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Nordic European Cutaneous Oncodermatology Management (NECOM 6): A Practical Algorithm Integrating Skincare for the Prevention and Treatment of Cutaneous Side Effects of Hormonal Cancer Therapy

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 ORIGINAL ARTICLE

A Practical Algorithm for the Prevention and Treatment of Cutaneous Side Effects of Hormonal Cancer Therapy

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ABSTRACT

Introduction: Hormonal therapies, typically used in the treatment of breast and prostate cancer patients, have been associated with numerous skin toxicities that can impact quality of life and interfere with treatment adherence. Appropriate management is necessary to improve the quality of life for cancer patients and survivors who experience hormonal therapy-related dermatologic toxicities.

Objectives: To develop a practical, physician-developed algorithm for the management of hormonal therapy-related cutaneous adverse events using prescription treatment and non-prescription skincare.

Methods: The Nordic European Cutaneous Oncodermatology Management (NECOM) 6 advisory board integrated evidence from a structured literature search with the panel's expertise and clinical insights to create a practical algorithm for preventing and treating flushing/hot flashes, pruritus/urticaria, rosacea, alopecia, hirsutism, and hyperhidrosis associated with hormonal therapy.

Results: An algorithm that aims to improve patient comfort during and after treatment, reduce the incidence of hormonal therapy-related cutaneous adverse events, and promote healing of affected skin areas by using prescription medication and skincare. Suggested management recommendations supplement the algorithm.

Conclusions: Preventing and treating common dermatologic toxicities associated with hormonal cancer therapies is an essential component of care to improve patient quality of life, adherence to cancer treatment, and treatment outcomes. The NECOM 6 algorithm provides management strategies for all HCPs who treat oncology patients to prevent and treat common cutaneous adverse events associated with hormonal cancer therapies.

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INTRODUCTION

In Nordic European countries, the annual incidence of new cancer cases between 2018 and 2022 was 642.4 per 100,000 in males and 520.3 per 100,000 in females, with a lifetime risk of developing cancer before age 75 estimated at 32.0% for males and 28.6% for females.[1] In 2022, the four most commonly diagnosed cancers in Europe were breast, colorectal, lung, and prostate, accounting for almost half of all cancer diagnoses.[2] While cancer incidence continues to rise, advancements in cancer treatment have significantly improved survival rates. Age-standardized death rates in Nordic European countries have declined over the past decade, decreasing annually by 1.9% for males and 1.4% for females.[1] However, as cancer care evolves, so does the challenge of managing treatment-related toxicities.

Hormonal therapies used in the treatment of breast and prostate cancer patients have been associated with numerous skin toxicities.[3-8] Although healthcare providers (HCPs) may consider cutaneous adverse effects (cAEs) of hormonal cancer therapy an inevitable occurrence that does not need to be addressed, these side effects can significantly reduce quality of life (QoL) and may be burdensome enough for some patients to discontinue their cancer treatment or forego them altogether.[3,9]

Skincare remains an underrecognized and underused modality for mitigating these adverse events. Although cAEs are a common consequence of cancer treatment, most guidelines do not include skincare measures, highlighting the gap in skincare recommendations in the literature. The aim of this algorithm is to improve patient comfort during/after cancer treatment, to reduce the incidence and severity of hormonal therapy-related cutaneous adverse events, and to promote healing of affected skin areas by using prescription medication and skincare.

Project Update

The Nordic European Cutaneous Oncodermatology Management (NECOM) project aims to improve cancer patients' and survivors' QoL by offering tools to support HCPs treating oncology patients in preventing and managing cAEs. This includes a broad range of

HCPs, such as dermatologists, oncologists, surgeons, surgical oncologists, nurses, nurse practitioners, physician assistants, GPs, and pharmacists. The publications to date include:

NECOM 1: A review paper and an algorithm to reduce the incidence of cAEs, treat cAEs, and maintain healthy skin using general measures and non-prescription agents.[10]
NECOM 2: Skincare algorithm for patients with cancer and survivors.[11]
NECOM 3: A practical algorithm on skincare for the prevention and treatment of acute radiation dermatitis related to radiation treatment.[12]
NECOM 4: Practical algorithm addressed the prevention and management of cutaneous immunotherapy-related adverse events, improving cancer patients' QoL and outcomes.[13]
NECOM 5: Practical algorithm is to prevent and manage cutaneous targeted therapy-related adverse events (TTcAEs), improving cancer patients' QoL and outcomes.
NECOM 6: Practical algorithm is to prevent and manage cutaneous hormonal therapy-related adverse events (HTcAEs), improving cancer patients' QoL and outcomes.

METHODS

A selected group of multidisciplinary advisors used the AGREE II instrument following the modified Delphi method to develop the NECOM 6 practical algorithm for the prevention and treatment of HTcAEs. The modified Delphi method is a communication technique for interactive decision-making for medical projects.

During a face-to-face meeting on September 27, 2024, the outcome of a structured literature review identifying the spectrum of cAEs and addressing their prevention and treatment was discussed. The practical algorithm was developed based on the assembled evidence coupled with the panel's experience and opinion. An online process was used to fine-tune the practical algorithm and prepare and review the publication.

Literature Review

The literature review looked for papers describing current best practices in improving comfort during hormonal therapy, reducing/treating cAEs, and promoting healing of affected skin areas. Guidelines, consensus papers, reviews, and best practices published in English from January 2010 to January 2024 were included. Papers with no original data, not dealing with prescription treatment and/or skincare for cAEs related to hormonal therapy, and those in a language other than English were excluded (Figure 1).

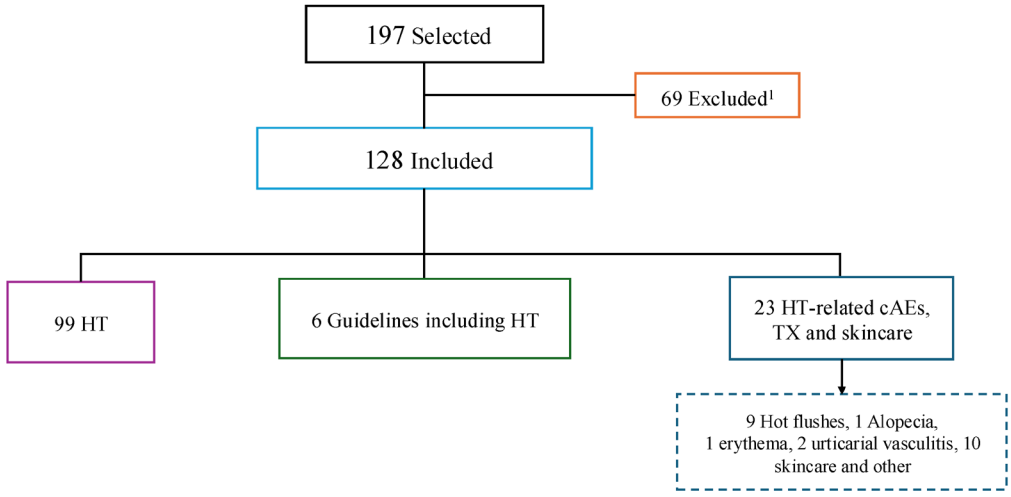
A dermatologist and a physician-scientist conducted the searches on July 25 and 26, 2024 using PubMed as the primary search engine, with Google Scholar as a secondary source. The search focused on reducing adverse events of hormonal therapy and promoting comfort during therapy. The search criteria used were as follows: *cAEs related to hormonal therapy AND QoL of patients/survivors OR education of staff and patients/survivors OR communication strategies OR prescription medications OR skincare OR topical regimes for prevention OR treatment OR maintenance OR adjunctive skincare OR adherence OR concordance OR efficacy OR safety OR tolerability OR skin irritation.*

The 128 publications that met the search criteria included clinical guidelines, algorithms, consensus papers, systematic literature reviews, and clinical studies. The publications were evaluated and graded by two independent reviewers and, on this basis, selected or excluded from the final list.

The Algorithm

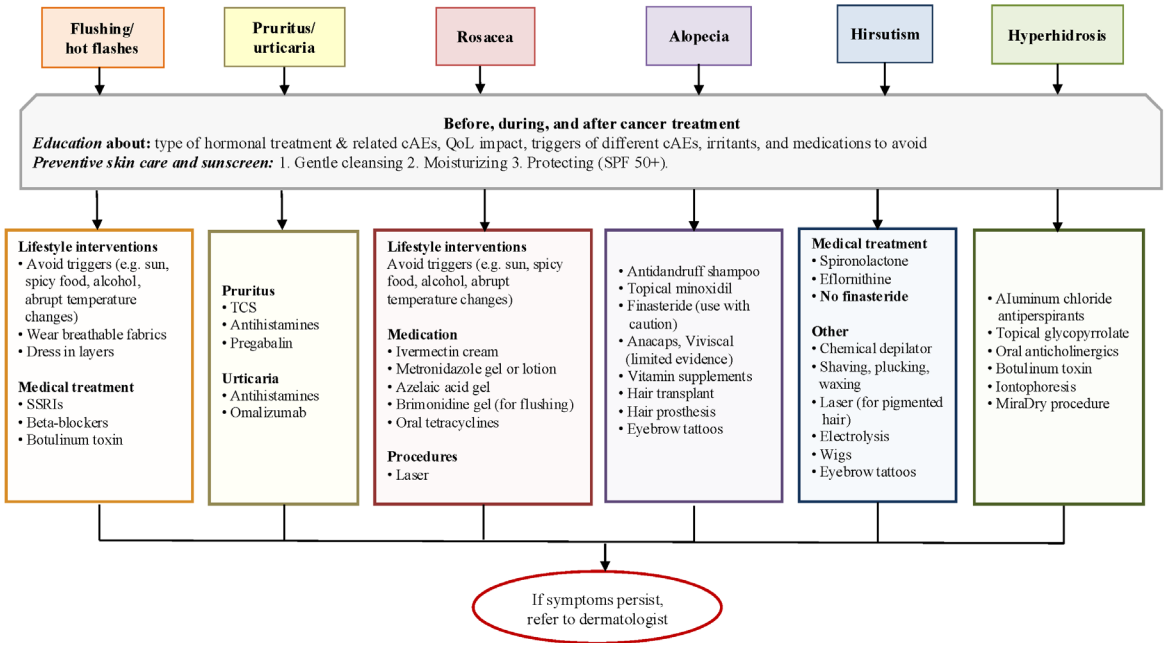
An algorithm for preventing and managing hormonal cancer therapy-related cAEs was created based on the evidence from the structured literature review and expert experience (Figure 2). Early identification of severe cAEs, which may be detected by signs and symptoms including fever, skin pain, epidermal changes, or laboratory abnormalities, is an essential first step because, regardless of

FIGURE 1. Structured literature search results.



[1]Duplications were excluded, Hormonal treatment (HT), prescription treatment (TX).
Clinically relevant to the algorithm, including guidelines, consensus papers, reviews, and best practices in cAEs-related to hormonal approaches in English from January 2010 to July 2024. Literature describing current best practices in improving comfort during hormonal therapy, reducing/treating cAEs, and promoting healing of affected skin areas.

FIGURE 2. NECOM 6 algorithm.



cAE = cutaneous adverse event; QoL = quality of life; SSRI = selective serotonin reuptake inhibitor; TCS = topical corticosteroids

the cutaneous reaction, the patient will require immediate evaluation by a dermatologist and often inpatient or ICU-level care. When red flag signs or symptoms are absent, recommendations become specific to the type of cutaneous reaction with therapeutic distinctions.

Interventions are stepwise based on cAE severity. The patient should be referred to a dermatologist if symptoms persist despite treatment.

Type of Cancers Treated With Hormonal Therapy

In Nordic European countries, breast cancer accounts for 25.0% of all new cancer cases in women, while prostate cancer accounts for 26.6% of all new cancer cases in men.[14] Hormonal therapy is often used in the treatment of these cancers to reduce hormone levels that can stimulate cancer cell growth.[4,5]

Hormone therapy for breast cancer includes aromatase inhibitors (AIs), selective estrogen receptor modulators (SERMs), and selective estrogen receptor degraders (SERDs). These agents lower the levels of estrogen in the body or block its effects.[4] In contrast, hormone therapy for prostate cancer includes luteinizing hormone-releasing hormone (LHRH) agonists, gonadotrophin-releasing hormone (GnRH) antagonists, anti-androgens, and second-generation hormone therapy. These agents work by either interfering with androgen production or blocking androgen action.[5]

Hormone therapies for breast and prostate cancer are associated with various cAEs (Table 1).[3–8] For example, the decrease in estrogen levels from SERMs and AIs, and the reduction in androgen levels from GnRH agonists, can result in a pharmacologic menopause reaction characterized by hot flashes/flushing and hyperhidrosis.[8] In addition to symptoms of menopause, medications used to treat breast cancer can also cause pruritus, rosacea, alopecia, and hirsutism. Meanwhile, the most common cAEs associated with androgen deprivation therapy (ADT) for prostate cancer are hot flashes, alopecia, and pruritus.[5,6]

General Principles for Managing Cutaneous Adverse Events of Hormonal Cancer Therapy

Skin reactions associated with hormonal cancer therapy can reduce quality of life and threaten treatment adherence.[3,9] Studies in women receiving systemic cancer therapy have shown that dermatologic toxicities can significantly alter a woman's self-image, cultural identity, femininity, sexuality, and mental health. In severe instances, they can lead to premature treatment discontinuation and may therefore affect overall survival and treatment response.[8] Therefore, timely diagnosis and management of emergent cAEs is crucial in the multidisciplinary care of patients receiving hormonal cancer therapy.

Pretherapy counseling is essential to educate patients about the risks of cAEs associated with their specific hormonal cancer treatment. It also provides an opportunity to discuss potential triggers for cAEs, highlight the importance of avoiding triggers and irritants, and discuss interventions that may support treatment adherence. Patients should also be counseled on preventive skincare using gentle cleansers and moisturizers and regular use of sunscreen with a minimum SPF of 50 (Table 2). Cleansers should be non-abrasive and fragrance-free, with a pH close to that of skin (~5).[15] Topical moisturizers, applied twice daily can help maintain skin hydration and reduce the risk of xerosis induced by treatments.[15]

When patients present with skin concerns, it is important for HCPs to assess the severity of the cAEs, provide appropriate treatment recommendations, and refer severe cases to a specialist (oncologist and/or dermatologist). In more severe cases, treatment interruption or discontinuation may be warranted.[16]

TABLE 1.

Hormonal Therapies and Associated Cutaneous Adverse Effects[3-8]			
Drug Class	**Drug Name**	**Oncologic Indication**	**Cutaneous Adverse Events**
Aromatase inhibitors	Anastrozole, exemestane, letrozole	Breast	Hot flashes/flushing, pruritus, alopecia, hirsutism, hyperhidrosis
SERMs	Tamoxifen, raloxifene, toremifene	Breast	Hot flashes/flushing, alopecia, hirsutism, hyperhidrosis
SERDs	Fulvestrant	Breast	Hot flashes/flushing, alopecia
Anti-androgens	Bicalutamide, cyproterone acetate, flutamide, nilutamide	Prostate	Hot flashes/flushing, alopecia, hyperhidrosis, pruritus
LHRH agonists	Goserelin, leuprorelin acetate, triptorelin, buserelin acetate	Prostate	Hot flashes/flushing, pruritus, alopecia, hyperhidrosis
GnRH antagonists	Degarelix	Prostate	Hot flashes/flushing, pruritus, alopecia, hyperhidrosis
Second-generation hormone therapy	Abiraterone, enzalutamide, apalutamide, darolutamide, nilutamide	Prostate	Hot flashes/flushing, pruritus, alopecia, hyperhidrosis

SERMs, selective estrogen receptor modulators; SERDs, selective estrogen receptor degraders. LHRH, luteinizing hormone-releasing hormone; GnRH, gonadotrophin-releasing hormone.

Treatment for Specific Cutaneous Adverse Effects

Flushing/Hot flashes

Hot flashes are a common side effect of hormonal cancer therapy. These transient episodes of sudden heat, flushing, and sweating are often accompanied by redness, nausea, palpitations, or anxiety.[9,17,18] According to a population-based survey, breast cancer survivors are 5.3 times more likely to experience menopausal symptoms, like flushing, compared to the general female population. In the Anastrozole vs Tamoxifen Alone or in Combination (ATAC) trial, hot flashes were reported in 35.7% of patients treated with anastrozole and 40.9% of those treated with tamoxifen. Similarly, in the Intergroup Exemestane Study (IES) trial, 42% of patients receiving exemestane experienced hot flashes, while the BIG 1-98 trial reported an incidence of 33.5% among those treated with letrozole.[17]

Hot flashes also affect 58 to 80% of patients receiving ADT at varying levels of severity.[9] Although some men notice an improvement in hot flashes over time, they typically peak in frequency three months after starting ADT treatment and often persist long-term.[5,9]

For most patients with breast cancer or prostate cancer, hot flash intensity is moderate to severe.[18] Up to 27% of patients treated with ADT describe hot flashes as the most significant adverse QOL effect, with debilitating hot flashes even leading to ADT discontinuation in some cases.[9] Meanwhile, in patients with breast cancer, severe hot flashes have been associated with sleep difficulty, higher pain severity, and poor psychological functioning. In some cases, the debilitating impact of severe flushing from tamoxifen can lead to treatment discontinuation.[19]

Before starting hormonal cancer treatment, HCPs should inform patients about this potential side effect and advise them to keep a diary of the frequency and severity of hot flashes.[9] When assessing hot flashes, HCPs should evaluate their onset, baseline frequency and severity, impact on QoL (eg, sleep and work), and possible patterns or triggers.

First-line treatment involves avoiding patient-specific triggers, which may include heat, alcohol, caffeine, smoking, or stress.[8] Additional lifestyle interventions such as dressing in layers and wearing breathable fabrics (ie, cotton) can also be recommended.[17]

If lifestyle interventions fail, pharmacologic management may be necessary. Although estrogen replacement is the most effective treatment for menopausal symptoms, hormone replacement therapy (HRT) is contraindicated in patients with advanced breast cancer, and should not be used to treat postmenopausal symptoms, particularly in patients with ER-positive disease.[20]

To control hot flashes, clinicians can consider nonhormonal pharmacological treatment interventions that have reported efficacy in women with a history of breast cancer and in some men who have undergone ADT, such as SSRIs, SNRIs, certain anticonvulsants, anticholinergics, alpha-adrenergic agonists, and beta-blockers (Table 3).[20] Venlafaxine ER, paroxetine, gabapentin, and pregabalin are associated with a 55% to 60% reduction in hot flashes, while citalopram and fluoxetine, have been found to reduce hot flashes by approximately 50%.[18]

If prescribing SSRIs, clinicians should be mindful of the potential for drug interactions, as many SSRIs can inhibit the cytochrome P450 enzymes involved in the metabolism of tamoxifen.[18] Tamoxifen is metabolized primarily by CYP2D6 into its active form, which is crucial for its therapeutic effect in breast cancer treatment. Drugs that inhibit CYP2D6 activity can reduce the conversion of tamoxifen to its active form, potentially decreasing its efficacy. Citalopram and venlafaxine are least likely to affect CYP2D6 activity and may be more appropriate for use in patients taking tamoxifen. In contrast, paroxetine and fluoxetine are potent CYP2D6 inhibitors and should be avoided.[17]

TABLE 2.

Preventive Skincare and Sunscreen Recommendations[15]		
Dermatologic Process	**Products/Ingredients To Look For**	**Products/Ingredients To Avoid**
Cleansing	Mild cleanser with a mildly acidic to neutral pH (4-6.5)	Abrasive ingredients, alkaline cleansers, fragrances
Moisturizing	Moisturizers with emollients or occlusives	Fragrances
Sun protection	Broad-spectrum sunscreen with SPF of 50 or higher	--

SPF, sun protection factor.

TABLE 3.

Treatment for Flushing/Hot Flashes[18,24]			
Drug Class	**Medication**	**Common Dosage**	**Comments**
SNRI	Venlafaxine	37.5-150 mg/day	First-line option for hot flashes;[24] frequently used in clinical practice; best studied agent in men
	Desvenlafaxine	100-150 mg/day	
	Duloxetine	30 mg/day x 1 wk, then 60 mg/day	Moderate CYP2D6 inhibitor[24]
SSRI	Paroxetine	10-25 mg/day	Avoid in patients receiving tamoxifen due to potent CYP2D6 inhibition
	Citalopram	10-20 mg/day	First-line option for hot flashes[24]
	Escitalopram	10-20 mg/day	First-line option for hot flashes[24]
	Fluoxetine	20 mg/day	Potent CYP2D6 inhibitor; avoid use with tamoxifen
	Sertraline	25-100 mg/day	Moderate CYP2D6 inhibitor
Anticonvulsant	Gabapentin	300-900 mg/day	Can cause drowsiness
	Pregabalin	150-300 mg/day	--
Alpha-adrenergic agonists	Clonidine	0.1 mg/day	Sudden cessation can result in significant hypertension; no efficacy demonstrated in men with post-orchiectomy hot flashes.[18]

Oral clonidine has been found to reduce hot flashes by approximately 40%.[18] However, the oral preparation of clonidine is associated with potential side effects such as xerostomia, dizziness, constipation, and hypotension.[19]

Some studies also suggest that botulinum toxin injections may have a potential beneficial effect on menopausal flushing.[21] While Eshghi et al[22] demonstrated that injecting a total dose of up to 30 units of botulinum toxin into the cheeks (1 unit per square cm) significantly decreased patients' Dermatology Life Quality Index after 2 months, Odo et al[23] employed a different dosing regimen. Using a 40-point injection technique with 6.2 units at each selected point across the head, neck, and chest, they observed a significant reduction in the frequency of menopausal flushing episodes after 2 months compared to saline controls.[23] These studies highlight the variability in dosing and injection techniques, and the need for further randomized clinical trials with larger patient populations to better understand the long-term efficacy and safety of botulinum toxin for treating hot flashes.

According to the 5th ESO-ESMO international consensus guidelines, there is no convincing evidence that phytotherapeutic (herbal) drugs improve postmenopausal symptoms; they are therefore not recommended.[20]

Pruritus and Urticaria

Pruritus is frequently experienced by patients undergoing treatment for prostate cancer. In a study of 303 prostate cancer patients treated with apalutamide, 28% experienced associated grade 1/2 pruritus.[6] Left untreated, pruritus may lead to excoriations from scratching or skin infections.

As dry skin is a common precursor to pruritus, it is important to implement preventative measures to prevent skin dryness.[25] Regular use of moisturizers may mitigate dry skin and help maintain skin integrity, thus minimizing the risk of pruritus.[15,26] Emollients with ceramides and hyaluronic acid can help maintain skin hydration and decrease transepidermal water loss.[15] Providers should also educate patients to avoid harsh soaps and basic pH cleansers, limit shower time, avoid hot water, and avoid products containing fragrances, irritants, or sensitizing agents.[15]

If pruritus occurs, clinicians should advise patients to continue using their daily emollients and can add on medical treatment. Medical treatment for pruritus includes topical corticosteroids, oral antihistamines, and GABA agonists (pregabalin/gabapentin) according to the severity of pruritus (Table 4).[25] For mild-to-moderate pruritus, topical corticosteroids (eg, mometasone furoate 0.1% ointment or betamethasone valerate 0.1% ointment) can be considered.[25] Nonsedating, second-generation antihistamines (eg, loratadine 10 mg daily) may be recommended as the first choice for systemic therapy for daytime pruritus, while patients who suffer from nighttime pruritus may benefit from the sedating properties of first-generation antihistamines (eg, diphenhydramine 25-50 mg daily).[25] Pregabalin (25-150 mg daily) and gabapentin (900-3600 mg daily) may be considered as second-line treatment in patients who fail antihistamines and continue to experience clinically significant pruritus.[25] In refractory cases, the patient should be referred to a dermatologist to optimize the treatment.

Urticaria is a debilitating mast cell-driven skin disease presenting with itchy wheals, angioedema, or both.[27] Evidence for the treatment

TABLE 4.

Treatment for Pruritus[25]		
Line of Therapy	**Intervention**	**Notes**
First-line treatment	Topical low/medium potency steroids Second-generation oral antihistamines (daytime pruritus) First-generation oral antihistamines (nighttime pruritus)	Continue drug at current dose and monitor for change in severity. Reassess after 2 weeks (either by HCP or patient self-report); if reactions worsen or do not improve, proceed to next step.
Second-line treatment	Topical medium/high potency steroid OR GABA agonists (pregabalin/gabapentin)	Continue drug at current dose and monitor for change in severity. Reassess after 2 weeks (either by HCP or patient self-report); if reactions worsen or do not improve, interrupt treatment until symptom improvement.

HCP, healthcare provider; GABA, gamma-aminobutyric acid.

TABLE 5.

Treatment for Rosacea[30]			
Therapy	**Formulation and Dosage**	**Type of Rosacea**	**Adverse Effects**
Metronidazole	0.75% gel, cream, or lotion BID; 1% gel QD	PP	Pruritus, stinging, irritation, dryness
1% gel QD	15% gel QD or BID	PP	Stinging, irritation, burning
Azelaic acid	0.33% gel QD	Erythema	Pruritus, burning, irritation, dryness, erythema
Brimonidine	1% cream QD	PP	Burning, skin irritation
Ivermectin	Gel 1%/BID	PP	Pruritus, burning, irritation, dryness
Clindamycin	100 mg QD or BID	PP	Photosensitivity, candidal
Doxycycline	100 mg QD or BID	PP	vaginitis, diarrhea
Isotretinoin	0.3 mg/kg QD OR 10-20 mg QD x 4-6 months, followed by microdose therapy (0.03 to 0.17 mg/kg/day)	Refractory PP and phymatous subtypes	Dry skin, photosensitivity, hepatotoxicity, impaired night vision

QD, once daily; BID, twice daily; PP, papulopustular.

of urticaria in oncology is limited. Current management guidelines for chronic urticaria recommend step-up administration of second-generation H1 antihistamines to four-fold the approved dose, followed by omalizumab.[27,28]

While antihistamines are the mainstay of treatment for urticaria, the lack of head-to-head studies makes it difficult to determine if one is more effective than the others.

Although malignant diseases were one of the exclusion criteria in most controlled trials of omalizumab in chronic spontaneous urticaria, clinicians are often asked if omalizumab can be used in patients with malignant diseases. There are no published data on the effects of omalizumab in patients with malignant disease; however, there are also no reports that the use of omalizumab is less safe or effective in patients with comorbid malignancy. Therefore, omalizumab may be considered for the treatment of urticaria in patients with comorbid malignancy after oncology consulation.[29]

Rosacea

Rosacea is characterized by transient or persistent facial flushing, telangiectasia, inflammatory papules and pustules, and connective tissue hyperplasia.[30] Numerous triggers can aggravate rosacea, including sun exposure, stress, exercise, heat, spicy foods, hot beverages, and alcohol.[30,31] Patients should be informed about these triggers and encouraged to avoid them.

Proper skincare may also help improve and maintain the integrity of the skin barrier and reduce skin sensitivity. Therefore, the use of mild, non-alkaline, fragrance- and abrasive-free cleansers and moisturizers, as well as photoprotection with wide-brimmed hats and broad-spectrum sunscreens with SPF 50 or higher is recommended.[30]

The older classification of rosacea, preferred by the panel, divides the condition into four subtypes: erythematotelangiectatic, papulopustular, phymatous, and ocular. These subtypes are diagnosed clinically and treatment varies according to the clinical presentation (Table 5). For inflammatory lesions, first-line treatments are topical metronidazole or azelaic acid. Once-daily brimonidine is also effective for reducing erythema. Papulopustular rosacea can be treated with topical ivermectin or systemic tetracyclines, most commonly subantimicrobial-dose doxycycline. For refractory cases, isotretinoin may be used. Phymatous rosacea, characterized by thickened skin, is treated primarily with laser or light-based therapies.[30,31] Surgical procedures (ie, electrosurgery, tangential excision, scissor sculpting) can be considered in severe cases.[30]

Alopecia

A non-scarring, androgenetic pattern of alopecia is a common, yet underreported, adverse event of hormonal cancer therapies.[32] This type of alopecia often presents as female pattern hair loss, characterized by diffuse thinning over the crown without frontal hairline recession, often forming a "Christmas tree pattern" along the center part.[8,25]

A meta-analysis of 35 studies with over 13,000 patients treated with hormonal therapy reported an overall incidence of all-grade alopecia at 4.4%. The highest incidence (25%) was observed in patients treated with tamoxifen, followed by treatment with anastrozole (14.7%).[32] The incidence of alopecia increases when endocrine therapies are combined or sequentially administered.[8]

Alopecia has been cited as the most traumatic dermatologic adverse event in approximately 58% of women receiving breast cancer treatment,[32] with women reporting lower self-esteem, poorer body image, and lower QoL.[33] Up to 8% of survivors have indicated that they would discontinue therapy because of this adverse effect.[34] Even mild cases of alopecia can have a substantial negative emotional impact, highlighting the importance of considering the distress that alopecia may have on cancer survivors' QoL.[7]

Before initiating hormonal therapy, clinicians need to communicate the risk of alopecia with patients and provide guidance on options for concealing hair loss, such as hats, scarves, extensions, or wigs.[8,25] When patients on hormonal therapy present with alopecia, other potential causes of hair loss should first be ruled out by evaluating serum iron, serum ferritin, total iron binding capacity, TSH levels, vitamin D, zinc levels, and a complete blood count.[3,25] Patients must be educated on their prognosis, informed that the goal of treatment (Table 6) is to minimize hair loss, and understand that therapy may focus on maintenance, rather than hair regrowth.[34]

Topical minoxidil 5% once daily for women and twice daily for men

TABLE 6.

Treatment for Alopecia[41]			
Line of Treatment	**Medication**	**Formulation/Dosage**	**Comments**
First-line treatment	Topical minoxidil	5% daily (women) or BID (men)	Before starting treatment, check TSH, iron, ferritin, vitamin D, zinc.
Second-line treatment	Spironolactone	50-200mg/day	Topical treatments can be started during chemotherapy. Therapeutic decisions about spironolactone should be made in consultation with the oncologist.

BID, twice daily; TSH, thyroid stimulating hormone.

is first-line treatment for individuals with alopecia. Treatment with 5% topical minoxidil has been shown to result in a moderate to significant improvement of alopecia in 80% of female patients with breast cancer.[35] Topical ketoconazole can be used as adjunctive or alternative therapy. Although large-scale prospective studies are lacking, a systematic review found positive results to support the use of 2% ketoconazole shampoo for the treatment of androgenetic alopecia, even with the most infrequent use of 2 to 3 times per week.[36] In cases refractory to minoxidil, spironolactone may be considered after discussion with the oncologist. Although spironolactone (50-200 mg daily) has been used in women with breast cancer on endocrine therapy, there was a theoretical risk for breast cancer recurrence due to the estrogenic effects of spironolactone. However, a retrospective analysis published in the Journal of the American Academy of Dermatology concluded that spironolactone was not independently associated with increased breast cancer recurrence and may be considered for the treatment of alopecia in breast cancer survivors.[37]

Finasteride should be used with caution in male breast cancer patients; finasteride is not recommended for use in breast cancer patients or survivors.[8] Vitamin supplements, such as biotin, are not recommended due to a lack of supporting data and the potential to interfere with lab results, including thyroid function and cardiac enzyme studies.[38] Similarly, food supplements have limited evidence to support their use, especially in oncology settings. Further investigations are needed to evaluate efficacy and safety in this population. Hair transplants may be suitable for patients with areas of high-density donor hair, allowing for transplantation to localized areas of hair loss, rather than patients with diffuse thinning over the entire scalp.[8]

Hirsutism

Hirsutism, defined as the presence of excessive hair in androgen-dependent areas of a woman's body, is an underreported side effect of hormonal therapies.[39,25,40] Hirsutism can not only lead to the avoidance of social situations, but also to symptoms of anxiety and depression.[41] Local measures, such as shaving, bleaching, depilatories, and electrolysis (Table 7) can be used as first-line treatment.[39] Patients can also be treated with laser therapy, with the patient's Fitzpatrick skin type guiding wavelength selection.[39] Topical eflornithine cream, applied twice daily, can be used as second-line treatment. It has been shown to slow the rate of hair growth significantly in up to 32% of patients and can be used adjunctively with local methods of hair removal.[40–42] If used in conjunction with local hair removal methods, topical eflornithine should be applied at least 5 minutes after hair removal. Makeup and sunscreen can be applied over treated areas after the cream has dried.[42] Although spironolactone can be considered in doses up to 200 mg/day, caution is warranted due to the potential risk of hormonal stimulation in patients with hormone-receptor-positive breast cancer.[34,40]

Hyperhidrosis

Patients undergoing hormonal therapy for breast or prostate cancer may develop hyperhidrosis. Excessive sweating is a recognized side effect associated with certain hormone treatments including anastrozole, tamoxifen, and raloxifene.[43] Hyperhidrosis can significantly impact QoL and cause social, emotional, and work impairment.[44] Disease severity and location of hyperhidrosis can be used to guide treatment (Table 8).[44] In most cases, topical 20% aluminum chloride is recommended as first-line treatment regardless of severity and location.[44] This solution is applied nightly to the affected areas for six to eight hours until improvement is observed, at which time the application interval can be lengthened to maintain sweat control. For patients with craniofacial sweating, topical glycopyrrolate, applied once every two to three days, is recommended as first-line treatment. It has shown a 96% success rate with minimal adverse effects (mild skin irritation). Botulinum toxin injection, administered intradermally in the affected area, is considered first- or second-line treatment for axillary, palmar, plantar, or craniofacial hyperhidrosis.[44] Iontophoresis is an effective first- or second-line treatment for hyperhidrosis of the palms and soles. In severe cases of hyperhidrosis, when other treatments fail, oral anticholinergics can be considered as adjunctive therapy.[44] Local microwave therapy is a newer treatment option for axillary hyperhidrosis that targets and permanently destroys sweat glands, odor glands, and hair follicles in the axilla.[44]

TABLE 7.

Treatment for Hirsutism[34,39,40]		
Line of Therapy	**Treatment**	**Notes**
First-line treatment	Depilatories, shaving, waxing, electrolysis, bleaching	--
	Laser therapy	--
Second-line treatment	Eflornithine topical cream BID	Can be combined with local hair removal methods
	Spironolactone, 50 to 200 mg/QD	Decision should be made in consultation with the oncologist

HCP, healthcare provider; GABA, gamma-aminobutyric acid.

TABLE 8.

Treatment for Hyperhidrosis[44]

Medication	Common Dosage	Location of Hyperhidrosis	Comments
Aluminum chloride	20% topical solution	20% solution appropriate for palmoplantar 6.25% - 12% solution appropriate for folds	First-line treatment
OnabotulinumtoxinA	Intradermally into affected areas	Axillary, palmar, plantar, or craniofacial hyperhidrosis	Use when patients fail aluminum chloride or in severe cases
Iontophoresis		Plantar, palmer	--
Topical glycopyrrolate	2%	Appropriate for all locations	--
Oxybutynin	2.5%/day or BID	Generalized or failed above	Adjunctive therapy
Oral glycopyrrolate	2mg /BID	Generalized or failed above	Adjunctive therapy

CONCLUSION

Quality of life is a crucial consideration for cancer patients undergoing hormonal therapy. Although cAEs commonly occur, they should not be dismissed as issues that patients must simply endure. Effective management strategies exist to prevent, reduce, or treat cAEs from hormonal cancer therapy. Integrating an appropriate skincare regimen into a patient's care plan not only improves patient comfort but can also help support adherence to cancer treatment. Carefully selecting and recommending products with appropriate active ingredients and delivery vehicles is essential for optimizing outcomes. When discussing skincare with patients, clinicians should empower patients to take a proactive approach to caring for their skin, starting before treatment and continuing through and after cancer therapy. By addressing cAEs, healthcare providers can improve patient comfort during and after treatment, reduce the risk of some cAEs, and manage AEs through the use of appropriate prescription medication and skincare.

DISCLOSURES

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