National Community Oncology Dispensing Association, Inc.
PASSION FOR PATIENTS

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Positive Quality Intervention: Oral Chemotherapy-Induced Peripheral Neuropathy

Description:

Chemotherapy-induced peripheral neuropathy (CIPN) is a serious side effect that can occur with chemotherapeutics, including certain oral chemotherapy agents. Appropriate patient education and monitoring may assist with identifying early signs of peripheral neuropathy, but no agents have demonstrated efficacy in preventing CIPN. When patients experience chronic peripheral neuropathy not relieved by dose reductions or interruptions, further treatment may be warranted. Currently, the strongest evidence supports the use of duloxetine as treatment for CIPN. Other agents have demonstrated mixed results but may be useful for individual patients.

Background:

CIPN can greatly affect a patient's quality of life and influence their cancer treatment regimen. Definitive algorithms for the management of CIPN are currently lacking as most trials on prevention and/or treatment have failed to produce clinically significant results. The presentation of CIPN varies depending on the mechanism of the chemotherapy agent, which could have implications on treatment choice[1]. The American Society of Clinical Oncology 2014 CIPN guidelines recommend only duloxetine for treatment and other agents as "reasonable to try;" the European Society for Medical Oncology and the National Comprehensive Cancer Network extrapolate treatments for non-cancer peripheral neuropathy to CIPN in their cancer pain guidelines[2-4]. Due to the paucity of evidence specific to CIPN and no evidence specific to oral CIPN, drug therapy is frequently based on trial and error with individual patients.

<u>Oral chemotherapy agents that commonly cause peripheral neuropathy</u> (incidence >10%)[5]

Brigatinib, capecitabine, crizotinib, encorafenib, imatinib, ivosidenib, ixazomib, lenalidomide, lorlatinib, pomalidomide, ponatinib, sorafenib, thalidomide, tretinoin, vemurafenib

Patient-specific considerations:

- Other causes of peripheral neuropathy
  - Diabetes[6,7]
    - If potential diabetic component to neuropathy, exploration of treatment options shown to be efficacious for diabetic neuropathy should be tried
    - E.g. glycemic control, pregabalin, tricyclic antidepressants, etc.
  - Vitamin B12 deficiency
  - Vasculitis

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- Comorbidities: Renal function, Cardiac function
- Drug interactions

Non-pharmacologic interventions[8]

- Consider integration of non-pharmacologic interventions into treatment plan such as using assistive devices, wearing hand/foot protection (oven mitts, gloves, socks/shoes), checking temperature of shower/bath before use with thermometer, and inspecting skin for cuts, abrasions, and burns that may not be felt daily.

Drug therapy[1-4, 9]

- Duloxetine[10]
  - Initiate at 30 mg by mouth daily x 1 week, then increase to 60 mg daily
  - Taper over 1-2 weeks if discontinuing therapy
  - Avoid use in severe renal insufficiency (CrCl < 30mL/min) and hepatic impairment
- Consider alternatives (less evidence)
  - Gabapentin
    - Initiate at 100 to 300 mg by mouth nightly, then divided 2-3 times per day as dose increases to maximum dose of 3600 mg/day
    - Titrate every 3 days to effect with slower titration for the elderly or frail
    - Adjust for renal insufficiency (CrCl < 60 mL/minute)
    - Taper over at least 1 week if discontinuing therapy
  - Pregabalin
    - Initiate at 25 mg by mouth nightly, then divided 2-3 times per day as dose increases to maximum dose of 600 mg/day
    - Titrate every 3 days to effect with slower titration for the elderly or frail
    - Adjust for renal insufficiency (CrCl < 60 mL/minute)
    - Taper over at least 1 week if discontinuing therapy
  - Venlafaxine
    - Initiate at 37.5 mg by mouth daily
    - Titrate every week to effect up to maximum 225 mg daily
    - Adjust for renal insufficiency (CrCl < 90 mL/minute for extended release and ≤ 70 mL/minute for immediate release)
    - Adjust for hepatic insufficiency (Child-Pugh class A-C)
    - Taper by approximately 75 mg every 4 days when discontinuing therapy
  - Tricyclic antidepressants
    - Initiate at low dose and increase every 5 to 7 days if tolerated

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        - Use with caution in patients with conduction abnormalities
        - Taper over approximately 4 weeks if discontinuing therapy
    - Opioids in combination with adjuvant therapy
    - Topical agents
        - Baclofen, amitriptyline, and ketamine
        - Gabapentin
        - Low-concentration menthol
        - Lidocaine

PQI Process: Upon receipt of an order for an oral chemotherapeutic with a known peripheral neuropathy side effect:

- Assess for baseline peripheral neuropathy prior to initiation of oral chemotherapy agent
- Patient education (refer to Patient-Centered Activities)
- Regularly assess patient for development of peripheral neuropathy throughout therapy
- If peripheral neuropathy develops, ensure provider visit to address CIPN occurs
- Recommend appropriate dose interruptions or modifications as indicated
- If further intervention is necessary, recommend drug therapy options for the treatment of CIPN based on patient-specific factors such as comorbidities and drug interactions
- Assess patient for change in symptoms within first 2 weeks of starting CIPN treatment

Patient Centered Activities:

- Counsel patient on peripheral neuropathy
    - Signs and symptoms (discomfort or pain, numbness, tingling, burning, weakness, impaired hot/cold sensory perception in hands or feet)
    - Potential timeline for onset if known
    - Management options if neuropathy develops
- For initiation of CIPN treatment, counsel patient on new therapy
    - Titration schedule
    - Side effects
        - Duloxetine: drowsiness, fatigue, nausea, sexual dysfunction
        - Gabapentin: peripheral edema, emotional lability, drowsiness, dizziness
        - Pregabalin: peripheral edema, weight gain, drowsiness, dizziness
        - Venlafaxine: insomnia, drowsiness, nausea, sexual dysfunction, anorexia
        - Tricyclic antidepressants: sedation, arrhythmia, weight gain, dry mouth
    - Risks of abrupt discontinuation
- Ensure patients have contact information for the clinic and know when to call in

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