National Community Oncology Dispensing Association, Inc.
PASSION FOR PATIENTS

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Positive Quality Intervention: Afatinib (Gilotrif®) Management in Non-Small Cell Lung Cancer

Description: The purpose is to provide management of common adverse events, follow-up with patients, and dose modifications. Dose adjustments are common and greatly reduced frequency and severity of adverse reactions. In Lux-Lung 3, 43% maintained the 40mg starting dose, 38% reduced to 30mg and 19% further reduced to 20mg. Progression free survival remained consistent in patients with or without dose adjustments.

Background: Afatinib is indicated for the first-line treatment of EGFR positive (exon 19 or exon 21) metastatic non-small cell lung cancer (NSCLC). In addition, it is also indicated for the treatment of patients with metastatic squamous NSCLC progressing after platinum-based chemotherapy. Proper follow up including patient assessment is essential when new patients start on therapy. An increase number of patient touches are needed to ensure patients are being managed properly and are dose reduced appropriately. Weekly follow ups are ideal to assess adverse events.

PQI Process: Upon receipt of afatinib prescription:

- Ensure appropriate indication and dose. Keep in mind that dose holds and modifications occurred frequently in the clinical trials
- Afatinib Dose Management:
    - Hold therapy:
        - ≥ grade 3 adverse reactions
        - ≥ grade 2 diarrhea (persisting for 2 or more consecutive days while taking anti-diarrheal)
        - Cutaneous reactions (prolonged, lasting more than 7 days, or intolerable)
        - Renal impairment
        - Resume treatment at 10 mg less per day when adverse reaction fully resolves, returns to baseline, or improves to grade 1
    - Permanently Discontinue:
        - Life-threatening bullous, blistering, or exfoliative skin lesions
        - Confirmed interstitial lung disease (ILD)
        - Severe drug-induced hepatic impairment
        - Persistent ulcerative keratitis
        - Symptomatic left ventricular dysfunction
        - Severe or intolerable adverse reaction occurring at a dose of 20 mg per day

Patient Centered Activities:

- Provide Oncology Chemotherapy Education (OCE) sheet
- Counsel Patient
    - **Day 1 – Initial Patient Counseling**

Patient Centered Activities Continued:

- Educate patients on adverse events, **especially diarrhea and rash/acne** are expected and reassure patients that **dose modifications are common**
  - Provide patients with loperamide. Advise patients to take loperamide and call the office at the onset and continue anti-diarrheal until loose stools cease for 12 hours
  - Advise patients to call office at the onset of rash
  - Advise patients to immediately report any new or worsening lung symptoms, or any combination of the following symptoms: trouble breathing or shortness of breath, cough, fever
  - Advise patients to immediately report any symptoms of a liver problem: skin or the whites of eyes turn yellow, urine turns dark or brown (tea colored), pain on the right side of stomach, bleeds or bruises more easily than normal, lethargy

- **Days 7, 14, 21, 28– Patient Follow-Up**
  - Follow up on diarrhea and rash/acne
  - Follow up on other common reactions – Stomatitis and Paronychia
  - Follow up on less common reactions – dry skin, pruritus, keratitis, interstitial lung disease, hepatic toxicity

Supplemental Information

Diarrhea	Grade 1	Grade 2	Grade 3	Grade 4
	< 4 stools	4-6 stools	7 or more stools	Life-Threatening
	Increase of <4 stools/day over baseline, mild increase in ostomy output compared to baseline	Increase of 4-6 stools/day over baseline; not interfering with daily activities; IV fluids indicated, 24 hrs; moderate increase in ostomy output compared to baseline	Increase of +7 stools/day over baseline; incontinence; interfering with daily activities; IV fluid fluids ≥ 24 hrs; hospitalization; severe increase in ostomy output compared to baseline	Life-Threatening consequences (ex. hemodynamic collapse)
	Maintain dose	**Consider pausing**	**Hold**	**Hold**
	Continue same dose. Stop laxatives and advise patient to drink 8-10 glasses of water or clear fluids/day. Prescribe 4 mg loperamide taken immediately; followed by 2 mg after each loose stool (max. 16 mg/day) until bowel movements cease for 12 hours	Continue same dose unless grade 2 diarrhea continues for ≥ 48 hours, hold until reduced to grade 1 or below; resume with dose reduction; see grade 1; continue loperamide; assess for dehydration and electrolyte imbalance; consider IV fluid and electrolyte replacement	Hold until recovered to grade 1 or below and follow with dose reduction. In addition to grade 2 interventions, an infection process should be ruled out with stool cultures; aggressive IV fluid replacement for ≥ 24 hours; hospitalization to monitor progress; consider prophylactic antibiotics if patient is neutropenic	See Grade 3
Rash/ Acne	**Grade 1**	**Grade 2**	**Grade 3**	**Grade 4**
	Macular or papular eruptions or erythema without associated symptoms	Macular or papular eruptions with pruritus or other associated symptoms; localized desquamation or other lesions covering <50% of BSA	Severe, generalized erythroderma or macular, papular, or vesicular eruption; desquamation covering ≥ 50% of BSA; associated with pain, disfigurement, ulceration	Generalized exfoliative, ulcerative, or bullous dermatitis
	Maintain dose	**Hold**	**Hold**	**Discontinued**
	Topical Steroids or tacrolimus ointment alternative. Consider topical antibiotics twice daily. Recommend cream for isolated scattered lesions, and lotion for multiple scattered areas.	Topical steroid treatment as for grade 1 oral antibiotic (6 weeks) e.x. doxycycline 100 mg b.i.d., minocycline HCL 100 mg b.i.d., or, if available, oxytetracycline 500 mg b.i.d. Stop topical antibiotic if being used	Topical and systemic treatment as for grade 2. If Infection suspected, switch oral antibiotic to broad spectrum/gram negative coverage and consider skin swab for bacterial culture	Permanently discontinue for life-threatening bullous, blistering, or exfoliative skin lesions

Paronychia (Nails)	Grade 1	Grade 2	Grade 3	Grade 4
	Nail fold edema or erythema; disruption of the cuticle	Localized intervention indicated; oral intervention indicated (ex. antibiotic, antifungal, antiviral); nail fold edema or erythema with pain; associated with discharge or nail plate separation; limiting instrumental ADL	Surgical intervention or IV antibiotics indicted; limiting self-care activities of daily living (ADL)	N/A
	Maintain dose	**Prolonged: Pause**	**Hold**	N/A
	Topical antibiotics/antiseptics, vinegar soaks, and topical ultrapotent steroids	Topical antibiotics, vinegar soaks, silver nitrate application weekly, and topical ultrapotent steroids	Topical antibiotics, vinegar soaks, silver nitrate application weekly/ consider nail avulsion and systemic antibiotics	N/A
Stomatitis	**Grade 1**	**Grade 2**	**Grade 3**	**Grade 4**
	Erythema of the mucosa	Patchy ulcerations or pseudomembranes	Confluent ulcerations or pseudomembranes; bleeding with minor trauma	Tissue necrosis; significant spontaneous bleeding; life-threatening consequences
	Maintain dose	**Prolonged: Hold**	**Hold**	**Hold**
	Oral rinses with agents such as non-alcoholic mouthwash, normal saline, diluted salt and baking soda solution	Addition of topical analgesic mouth treatments, topical corticosteroids, antiviral therapy if herpetic infection confirmed, antifungal therapy preferably topical on a case by case basis	Same as for grade 2; institute additional symptomatic therapy (topical or systemic) as clinically indicated	Same as for grade 2; institute additional symptomatic therapy (topical or systemic) as clinically indicated