodular/morpheaform BCC, due to a lack of dermal tumor invasion and higher histologic clearance rates in this subtype.
- D. Cutaneous squamous cell carcinoma (cSCC):** is the second most common skin cancer arising from epidermal keratinocytes and may develop on any skin surface including the head, trunk, extremities, oral mucosa, periungual skin, and anogenital areas. Although rarely metastatic, cSCC has a greater potential to recur and metastasize and can cause local destruction and disfigurement that can extend to areas of soft tissue, cartilage, and bone. There are two subtypes of cSCC: 1. Bowen's disease, an in situ cSCC, which is similar to actinic keratosis (AK), a premalignant lesion and 2. Non-Bowen disease type, also referred to as invasive cSCC. Clinical variants of invasive cSCC may include: spindle cell (sarcomatoid), acantholytic (adenoid), clear cell, adenosquamous (mucin-producing), desmoplastic, and single-cell cSCC.
- E. Risk Factors for BCC/cSCC:** include UV light exposure, exposure to ionizing radiation, chronic immunosuppression (e.g., from organ transplant, from glucocorticoid use, from immunosuppressive diseases), viral infections (e.g. HPV infection), exposure to chemical carcinogens (e.g., arsenic), and genetics (e.g., Xeroderma pigmentosum).
- F. Risk Factors for Recurrence of BCC/cSCC:** increased size of lesions, anatomic location of lesions, poorly defined tumor borders, presence of immunosuppression, recurrent disease (versus primary disease), site/history of prior RT, aggressive growth sclerosing pattern (versus nodular or superficial), histologic subtypes, thickness or level of invasion, and presence of perineural involvement. *Please refer to Attachment A for BCC and cSCC risk for recurrence factors.*
- G. Preventive measures to reduce the development of BCC/cSCC:** minimize exposure to UV radiation and use of sunscreen, use of acitretin/isotretinoin (both are retinoid treatment for premalignant SCC lesion), and nicotinamide treatment.
- H. Treatment of BCC/cSCC:** the goal of local treatment is cure and the best chance for cure is with the most effective primary therapy and surgery affords the highest cure rate. The treatment modalities include the following, in order of descending cure rates: surgery (e.g., Moh's micrographic surgery, surgical excision, curettage and electrodesiccation), radiation therapy, and superficial therapies (e.g., photodynamic therapy, cryotherapy, topical imiquimod, topical fluorouracil). *Please refer to Attachment B for the management of BCC and cSCC by Risk Factors.*
- I. Follow-up Monitoring For Primary and Recurrent Local/Regional BCC/cSCC [surveillance using CT or MRI as clinically indicated for deeply invasive lesions]:**
 - 1. BCC: every 6-12 months for 5 years, then annually for life.
 - 2. Local cSCC: every 3-12 months for 2 years, then every 6-12 months for another 3 years, then annually for life.

3. Regional cSCC: every 1-3 months for 2 years, every 2-4 months for another 1 year, every 4-6 months for another 3 years, then every 6-12 months for life.

J. Follow-up Monitoring For Primary Cutaneous Lymphomas: Routine imaging tests are not recommended in indolent or localized cutaneous lymphomas without systemic involvement. PET/CT Imaging tests are recommended, when clinically indicated, for extracutaneous or progressive disease.

III. INDICATIONS FOR USE/INCLUSION CRITERIA

A. Continuation requests for a not-approvable medication shall be exempt from this Evolent policy provided:

1. The requested medication was used within the last year, **AND**
2. The member has not experienced disease progression and/or no intolerance to the requested medication, **AND**
3. Additional medication(s) are not being added to the continuation request.

B. Basal Cell Carcinoma (BCC)

1. **NOTE:** This policy covers topical therapies for BCC. For systemic therapy used in the treatment of advanced high risk, recurrent unresectable, or metastatic BCC, please refer to the following drug policies:
 - a. UM ONC_1222 Erivedge (vismodegib)
 - b. UM ONC_1312 Odomzo (sonidegib)
 - c. UM ONC_1089 Libtayo (cemiplimab-rwlc)
2. The following may be used as monotherapy, or as combination therapy following the failure of monotherapy, for the topical/intralesional treatment of primary or recurrent low risk BCC, in members who are not candidates for surgery and/or radiation therapy:
 - a. Levulan Kerastick (aminolevulinic acid hydrochloride): for use as photodynamic therapy for superficial BCC.
 - b. Carac, Efudex, or Fluoroplex (topical fluorouracil): for use as topical therapy for superficial BCC.
 - c. Aldara (topical imiquimod): for use as topical therapy for superficial BCC.
 - d. The use of intralesional therapies is recommended as palliative treatment of low risk superficial BCC, when there are no other alternative treatments, may include the following: fluorouracil (5FU), methotrexate (MTX), bleomycin, and interferon (IFN alfa 2a/2b, beta, and gamma). Unlike topical therapies, this recommendation is derived from small retrospective case series and are not supported by robust study design, study size, and long term follow up and cure rate data. *Please refer to Attachment C for details on dose and administration.*

C. Cutaneous Squamous Cell Carcinoma (cSCC)

1. **NOTE:** This policy covers topical therapies for cSCC. For systemic therapy used in the treatment of advanced high risk, recurrent, or metastatic cSCC, please refer to the following drug policies:
 - a. UM ONC_1089 Libtayo (cemiplimab-rwlc)
 - b. UM ONC_1263 Keytruda (pembrolizumab)
2. Other systemic therapies used for higher risk disease/residual positive margins, as monotherapy or in combination with chemotherapy +/- radiation therapy, may include: capecitabine, carboplatin, cetuximab, cisplatin, and paclitaxel.

3. The following may be used as monotherapy, or as combination therapy following the failure of monotherapy, for the topical/intralesional treatment of primary or recurrent low risk cSCC in members who are not candidates for surgery and/or radiation therapy:
 - a. Levulan Kerastick (aminolevulinic acid hydrochloride): for use as photodynamic therapy for superficial cSCC.
 - b. Carac, Efudex, or Fluoroplex (topical fluorouracil): for use as topical therapy for actinic keratoses OR for cSCC in situ (Bowen's disease).
 - c. Aldara (topical imiquimod): for use as topical therapy for actinic keratoses OR for cSCC in situ (Bowen's disease).
 - d. Klisyri (topical tirbanibulin): topical therapy for actinic keratoses.
 - e. The use of intralesional therapies as palliative treatment of low risk cSCC, when all alternate treatment modalities have failed or are not possible, may include the following: fluorouracil (5FU), methotrexate (MTX), bleomycin, and interferon (IFN alfa 2a/2b, beta, and gamma). Unlike topical therapies, this recommendation is derived from small retrospective case series and are not supported by robust study design, study size, and long term follow up and cure rate data. *Please refer to attachment C for details on dose and administration.*

D. Primary Cutaneous Lymphomas

1. NOTE: This policy covers topical therapies for primary cutaneous lymphoma, stage IA to IIA T-cell lymphoma and stage T1-3 -B-cell lymphoma. For systemic therapy used in the primary treatment of Stage IIB-IV T-cell lymphoma, extracutaneous (N1 or M1 disease) B-cell lymphoma, or refractory disease, please refer to the following drug policies:
 - a. UM ONC_1203 Adcetris (brentiximab)
 - b. UM ONC_1227 Zolinza (vorinostat)
 - c. UM ONC_1230 Istodax (romidepsin)
 - d. UM ONC_1260 Beleodaq (belinosat)
 - e. UM ONC_1344 Poteligeo (mogamulizumab-kpkc)
 - f. UM ONC_1384 Targretin (oral bexarotene)
2. The following topical treatments may be used as monotherapy, or as combination therapy following the failure of monotherapy, for primary cutaneous lymphomas, with or without local phototherapy [e.g., PUVA, total skin electron beam therapy (TSEBT), or involved-site radiation therapy (ISRT)]:
 - a. For members with primary cutaneous T-cell lymphoma (including mycosis fungoides, Sezary syndrome, primary cutaneous CD30+ T-cell lymphoproliferative disorders):
 - i. Valchlor (topical mechlorethamine)
 - ii. Targretin (topical bexarotene)
 - b. For members with primary cutaneous B-cell lymphoma (including marginal zone or follicle center lymphoma):
 - i. Valchlor (topical mechlorethamine)
 - ii. Targretin (topical bexarotene)

IV. EXCLUSION CRITERIA

- A. Use of topical or intralesional therapies for any of the following in NMSC (BCC/cSCC):
 1. For tumor greater than or equal to 2cm in size.
 2. For the primary treatment of high-risk or recurrent unresectable NMSC (BCC/cSCC).

3. For nodular and morphea-form BCC. This exclusion is based on the lack of data in these subtypes of BCC, reduced cure rates when compared to superficial BCC, including lack of long term follow up greater than 2 years.
- B. Dosing exceeds the available topical package size per single treatment: Levulan Kerastick 20% solution (1 applicator), Carac 0.5% cream (30 gm), Efidex 5% cream (40 gm), Fluoroplex 1% cream (30 gm), Aldara 5% cream (12 pack), Targretin 1% gel (60 gm), and Valchlor 0.016% gel (60 gm), Klisyri 1% (1 applicator),
 - C. Dosing exceeds the total intralesional dose per single treatment (*see Attachment C*).
 - D. Investigational use of topical and intralesional therapies with an off-label indication that is not sufficient in evidence or is not generally accepted by the medical community. Sufficient evidence that is not supported by CMS recognized compendia or acceptable peer reviewed literature is defined as any of the following:
 1. Whether the clinical characteristics of the patient and the cancer are adequately represented in the published evidence.
 2. Whether the administered chemotherapy/biologic therapy/immune therapy/targeted therapy/other oncologic therapy regimen is adequately represented in the published evidence.
 3. Whether the reported study outcomes represent clinically meaningful outcomes experienced by patients. Generally, the definition of Clinically Meaningful outcomes are those recommended by ASCO, e.g., Hazard Ratio of less than 0.80 and the recommended survival benefit for OS and PFS should be at least 3 months.
 4. Whether the experimental design, in light of the drugs and conditions under investigation, is appropriate to address the investigative question. (For example, in some clinical studies, it may be unnecessary or not feasible to use randomization, double blind trials, placebos, or crossover).
 5. That non-randomized clinical trials with a significant number of subjects may be a basis for supportive clinical evidence for determining accepted uses of drugs.
 6. That case reports are generally considered uncontrolled and anecdotal information and do not provide adequate supportive clinical evidence for determining accepted uses of drugs.
 7. That abstracts (including meeting abstracts) without the full article from the approved peer-reviewed journals lack supporting clinical evidence for determining accepted uses of drugs.

V. MEDICATION MANAGEMENT

- A. Please refer to the FDA label/package insert for details regarding these topics.

VI. APPROVAL AUTHORITY

- A. Review – Utilization Management Department
- B. Final Approval – Utilization Management Committee

VII. ATTACHMENTS

- A. Attachment A: BCC and cSCC Risk Factors for Recurrence
- B. Attachment B: Management of BCC and cSCC
- C. Attachment C: Intralesional Therapies

VIII. REFERENCES

- A. Levulan Kerastick, Carac, Efudex, Fluoroplex, Aldara, Picato, Targretin, Valchlor, Tazorac prescribing information accessed on March 13, 2023.
- B. Work Group; Invited Reviewers, Kim JYS, Kozlow JH, Mittal B, Moyer J, Olencki T, Rodgers P. Guidelines of care for the management of basal cell carcinoma. *J Am Acad Dermatol*. 2018 Mar;78(3):540-559.
- C. Work Group; Invited Reviewers, Kim JYS, Kozlow JH, Mittal B, Moyer J, Olencki T, Rodgers P. Guidelines of care for the management of cutaneous squamous cell carcinoma. *J Am Acad Dermatol*. 2018 Mar;78(3):560-578.
- D. Kauvar AN, Cronin T Jr, Roenigk R, Hruza G, Bennett R; American Society for Dermatologic Surgery. Consensus for nonmelanoma skin cancer treatment: basal cell carcinoma, including a cost analysis of treatment methods. *Dermatol Surg*. 2015 May;41(5):550-71.
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- J. National Comprehensive Cancer Network. Cancer Guidelines and Drugs and Biologics Compendium 2023.
- K. Clinical Pharmacology Elsevier Gold Standard 2023.
- L. Micromedex® Healthcare Series: Micromedex Drugdex Ann Arbor, Michigan 2023.
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- N. Ellis LM, et al. American Society of Clinical Oncology perspective: Raising the bar for clinical trials by defining clinically meaningful outcomes. *J Clin Oncol*. 2014 Apr 20;32(12):1277-80.
- O. Medicare Benefit Policy Manual Chapter 15 Covered Medical and Other Health Services: <https://www.cms.gov/Regulations-and-Guidance/Guidance/Manuals/Downloads/bp102c15.pdf>.

Attachment A: BCC Risk Factors for Recurrence

STRATIFICATION TO DETERMINE TREATMENT OPTIONS FOR LOCAL BCC BASED ON RISK FACTORS FOR RECURRENCE^a

Risk Group	Low Risk	High Risk
Treatment options	BCC-2	BCC-3
H&P		
Location/size	Trunk, extremities <2 cm	Trunk, extremities ≥2 cm
		Head, neck, hands, feet, pretibia, and anogenital (any size) ^c
Borders	Well-defined	Poorly defined
Primary vs. recurrent	Primary	Recurrent
Immunosuppression	(-)	(+)
Site of prior RT	(-)	(+)
Pathology (BCC-A)		
Subtype	Nodular, superficial ^b	Aggressive growth pattern ^d
Perineural involvement	(-)	(+)

National Comprehensive Cancer Network Cancer Guidelines (version: 1.2023): Basal Cell Skin Cancer

cSCC Risk Factors for Recurrence

STRATIFICATION TO DETERMINE TREATMENT OPTIONS AND FOLLOW-UP FOR LOCAL CSCC BASED ON RISK FACTORS FOR LOCAL RECURRENCE, METASTASES, OR DEATH FROM DISEASE

Risk Group ^a	Low Risk	High Risk	Very High Risk
Treatment options	SCC-2	SCC-3	SCC-3
H&P			
Location/size ^b	Trunk, extremities ≤2 cm	Trunk, extremities >2 cm – ≤4 cm	>4 cm (any location)
		Head, neck, hands, feet, pretibia, and anogenital (any size) ^e	
Clinical extent	Well-defined	Poorly defined	
Primary vs. recurrent	Primary	Recurrent	
Immunosuppression	(-)	(+)	
Site of prior RT or chronic inflammatory process	(-)	(+)	
Rapidly growing tumor	(-)	(+)	
Neurologic symptoms	(-)	(+)	
Pathology (SCC-A)			
Degree of differentiation	Well or moderately differentiated		Poor differentiation
Histologic features: Acantholytic (adenoid), adenosquamous (showing mucin production), or metaplastic (carcinosarcomatous) subtypes	(-)	(+)	Desmoplastic SCC
Depth ^{c,d} : Thickness or level of invasion	<2 mm thick and no invasion beyond subcutaneous fat	2–6 mm depth	>6 mm or invasion beyond subcutaneous fat
Perineural involvement	(-)	(+)	Tumor cells within the nerve sheath of a nerve lying deeper than the dermis or measuring ≥0.1 mm
Lymphatic or vascular involvement	(-)	(-)	(+)

National Comprehensive Cancer Network Cancer Guidelines (version: 1. 2023): Squamous Cell Skin Cancer

Attachment B: Management of BCC and cSCC

Low risk BCC	Curettage and electrodesiccation OR Surgical or shave excision Excision with postoperative margin assessment OR Topical therapy (imiquimod, topical 5-fluorouracil, photodynamic therapy, or cryotherapy) Radiation therapy*
High risk BCC	Excision with postoperative margin assessment OR Mohs or other forms of f peripheral and deep en face margin assessment (PDEMA) OR Radiation therapy/systemic therapy (vismodegib, sonidegib, cemiplimab)*
Low risk cSCC	Curettage and electrodesiccation or shave excision OR Excision with postoperative margin assessment OR Mohs or other forms of f peripheral and deep en face margin assessment (PDEMA) OR Radiation therapy*
High risk/Very High Risk cSCC	Excision with postoperative margin assessment OR Mohs or other forms of f peripheral and deep en face margin assessment (PDEMA) OR Radiation therapy* +/- systemic therapy OR Systemic therapy if curative RT not feasible
cSCC with palpable LN	FNA/Core Biopsy – if LN is positive- excision of primary tumor and regional LN dissection

*RT is reserved for the following: 1. Non-surgical candidates, 2. Patients older than 60 years because of concern with long term complications, or 3. For extensive perineural involvement or high risk features, adjuvant RT may be considered. RT is contraindicated in genetic conditions (e.g., basal cell nevus syndrome) or relatively contraindicated in patients with connective tissue disorder (e.g., scleroderma). Re-irradiation should not be performed for recurrent disease within a prior radiation field.

Attachment C: Intralesional Therapies

TABLE 4. Efficacy of Intralesional 5-Fluorouracil, Methotrexate, and Bleomycin in the Treatment of Non-Melanoma Skin Cancer (NMSC). All Uses are Off-Label					
Drug	NMSC Subtype	Study	Mean Total Dose per Tumor (mg)	Mean Number of Treatments per Tumor	Clearance Rate, % (Lesions Cleared/Lesions Treated)
5-fluorouracil	BCC	Avant ³⁶	NR	NR (Range: 4–14)	95 (20/21)
		Kurtis ³⁷	612.5	5.5	100 (2/2)
		Aggregate	612.5	5.5	96 (22/23)
	KA	Klein ³⁸	86.75	20	100 (2/2)
		Kurtis ³⁷	354	8.3	100 (3/3)
		Goette ³⁹	NR	3	98 (40/41)
		Parker ⁴⁰	360	3.8	100 (5/5)
Methotrexate	KA	Aggregate	304	4.1	98 (50/51)
		Melton ⁴¹	21.9	1.7	100 (9/9)
		Cuesta-Romero ⁴²	41.7	2.7	100 (6/6)
		Annest ⁴³	38.2	2	83 (15/18)
		Aggregate	34.3	2	91 (30/33)
Bleomycin	BCC	Mishima ⁴⁴	NR	NR	100 (3/3)
	KA	Sayama ⁴⁵	0.38	1.5	100 (6/6)

BCC, basal cell carcinoma; KA, keratoacanthoma; NR, not reported; SCC, squamous cell carcinoma.

TABLE 5. Efficacy of Interferon Alfa in the Treatment of Non-Melanoma Skin Cancer (NMSC). All Uses are Off-Label					
Drug	NMSC Subtype	Study	Mean Total Dose per Tumor (mU)	Mean Number of Treatments per Tumor	Clearance Rate, % (Lesions Cleared/Lesions Treated)
Interferon alfa-2	Superficial BCC	Greenway ⁴⁶	13.5	9	100 (5/5)
		Wickramasinghe ⁴⁷	8.1	9	0 (0/1)
		Aggregate	12.6	9	83 (5/6)
	BCC	Greenway ⁴⁶	13.5	9	100 (5/5)
		Wickramasinghe ⁴⁷	8.1	9	10 (1/10)
		Aggregate	9.9	9	40 (6/15)
	KA	Wickramasinghe ⁴⁷	8.1	9	100 (1/1)
SCC		Wickramasinghe ⁴⁷	8.1	9	100 (3/3)
Interferon alfa-2a	Superficial BCC	Grob ⁴⁸	74.6	23	100 (1/1)
		Dogan ⁴⁹	36 or 54	12	50 (1/2)
		Alpsoy ⁵¹	15 or 30	10	0 (0/1)
	BCC	Bostanci ⁵²	13.5 or 27	9	29 (2/7)
		Aggregate	UC	10.8	36 (4/11)
		Grob ⁴⁸	74.6	23	100 (7/7)
		Dogan ⁴⁹	36 or 54	12	91 (10/11)
		LeGrice ⁵⁰	13.5	9	73 (8/11)
		Alpsoy ⁵¹	15 or 30	10	71 (10/14)
		Bostanci ⁵²	13.5 or 27	9	69 (9/13)
	KA	Aggregate	UC	11.6	79 (44/56)
		Grob ⁵³	57	12	83 (5/6)
		Superficial BCC	Cornell ⁵⁴	13.5	9
Interferon alfa-2b	Superficial BCC	Edwards ⁵⁵	10	1	44 (7/16)
			30	3	75 (12/16)

TABLE 5. continued

Drug	NMSC Subtype	Study	Mean Total Dose per Tumor (mU)	Mean Number of Treatments per Tumor	Clearance Rate, % (Lesions Cleared/Lesions Treated)
		Mozzanica ⁵⁶	13.5	9	50 (2/4)
		Thestrup-Pedersen ⁵⁷	13.5	9	75 (6/8)
		Boneschi ⁵⁸	13.5	9	64 (9/13)
		Healsmith ⁵⁹	13.5	9	100 (1/1)
		Pizarro ⁶⁰	13.5	9	80 (4/5)
		Chimenti ⁶¹	NR	NR	62 (16/26)
		Alpsoy ⁵¹	15 or 30	10	50 (1/2)
		Tucker ⁶²	13.5	9	100 (44/44)
	Aggregate	UC	7.7	79.2 (152/192)	
	BCC	Cornell ⁵⁴	13.5	9	83 (55/66)
		Edwards ⁵⁵	10	1	59 (10/17)
			30	3	75 (12/16)
		Mozzanica ⁵⁶	13.5	9	0 (0/2)
		Thestrup-Pedersen ⁵⁷	13.5	9	0 (0/2)
		Boneschi ⁵⁸	13.5	9	38 (5/13)
		Healsmith ⁵⁹	13.5	9	56 (5/9)
		Stenquist ⁶³	13.5	9	27 (4/15)
		Pizarro ⁶⁰	13.5	9	5 (15/20)
		Chimenti ⁶¹	NR	NR	68 (78/114)
		Alpsoy ⁵¹	15 or 30	10	69 (9/13)
		Kim ⁶⁴	13.5	9	100 (5/5)
		Tucker ⁶²	13.5	9	94 (51/54)
	Aggregate	UC	7.9	72 (250/346)	
	KA	Oh ⁶⁵	15	5	100 (4/4)
	SCC in situ	Edwards ⁶⁶	13.5	9	86 (6/7)
		Kim ⁶⁴	22	10	100 (2/2)
		Aggregate	15.4	9.2	89 (8/9)
	SCC	Edwards ⁶⁶	13.5	9	89 (24/27)
		Kim ⁶⁴	22	10	100 (1/1)
		Aggregate	13.8	9	89 (25/28)

BCC, basal cell carcinoma; KA, keratoacanthoma; NR, not reported; SCC, squamous cell carcinoma; UC, unable to calculate.

TABLE 6. Efficacy of Interferon Beta and Gamma in the Treatment of Non-Melanoma Skin Cancer (NMSC). All Uses are Off-Label

Drug	NMSC Subtype	Study	Mean Total Dose per Tumor (mU)	Mean Number of Treatments per Tumor	Clearance Rate, % (Lesions Cleared/Lesions Treated)
Interferon beta	BCC	Kowalick ⁶⁷	7.7	6.6	51 (35/69)
		Kowalick ⁶⁸	9	9	64 (85/133)
		Aggregate	8.6	8.2	59 (120/202)
Interferon gamma	Superficial BCC	Edwards ⁶⁹	1.8	9	14 (1/7)
			9	9	50 (4/8)
		Aggregate	5.6	9	33 (5/15)
	BCC	Tank ⁷⁰	1.6	8	0 (0/7)
		Edwards ⁶⁹	1.8	9	0 (0/8)
			9	9	50 (3/6)
		Aggregate	3.8	8.7	14 (3/21)

BCC, basal cell carcinoma; NR, not reported; UC, unable to calculate.

Chitwood K, Etzkorn J, Cohen G. Topical and intralesional treatment of nonmelanoma skin cancer: efficacy and cost comparisons. *Dermatol Surg.* 2013 Sep;39(9):1306-16.