Evolent Clinical Guideline 3068 for Topical and Intralesional Therapies Use in Non-Melanoma Skin Cancers (NMSC) and Primary Cutaneous Lymphomas

Guideline Number: Evolent_CG_3068	**Applicable Codes**	
"Evolent" refers to Evolent Health LLC and Evolent Specialty Services, Inc. 		
Original Date: September 2021	**Last Revised Date:** April 2025	**Implementation Date:** April 2025

TABLE OF CONTENTS

STATEMENT

Purpose

To define and describe the accepted indications for topical and intralesional therapies usage in the treatment of cancer, 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 this drug must be supported by one of the following: FDA approved product labeling, CMS-approved compendia, National Comprehensive Cancer Network (NCCN), American Society of Clinical Oncology (ASCO) clinical guidelines, or peer-reviewed literature that meets the requirements of the CMS Medicare Benefit Policy Manual Chapter 15.

DEFINITIONS

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.

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.

Basal Cell Carcinomas (BCC)

- 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.

Cutaneous Squamous Cell Carcinoma (cSCC)

- 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.

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).

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.*

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.

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.*

Follow-up Monitoring For Primary and Recurrent Local/Regional BCC/cSCC [surveillance using CT or MRI as clinically indicated for deeply invasive lesions]

- BCC: every 6-12 months for 5 years, then annually for life.
- Local cSCC: every 3-12 months for 2 years, then every 6-12 months for another 3 years, then annually for life.
- 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.

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.

INDICATIONS

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

- The member has not experienced disease progression on the requested medication AND
- The requested medication was used within the last year without a lapse of more than 30 days of having an active authorization AND
- Additional medication(s) are not being added to the continuation request.

Basal Cell Carcinoma (BCC)

- 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:
  - UM ONC_1222 Erivedge (vismodegib)
  - ECG 3060 Odomzo (sonidegib)
  - ECG 3013 Libtayo (cemiplimab-rwlc)
- 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:
  - Levulan Kerastick (aminolevulinic acid hydrochloride): for use as photodynamic therapy for superficial BCC.
  - Carac, Efudex, or Fluoroplex (topical fluorouracil): for use as topical therapy for superficial BCC.
  - Aldara (topical imiquimod): for use as topical therapy for superficial BCC.
  - 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.*

Cutaneous Squamous Cell Carcinoma (cSCC)

- 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:
  - ECG 3013 Libtayo (cemiplimab-rwlc)
  - UM ONC_1263 Keytruda (pembrolizumab)
- 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.
- 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:

- Levulan Kerastick (aminolevulinic acid hydrochloride): for use as photodynamic therapy for superficial cSCC.
- Carac, Efudex, or Fluoroplex (topical fluorouracil): for use as topical therapy for actinic keratoses OR for cSCC in situ (Bowen's disease).
- Aldara (topical imiquimod): for use as topical therapy for actinic keratoses OR for cSCC in situ (Bowen's disease).
- Klisyri (topical tirbanibulin): topical therapy for actinic keratoses.
- 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.*

Primary Cutaneous Lymphomas

- 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:
  - ECG 3031 Adcetris (brentiximab)
  - UM ONC_1227 Zolinza (vorinostat)
  - UM ONC_1230 Istodax (romidepsin)
  - UM ONC_1260 Beleodaq (belinosat)
  - UM ONC_1344 Poteligeo (mogamulizumab-kpkc)
  - UM ONC_1384 Targretin (oral bexarotene)
- 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)]:
  - For members with primary cutaneous T-cell lymphoma (including mycosis fungoides, Sezary syndrome, primary cutaneous CD30+ T-cell lymphoproliferative disorders):
    - Valchlor (topical mechlorethamine)
    - Targretin (topical bexarotene)
  - For members with primary cutaneous B-cell lymphoma (including marginal zone or follicle center lymphoma):
    - Valchlor (topical mechlorethamine)
    - Targretin (topical bexarotene)

CONTRAINDICATIONS/WARNINGS

- Contraindications
  - Levulan Kerastick (aminolevulinic acid hydrochloride)
    - Hypersensitivity to aminolevulinic acid or any component of the formulation
    - Known allergy/hypersensitivity to porphyrins
    - Known porphyria
    - Cutaneous photosensitivity at wavelengths of 400 to 450 nm
  - Carac, Efudex, or Fluoroplex (topical fluorouracil)
    - Hypersensitivity to fluorouracil or any component of the formulation
    - Dihydropyrimidine dehydrogenase (DPD) enzyme deficiency
    - Patients who are or may become pregnant
  - Valchlor (topical mechlorethamine)
    - Known severe hypersensitivity to mechlorethamine or any component of the formulation
  - Targretin (topical bexarotene)
    - Known hypersensitivity to bexarotene or any component of the formulation
    - Pregnancy

EXCLUSION CRITERIA

- Use of topical or intralesional therapies for any of the following in NMSC (BCC/cSCC):
  - For tumor greater than or equal to 2cm in size.
  - For the primary treatment of high-risk or recurrent unresectable NMSC (BCC/cSCC).
  - 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.
- Dosing exceeds the available topical package size per single treatment: Levulan Kerastick 20% solution (1 applicator), Carac 0.5% cream (30 gm), Efudex 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),
- Dosing exceeds the total intralesional dose per single treatment (*see Attachment C*).
- 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:
  - Whether the clinical characteristics of the patient and the cancer are adequately represented in the published evidence.

- Whether the administered chemotherapy/biologic therapy/immune therapy/targeted therapy/other oncologic therapy regimen is adequately represented in the published evidence.
- 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.
- 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).
- 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.
- That case reports are generally considered uncontrolled and anecdotal information and do not provide adequate supportive clinical evidence for determining accepted uses of drugs.
- 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.

CODING AND STANDARDS

Codes

- J7308 - Aminolevulinic acid hcl for topical administration, 20%, single unit dosage form (354 mg)
- J9999 - fluorouracil 0.5% topical cream, fluorouracil 5% topical cream, fluorouracil 1% topical cream, imiquimod 5% topical cream, bexarotene 1% topical gel, mechlorethamine 0.016% topical gel, tirbanibulin 1% topical ointment

Applicable Lines of Business

☐	CHIP (Children's Health Insurance Program)
☒	Commercial
☒	Exchange/Marketplace
☒	Medicaid
☐	Medicare Advantage

POLICY HISTORY

Date	Summary
April 2025	• Converted to new Evolent guideline template • This guideline replaces UM ONC_1445 Topical and Intralesional Therapies • Updated policy numbers in indication section
April 2024	• Updated NCH verbiage to Evolent

LEGAL AND COMPLIANCE

Guideline Approval

Committee

Reviewed / Approved by Evolent Specialty Clinical Guideline Review Committee

Disclaimer

Evolent Clinical Guidelines do not constitute medical advice. Treating health care professionals are solely responsible for diagnosis, treatment, and medical advice. Evolent uses Clinical Guidelines in accordance with its contractual obligations to provide utilization management. Coverage for services varies for individual members according to the terms of their health care coverage or government program. Individual members' health care coverage may not utilize some Evolent Clinical Guidelines. A list of procedure codes, services or drugs may not be all inclusive and does not imply that a service or drug is a covered or non-covered service or drug. Evolent reserves the right to review and update this Clinical Guideline in its sole discretion. Notice of any changes shall be provided as required by applicable provider agreements and laws or regulations. Members should contact their Plan customer service representative for specific coverage information.

REFERENCES

1. Levulan Kerastick, Carac, Efudex, Fluoroplex, Aldara, Picato, Targretin, Valchlor, Tazorac prescribing information accessed on March 19, 2025.
2. 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.
3. Work Group; Invited Reviewers, Kim JYS, Kozlow JH, Mittal B, Moyer J, Olenecki T, Rodgers P. Guidelines of care for the management of cutaneous squamous cell carcinoma. *J Am Acad* Dermatol. 2018 Mar;78(3):560-578.
4. 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.
5. Kauvar AN, Arpey CJ, Hruza G, Olbricht SM, Bennett R, Mahmoud BH. Consensus for Nonmelanoma Skin Cancer Treatment, Part II: Squamous Cell Carcinoma, Including a Cost Analysis of Treatment Methods. *Dermatol Surg*. 2015 Nov;41(11):1214-40.
6. 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.
7. Kirby JS, Miller CJ. Intralesional chemotherapy for nonmelanoma skin cancer: a practical review. *J Am Acad Dermatol*. 2010 Oct;63(4):689-702.
8. Perry A, Vincent BJ, Parker SR. Intralesional corticosteroid therapy for primary cutaneous B-cell lymphoma. *Br J Dermatol*. 2010 Jul;163(1):223-5.
9. Heinzerling L, Dummer R, Kempf W, Schmid MH, Burg G. Intralesional therapy with anti-CD20 monoclonal antibody rituximab in primary cutaneous B-cell lymphoma. *Arch Dermatol*. 2000 Mar;136(3):374-8.
10. Clinical Pharmacology Elsevier Gold Standard 2025.
11. Micromedex® Healthcare Series: Micromedex Drugdex Ann Arbor, Michigan 2025.
12. National Comprehensive Cancer Network. Cancer Guidelines and Drugs and Biologics Compendium 2025.
13. AHFS Drug Information. American Society of Health-Systems Pharmacists or Wolters Kluwer Lexi-Drugs. Bethesda, MD 2025.
14. 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.
15. Medicare Benefit Policy Manual Chapter 15 Covered Medical and Other Health Services: https://www.cms.gov/Regulations-and-Guidance/Guidance/Manuals/Downloads/bp102c15.pdf.
16. Current and Resolved Drug Shortages and Discontinuations Reported to the FDA: http://www.accessdata.fda.gov/scripts/drugshortages/default.cfm.

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]	Aggresive 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)
		Aggregate	304	4.1	98 (50/51)
Methotrexate	KA	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)
		Bostanci[52]	13.5 or 27	9	29 (2/7)
		Aggregate	UC	10.8	36 (4/11)
	BCC	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)
		Aggregate	UC	11.6	79 (44/56)
	KA	Grob[53]	57	12	83 (5/6)
Interferon alfa-2b	Superficial BCC	Cornell[54]	13.5	9	88 (50/57)
		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	Kowalzick[67]	7.7	6.6	51 (35/69)
		Kowalnick[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.