Care Step Pathway - Ocular Toxicity

Look:

- Does the patient look unwell (or ill)?
- Does the patient look uncomfortable?
- Is there eye drainage or tearing?
- Is there any eye redness?
- Is the patient sensitive to light?
- Is there lid or periocular edema?
- Are there skin lesions surrounding the eye(s)?
- Are pupils reactive?

Listen:

- Patient and family descriptions of ocular health and any current or prior history of eye problems (e.g., glaucoma, retinal issues, eye inflammation)
- Reports of specific eye complaints: redness, watering, drainage, change in acuity, diplopia (double vision), floaters, photophobia?
- When did symptoms start?
- Any recent eye injury, new medications, or exposure to toxic chemicals?
- Did the patient wear contact lenses?
- Is the patient diabetic?
- Associated symptoms: headache, vomiting, nausea?

Recognize:

- Patients at risk for ocular issues (history of glaucoma, dry eyes, uveitis, retinal disease, macular degeneration, or diabetes)
- The specific ocular complaint (if possible) and determine grade
- Other treatment-related symptoms

Grading Toxicity (Overall, Eye Disorders)

Grade 1 (Mild)	Grade 2 (Moderate)	Grade 3 (Severe)	Grade 4 (Potentially sight-threatening)
Asymptomatic; clinical or diagnostic observations only, no change in vision	Symptomatic (pain, irritation, photosensitivity, etc.); visual acuity decrease 1-3 lines in affected eye(s)	Highly symptomatic (pain, irritation, photosensitivity, etc.), vision decrease 3-6 lines in affected eye(s)	Vision decrease by >6 lines or 20/400 or worse in affected eye(s)

RED FLAGS:

- Sudden vision disturbances such as photosensitivity, eye pain, and redness
- Patient is unable to perform regular ADLs because of ocular issues
- Gradual or sudden visual loss
- Concern for permanent loss of vision

Management

Overall Strategy:

- Refer for baseline ophthalmic examination before beginning therapy (ophthalmologist should be made aware that patient is to start tisotumab vedotin-tftv therapy)
- Follow-up exams should be performed before each of the first nine cycles of tisotumab vedotin-tftv and if patient develops symptoms
- Advise patient to promptly report any changes in vision or any eye symptoms (and anticipate treatment hold pending further evaluation)
- Identify and closely monitor at-risk patients (including those with a history of glaucoma, dry eyes, uveitis, retinal disease, macular degeneration)
  - In patients with diabetes, promote good control of blood glucose since it reduces risk of retinal disease
- Advise patients to refrain from wearing contact lenses and be meticulous about eye hydration and hygiene

Specific Ocular Issues: drug can cause inflammation in any tissue of the eye, patients may complain for light sensitivity, pain, decrease vision

- Conjunctivitis/Episcleritis (inflammation of the eye surface): cool compresses, artificial tears/gels
- Keratitis (inflammation of cornea): artificial tears, lubricants, or corticosteroids drops, antibiotics
- Iritis/Uveitis/Vitritis (inflammation of various portions of the inside eye): corticosteroids drops, mydriatic ophthalmic drops
- Myositis (inflammation of the eye muscles): subtenon's corticosteroid injection or oral steroids
- Scleritis (inflammation of the white of the eye): topical steroids subtenon's corticosteroid injection or oral steroids
- Optic neuropathy/optic neuritis (jflammation of the optic nerve) subtenon's corticosteroid injection, oral or intravenous steroids and drug discontinuation
- Inflammatory orbitopathy (inflammation of the orbital tissue or lacrimal gland)- subtenon's corticosteroid injection, oral or intravenous steroids
- Retinopathy/vasculitis/retinal detachment (fluid accumulation under layers of retina): subtenon's corticosteroid injection, oral or intravenous steroids and drug hold/dose reduction/discontinuation
- Retinal vein occlusion (vascular event leading to vision changes, macular edema, glaucoma): anti-VEGF or steroid injection in addition to drug discontinuation
- Retinal pigment epithelial detachment (bilateral or multifocal separation of the retina from back of eye, leading to sudden vision changes): drug hold/dose reduction/discontinuation
- Choroidopathy/neovascular membrane- anti-VEGF injection drug hold/dose reduction/discontinuation

Grade 1 (Mild)

- Asymptomatic; clinical or diagnostic observations only, no change in vision
  - Conjunctivitis drug may be continued with caution; see ophthalmologist to start preservative free artificial tears (PFATs) or gels
  - Superficial punctate keratitis (SPK): drug may be continued with caution; see ophthalmologist to start PFATs or gels
  - Confluent superficial keratitis: 1st episode- recommend frequent gels
  - Anterior chamber reaction (mild)- start prednisone acetate 1% or difluprednate 0.05%, if posterior synechiae seen, start mydriatric like mydriacyl, cyclogel or atropine
- Support adherence to topical eye drops

Grade 2 (Moderate)

- Symptomatic (pain, irritation, photosensitivity, etc.); vision decrease 1-3 lines in affected eye(s)
- Urgent referral to ophthalmology (within 24 hours)
- Specific therapy dose modifications/holds/discontinuations:
  - Conjunctivitis or SPK: 2nd occurrence – reinforce use of PFATs and gels, withhold drug until </= grade 1, then resume at the same dose
  - Confluent SPK: 2nd occurrence – reinforce use of frequent PFATs and gels, withhold drug until </= grade 1, then resume at the same dose
  - Corneal ulceration: 1st occurrence – culture ulcer and start topical antibiotics withhold drug until complete corneal re-epithelialization, then resume drug at next lower level
  - Anterior chamber reaction (severe)- start prednisone acetate 1% or difluprednate 0.05%, if posterior synechiae seen, start mydriatric like mydriacyl, cyclogel or atropine
  - Retinal pigment epithelial detachment: withhold drug until </= grade 1, then resume at the same dose
  - Myositis/Orbitopathy- give subtenon's injection of triamcinolone acetonide 40mg/ml) up to 1ml) or start oral prednisone taper 60mg taper Uveitis (persistent Grade 2 or >6 weeks duration): hold drug (resume when improved to Grade 0/1)
- Support adherence to eye drops
- Anticipate drug holds/dose modifications of targeted therapy for other moderate ocular toxicities, per prescribing information
- Obtain ophthalmology clearance prior to restarting therapy

Grades 3 or 4 (Severe)

- Highly symptomatic (pain, irritation, photosensitivity, etc.), vision decrease >3 lines in affected eye(s)
- Urgent referral to ophthalmology (within 24 hours)
- Specific drug modifications/holds/discontinuations:
  - Ulcerative keratitis or perforation: start on topical antibiotics permanently discontinue drug,repair perforation
  - Posterior chamber reaction (mild to moderate)- give subtenon's injection of triamcinolone acetonide 40mg/ml) up to 1ml) or start oral prednisone taper 60mg taper Uveitis (persistent Grade 2 or >6 weeks duration): hold drug (resume when improved to Grade 0/1)
  - Posterior chamber reaction (severe)- give subtenon's injection of triamcinolone acetonide 40mg/ml) up to 1ml) or start oral prednisone taper 60mg taper over 6-8 weeks, hold drug until until </=grade 1, if persistant grade 2 or >6 weeks, discontinue drug
  - Corneal ulcer: 2nd occurrence – culture ulcer and start topical antibiotics, discontinue drug
  - Retinal pigment epithelial detachment: withhold drug until </= grade 1 then reduce dose or discontinue if no improvement after 3 weeks.
  - Serous retinal detachment: withhold drug until </= grade 1 then reduce dose or discontinue if no improvement after 3 weeks.
  - Retinal vein occlusion: start anti-VEGF therapy discontinue drug
  - Optic neuropathy/optic neuritis- oral or intravenous steroids and drug discontinuation
  - Obtain ophthalmology clearance prior to restarting therapy