Molina Clinical Policy
Topical and Intralesional Therapies Use in Non-Melanoma Skin Cancers (NMSC) and Primary Cutaneous Lymphomas
Policy Number: 423

Initial Policy Date: 8/10/2022

POLICY SECTIONS

DISCLAIMER

This Molina Clinical Policy (MCP) is intended to facilitate the Utilization Management process. Policies are not a supplementation or recommendation for treatment; Providers are solely responsible for the diagnosis, treatment and clinical recommendations for the Member. It expresses Molina's determination as to whether certain services or supplies are medically necessary, experimental, investigational, or cosmetic for purposes of determining appropriateness of payment. The conclusion that a particular service or supply is medically necessary does not constitute a representation or warranty that this service or supply is covered (e.g., will be paid for by Molina) for a particular Member. The Member's benefit plan determines coverage – each benefit plan defines which services are covered, which are excluded, and which are subject to dollar caps or other limits. Members and their Providers will need to consult the Member's benefit plan to determine if there are any exclusion(s) or other benefit limitations applicable to this service or supply. If there is a discrepancy between this policy and a member's plan of benefits, the benefits plan will govern. In addition, coverage may be mandated by applicable legal requirements of a State, the Federal government or CMS for Medicare and Medicaid Members. CMS's Coverage Database can be found on the CMS website. The coverage directive(s) and criteria from an existing National Coverage Determination (NCD) or Local Coverage Determination (LCD) will supersede the contents of this MCP and provide the directive for all Medicare members. References included were accurate at the time of policy approval and publication.

POLICY DESCRIPTION

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.

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.

RELATED POLICIES

Policy No.	Policy Title
N/A	

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.

INDICATIONS and/or LIMITATIONS OF COVERAGE

A. PREFERRED MEDICATION GUIDANCE FOR INITIAL REQUEST:

1. When health plan Medicaid coverage provisions—including any applicable PDLs (Preferred Drug Lists)—conflict with the coverage provisions in this drug policy, health plan Medicaid coverage provisions take precedence per the Preferred Drug Guidelines; **OR**

2. When health plan Exchange coverage provisions-including any applicable PDLs (Preferred Drug Lists)-conflict with the coverage provisions in this drug policy, health plan Exchange coverage provisions take precedence per the Preferred Drug Guidelines; **OR**

3. For Health Plans that utilize NCH UM Oncology Clinical Policies as the initial clinical criteria, the Preferred Drug Guidelines shall follow NCH L1 Pathways (http://pathways.newcenturyhealth.com/) when applicable, otherwise shall follow NCH drug policies; **AND**

4. Continuation requests of previously approved, non-preferred medication are not subject to this provision; **AND**

5. When applicable, generic alternatives are preferred over brand-name drugs; **AND**

6. When there is a documented drug shortage, disease progression, contraindication, or confirmed intolerance to a Preferred drug/regimen, per NCH Policy and Pathway, the available alternative product may be used if deemed medically appropriate and the indication is listed in a standard reference compendia or accepted peer review literature. For a list of current drug shortages, please refer to FDA drug shortage website in the reference section.

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. Note: Per NCH policy, Efudex (topical fluorouracil) and Aldara (topical imiquimod) are the preferred treatment options over other topical/intralesional therapies for the treatment of BCC. This recommendation is based on the lack of level 1 evidence (randomized trial and/or meta-analysis) showing superior outcomes over Efudex (topical fluorouracil) and Aldara (topical imiquimod).

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 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. Photofrin (porfimer sodium): for use as photodynamic therapy for superficial BCC.
   e. 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. NOTE: Per NCH policy, Efudex (topical fluorouracil) and Aldara (topical imiquimod) are the preferred treatment options over other topical/intralesional therapies (Picato, Carac, Fluroplex) for the treatment of cSCC. This recommendation is based on the lack of level 1 evidence (randomized trial and/or meta-analysis) showing superior outcomes over Efudex (topical fluorouracil) and Aldara (topical imiquimod).

4. 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. Picato (ingenol mebutate): for use as topical therapy for actinic keratoses.
   b. Carac, Efudex, or Fluoroplex (topical fluorouracil): for use as topical therapy for actinic keratoses with or without calcipotriene 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. Photofrin (porfimer sodium): for use as photodynamic therapy for actinic keratoses OR for cSCC in situ (Bowen's disease).
   e. Lactic acid/Salicylic acid: use as topical therapy for pre-treatment of hyperkeratotic actinic keratoses.
   f. Tazorac (tazarotene): use as topical therapy for pre-treatment of hyperkeratotic actinic keratoses.
   g. Urea: use as topical therapy for pre-treatment of hyperkeratotic actinic keratoses.
   h. 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. NOTE: Per NCH policy, Tazorac (topical tazarotene) is the preferred treatment option over other topical/intralesional therapies (e.g., Targretin, Valchlor, Aldara, Clobestasol, Kenalog, Rituxan) for the treatment of primary cutaneous lymphomas. This recommendation is based on the lack of level 1 evidence (randomized trial and/or meta-analysis) showing superior outcomes over Tazorac (topical tazarotene).

3. The following topical/intralesional 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)
      iii. Tazorac (topical tazarotene)
      iv. Aldara (topical imiquimod)

   b. For members with primary cutaneous B-cell lymphoma (including marginal zone or follicle center lymphoma):
      i. Valchlor (topical mechlorethamine)
      ii. Targretin (topical bexarotene)
      iii. Aldara (topical imiquimod)
      iv. Clobetasol propionate (topical corticosteroid)
      v. Kenalog injection (triamcinolone)- for intralesional use
      vi. Rituxan injection (rituximab) – for intralesional use.

EXCLUSION CRITERIA

A. Use of topical or intralesional therapies for any of the following in NMSC (BCC/cSCC):
   1. For tumor ≥ 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), Efudex 5% cream (40 gm), Fluoroplex 1% cream (30 gm), Aldara 5% cream (12 pack), Picato 0.05% gel (2 tubes),Targretin 1% gel (60 gm), Valchlor 0.016% gel (60 gm), and Tazorac 0.05% or 0.1% cream/gel (30/60/100 gm), and Clobetasol Propionate 0.05% cream/ointment (15/30/45/60 gm).

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. WhetherMthe administered chemotherapy/biologic therapy/immune therapy/targeted therapy/otheroncologic 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 < 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.

MEDICATION MANAGEMENT

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

ATTACHMENTS

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

Attachment A: BCC Risk Factors for Recurrence

STRATIFICATION TO DETERMINE TREATMENT OPTIONS FOR LOCAL BCC BASED ON RISK FACTORS FOR RECURRENCE[1]

Risk Group	Low Risk	High Risk
Treatment Options	See BCC-2	See BCC-3
H&P		
Location/size	Trunk, extremities <2 cm	Trunk, extremities ≥2 cm
		Cheeks, forehead, scalp, neck, and pretibia any size
		"Mask areas" of face (central face, eyelids, eyebrows, periorbital, nose, lips [cutaneous and vermilion], chin, mandible, preauricular and postauricular skin/sulci, temple, and ear), genitalia, hands, and feet[3]
Borders	Well-defined	Poorly defined
Primary vs. recurrent	Primary	Recurrent
Immunosuppression	(-)	(+)
Site of prior RT	(-)	(+)
Pathology (See BCC-A)		
Subtype	Nodular, superficial[2]	Aggressive growth pattern[4]
Perineural involvement	(-)	(+)

National Comprehensive Cancer Network Cancer Guidelines (version: 2.2021): 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[1]	Low Risk	High Risk	Very High Risk
Treatment Options	See SCC-2	See SCC-3	See SCC-3
H&P			
Location/size[2]	Trunk, extremities <2 cm	Trunk, extremities 2 cm – <4 cm	≥4 cm (any location)
		Head, neck, hands, feet, pretibia, and anogenital (any size)[5]	
Borders	Well-defined	Poorly defined	
Primary vs. recurrent	Primary	Recurrent	
Immunosuppression	(-)	(+)	
Site of prior RT or chronic inflammatory process	(-)	(+)	
Rapidly growing tumor	(-)	(+)	
Neurologic symptoms	(-)	(+)	
Pathology (See 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[3,4]: Thickness or level of invasion	≤6 mm and no invasion beyond subcutaneous fat		>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: 2.2021): Squamous Cell Skin Cancer

Attachment B: Management of BCC and cSCC

Low risk BCC	Curettage and electrodesiccation OR Excision with postoperative margin assessment OR Radiation therapy*
High risk BCC	Excision with postoperative margin assessment OR Moh's surgery or resection with complete circumferential peripheral and deep margin assessment with frozen/permanent section OR Radiation therapy*
Low risk cSCC	Curettage and electrodesiccation OR Excision with postoperative margin assessment OR Radiation therapy*
High risk/Very High Risk cSCC	Excision with postoperative margin assessment OR Moh's surgery or resection with complete circumferential peripheral and deep margin assessment with frozen/permanent section OR Radiation therapy*
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 longterm 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.

APPLICABLE CPT / HCPCS PROCEDURE CODES

None.

CODING DISCLAIMER. Codes listed in this policy are for reference purposes only and may not be all-inclusive. Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement. Listing of a service or device code in this policy does not guarantee coverage. Coverage is determined by the benefit document. Molina adheres to Current Procedural Terminology (CPT®), a registered trademark of the American Medical Association (AMA). All CPT codes and descriptions are copyrighted by the AMA; this information is included for informational purposes only. Providers and facilities are expected to utilize industry standard coding practices for all submissions. When improper billing and coding is not followed, Molina has the right to reject/deny the claim and recover claim payment(s). Due to changing industry practices, Molina reserves the right to revise this policy as needed.

REFERENCES

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APPENDIX

Reserved for State specific information. *Information includes, but is not limited to, State contract language, Medicaid criteria and other mandated criteria.*