Symptom Management Guidelines:
PALMAR-PLANTAR ERYTHRODYSESTHESIA (PPE)

### Definition
- **Palmar-Plantar Erythrodysesthesia (PPE)** – is a dermatologic toxicity characterized by redness and pain on the palm of the hand and sole of the foot, and occasionally other body surfaces, also known as hand and foot syndrome (HFS) and chemotherapy-induced acral erythema
- **Hand and foot skin reactions** – characterized by scaling surrounded by erythema commonly present on pressure bearing areas of the hands and feet (e.g. finger tips, heels)

### Contributing Factors

#### Chemotherapy
- Onset of symptoms of PPE vary with agent, dose, exposure, length of infusion and combination of 2 or more agents
- Chemotherapy that has microvasculature toxicity
- Capecitabine
- Pegylated liposomal doxorubicin
- Fluorouracil (5-FU)
- Sorafenib tosylate, sunitinib, lapatinib
- Cytarabine
- Docetaxel and Paclitaxel
- Etoposide

#### Relevant Medical History
- Severe renal dysfunction for drugs metabolized/excreted through the kidneys (e.g. fluorouracil, capecitabine, cytarabine)
- Severe hepatic dysfunction (elevated bilirubin, AST or alkaline phosphatase) for drugs metabolized/excreted through the liver (e.g. pegylated liposomal doxorubicin, fluorouracil, cytarabine, docetaxel, lapatinib).
- Previous dermatological conditions (e.g. seborrheic dermatitis, actinic keratoses).

#### Other
- Advanced age (over 65 years) and female gender – more common with infusional fluorouracil
- Ethnicity – non-white populations may have higher incidence & develop symptoms differently
- Alcoholism
- Increased body temperature (e.g. hot baths or showers, exercise, fever, weather, climate)
- Increased blood flow
- Friction or pressure to areas of the body caused by use or by obesity (e.g. behind the knees, groin, below the breast and axillae).
- Manual labour or vigorous exercise may exacerbate PPE (especially to hands and feet).
- Misalignment of joints

### Consequences
- Increased risk of altered skin integrity, infection
- Limited use of a potentially effective therapy for cancer
- Quality of life – pain, physical and/or psychological distress, sleep-wake disturbance, impaired mobility, altered role function

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<table>
<thead>
<tr>
<th><strong>GENERAL ASSESSMENT</strong></th>
<th><strong>SYMPTOM ASSESSMENT</strong></th>
<th><strong>PHYSICAL ASSESSMENT</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Contact &amp; General Information</strong></td>
<td>Normal</td>
<td>Vital Signs</td>
</tr>
<tr>
<td>• Physician name – oncologist, family physician</td>
<td>• Refer to pretreatment nursing or oncology assessment</td>
<td>• Frequency – as clinically indicated</td>
</tr>
<tr>
<td>• Pharmacy</td>
<td></td>
<td></td>
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<tr>
<td>• Home health care</td>
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<td></td>
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<tr>
<td>• Other health care providers</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Allergies</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Consider Contributing Factors</strong></td>
<td>Onset</td>
<td>Skin Assessment</td>
</tr>
<tr>
<td>• Cancer diagnosis and treatment(s) – note type and date of last treatment</td>
<td>• When did changes start?</td>
<td>• Ensure adequate light source and gloves if handling non-intact skin</td>
</tr>
<tr>
<td>• Medical history</td>
<td>• How are changes progressing?</td>
<td>• Assess all aspect of hands and feet, areas of cutaneous pressure/friction and intertriginous areas</td>
</tr>
<tr>
<td>• Pre-existing skin conditions (fungal disease, hyperkeratosis, eczema)</td>
<td></td>
<td>– Color</td>
</tr>
<tr>
<td>• Medication profile</td>
<td>Provoking / Palliating</td>
<td>• Degree of erythema – patchy or uniformly deeply red and any signs of pallor in areas of intense erythema. Hyper-pigmentation in non-white patients</td>
</tr>
<tr>
<td>• Recent lab or diagnostic reports</td>
<td>• What makes the symptoms better? Worse?</td>
<td>– Thickening</td>
</tr>
<tr>
<td></td>
<td>Quality</td>
<td>Hyperkeratosis of soles of feet and palmar surfaces</td>
</tr>
<tr>
<td></td>
<td>• What symptoms do you have? Tingling, burning, pain, blistering, ulceration, erythema, dryness, desquamation, cracking of skin, edema, white scaling, bullous lesions?</td>
<td>– Moisture</td>
</tr>
<tr>
<td></td>
<td>• When did symptoms begin in relation to last chemotherapy treatment?</td>
<td>• Any accumulation of fluid under skin</td>
</tr>
<tr>
<td></td>
<td>• Can you describe the nature of the symptom?</td>
<td>– Integrity</td>
</tr>
<tr>
<td>Region / Radiation</td>
<td>Severity / Other Symptoms</td>
<td>Any presence and size of flaking, peeling, rash, ulcers and/or blisters</td>
</tr>
<tr>
<td>• Where are the changes happening? Tops of hands, fingers/fingertips, palms, soles of feet, tops of feet, bra-line, waistline, intertriginous areas (two skin areas that may touch or rub together)</td>
<td>• How bothersome is this to you? (0-10 scale, with 0 not at all – 10 being worst imaginable)</td>
<td>– Desquamation</td>
</tr>
<tr>
<td></td>
<td>• Have you been experiencing any other symptoms: Fever? - possible infection</td>
<td>• Any associated bleeding</td>
</tr>
<tr>
<td></td>
<td>• Discharge from blisters? – possible infection</td>
<td>– Swelling</td>
</tr>
<tr>
<td></td>
<td>• Persistent bleeding? – possible thrombocytopenia</td>
<td>Degree of swelling</td>
</tr>
<tr>
<td>Treatment</td>
<td>Understanding / Impact on You</td>
<td>– Sensory changes</td>
</tr>
<tr>
<td>• Strategies used to avoid irritants, heat, and mechanical irritation?</td>
<td>• Are these symptoms affecting your ability to use your hands or feet or performs ADLs?</td>
<td>Tingling, numbness, pain, pruritus or burning</td>
</tr>
<tr>
<td>• Using any creams or ointments? If so, what type? Effective?</td>
<td></td>
<td></td>
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<tr>
<td>• Using any pain medications? If so, what type (topical, systemic)? Effective?</td>
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<tr>
<td>• Any other medications or treatments? (e.g. Vitamin B6)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Understanding / Impact on You</td>
<td>Value</td>
<td></td>
</tr>
<tr>
<td>• Are these symptoms affecting your ability to use your hands or feet or performs ADLs?</td>
<td>• What is your comfort goal or acceptable level for this symptom (0 – 10 scale)?</td>
<td></td>
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</tbody>
</table>
### PALMAR PLANTAR ERYTHRODYSESTHESIA GRADING SCALE*

#### NCI Common Terminology Criteria for Adverse Events (Version 4.03)

<table>
<thead>
<tr>
<th>Grade 1 (Mild)</th>
<th>Grade 2 (Moderate)</th>
<th>Grade 3 (Severe)</th>
<th>Grade 4 (Life-threatening)</th>
<th>Grade 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Minimal skin changes or dermatitis (e.g., erythema, edema, or hyperkeratosis) without pain</td>
<td>Skin changes (e.g., peeling, blisters, bleeding, edema, or hyperkeratosis) with pain; limiting instrumental ADL (e.g. preparing meals, shopping)</td>
<td>Severe skin changes (peeling, blisters, bleeding, edema or hyperkeratosis) with pain; limiting self-care ADLs (e.g. bathing, dressing, feeding self, using the toilet, taking medications)</td>
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<td>__</td>
</tr>
</tbody>
</table>

*A semicolon indicates ‘or’ within the description of the grade and a single dash (-) indicates a grade is not available.

### Step-Up Approach to Symptom Management:

Interventions Should Be Based On Current Grade Level and Include Lower Level Grade Interventions As Appropriate

#### Grade 1

**Non-Urgent:** Prevention, support, teaching & follow-up care as required

**Patient Care and Assessment**
- Screen for skin changes at first visit; re-assess at each visit and at peak times for onset
- Only known cure for PPE related to chemotherapy is dose reduction or interruption
- Timing of onset, appearance, distribution and skin changes varies with each chemotherapy

**Patient Self-assessment:**
- Assess skin daily. Notify oncologist at next scheduled visit or earlier if symptoms worsen
- Assess for early signs of PPE including:
  - Tingling and/or numbness (often first sign)
  - Dry, furrowed skin that becomes reddened or darker (in non-white patients)
  - Painless swelling or tenderness on the palms of the hands, pads of the fingers, soles of the feet and behind the knees, groin, axilla and below the breast

**Skin Care and Hygiene:**
- Clean hands, feet, and skin fold areas with lukewarm water; gently pat dry
- Wash sweat from skin
- Avoid hot water (e.g. while bathing, cleaning dishes)
- Apply emollient creams or lotions with lanolin to keep skin hydrated (e.g. Bag Balm®, Udderly Smooth®). Apply on intact skin liberally, gently, and often.
- Use keratolytics (urea & salicylic acid) to remove overgrown skin
- Avoid sun exposure during treatment- use sun block
- Avoid loose-fitting sandals or going bare feet outdoors

**Prevent Constriction of Skin:**
- Tight-fitting clothes, shoes, socks, belts and jewelry as well as harsh fabrics
- Tight bandages, dressings or adhesive tape to skin

**Avoid Abrasive Conditions and Mechanical Stress:**
- Immersing hands in strong detergent, bleach or other chemicals-use non-rubberized protective gloves
- Using hands for activities that might cause abrasion or mechanical stress (e.g. clapping, typing), require tight gripping (e.g. tools, musical instruments, driving) and vigorous activities (e.g. jogging, aerobics)
- Leaning on bony prominences (e.g. elbows, knees)
  - Sit or lie on padded surfaces

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- Raise legs with cushions when possible
- Place pillow between knees or wear pajamas if rubbing of legs occurs during sleep
- Gel shoe inserts for cushioning and reducing friction

**Regulate Temperature:**
- Avoid situations that raise body temperature (e.g. steam, saunas, hot baths, heating pads, vigorous exercise)
- Do not wear rubber gloves for dishwashing as they intensify heat

### Dietary Management
- Promote adequate hydration/nutrition during treatment to help prevent skin dryness/desquamation
- Recommend daily fluid intake of 8-12 cups (unless contraindicated) to help keep skin intact
- Promote a well-balanced diet high in protein, vitamins B and C

### Pharmacological Management
- Advise patient to avoid using topical anesthetics or diphenhydramine containing creams during treatment as these may exacerbate skin toxicity

### Patient Education and Follow-up
- Reinforce when to seek immediate medical attention:
  - Temperature greater than or equal to 38° C and/or presence of redness, discharge or odor from any open areas – possible infection
  - Unable to perform ADL – reflects deteriorating patient status and severity of PPE
  - Uncontrolled pain in hands, feet, intertriginous areas
- Instruct patient/family to call back if symptoms worsen or do not improve
- If indicated, arrange for nurse initiated telephone follow-up or physician follow-up for further assessment

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### Grade 2

#### URGENT:
Requires medical attention within 24 hours

### Patient Care and Assessment
- Collaborate with physician as patients may require:
  - Treatment delays, reductions or discontinuation of treatment. See Chemotherapy Protocols in Resources Section below for specific direction
  - New or change in prescriptions (analgesics, antibiotics, corticosteroids)
  - Lab and Diagnostic tests: CBC and blood cultures if infection suspected
- Arrange for further evaluation and assessment in an ambulatory setting
- Arrange for specific skin care and dressings as necessary

### Management of Skin Complications
**Pain:**
- Anticipate need for pain management; systemic or topical analgesics and/or topical steroids
- Cool packs on palms of hands or soles of feet may alleviate pain. Alternate on and off for 15 to 20 minutes at a time

**Local infection:**
- Review recent lab tests, culture any suspect areas, assess temperature
- Review prescribed medications with patient and consider antibiotic treatment and/or topical steroids

**Minor bleeding with trauma (stops after 2 minutes):**
- Review CBC and assess platelets and hemoglobin
- Apply pressure to control bleeding

**Alteration in skin integrity:**
- May need to apply dressing to prevent infection to altered area, consider hydrocolloid dressings

### Patient Education and Follow-Up
- Review correct technique and timing of application of prescribed skin care products
- Instruct patient/family to call back if symptoms worsen or do not improve. Arrange for further assessment if indicated

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### GRADE 3
OR
Presence of the following:
Temperature greater than or equal to 38°C, uncontrolled pain, blisters and/or desquamation

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**EMERGENT:**
Requires IMMEDIATE medical attention

### Patient Care and Assessment
- Patients will generally require hospital admission. Notify physician of assessment, facilitate arrangements as necessary
- If on active treatment, will require dose delays, reduction or discontinuation of treatment
- See Chemotherapy Protocols in Resources & Referrals Section below for direction

### Management of Skin Complications

#### Pain:
- Increase dose and frequency (i.e. around the clock) of analgesics may be indicated

#### Local or systemic infection:
- Review recent lab tests
- Culture: Blood and any suspect areas
- Assess temperature every 4 hours or as clinically indicated
- Administer topical and/or IV anti-infective medications as prescribed (e.g. antibiotics, antifungals, antiviral agents)

#### Persistent bleeding or bleeding without trauma:
- Platelet transfusion may be ordered

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### RESOURCES & REFERRALS

#### Referrals
- Patient support center or telephone care management
- Home Health Nursing
- Physician, oncologist
- Pain and Symptom Management/Palliative Care (PSMPC)
- Dermatology
- Podiatrist

#### Related Online Resources
- E.g. Fair Pharmacare; BC Palliative Benefits. Can be found in "Other Sources of Drug Funding Section"
  - [http://www.bccancer.bc.ca/health-professionals/professional-resources/pharmacy/drug-funding](http://www.bccancer.bc.ca/health-professionals/professional-resources/pharmacy/drug-funding)

#### Bibliography List
- [http://www.bccancer.bc.ca/health-professionals/professional-resources/nursing/symptom-management](http://www.bccancer.bc.ca/health-professionals/professional-resources/nursing/symptom-management)

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