CME

Herpes zoster: A primary care approach to diagnosis and treatment

Angela Kelley, PA-C

ABSTRACT

Herpes zoster, or shingles, caused by a reactivation of the chickenpox virus, can occur in patients of any age, but is more common in older adults. Patient history is critical in reaching a diagnosis, not only to manage the outbreak effectively, but also to prevent severe complications such as dissemination of the virus into the central nervous system. This article describes recent changes in diagnostic testing, treatment, prevention, and practice guidelines as well as the approach clinicians should take when evaluating patients with herpes zoster and assessing risk for complications.

Keywords: herpes zoster virus, vesicular rash, dermatomes, ophthalmic nerve, shingles, chickenpox

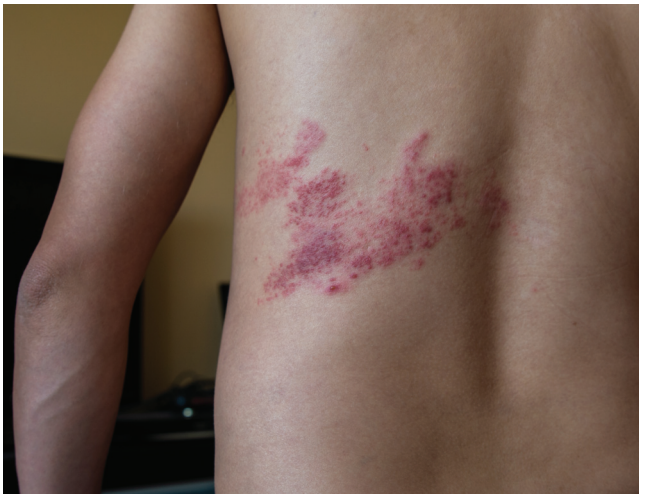
Learning objectives

- Identify clinical findings that would indicate HZV infections.
- Determine how aggressively to treat to prevent complications from HZV.
- Identify the common risk factors for HZV.
- Recognize how anatomy plays a role in the identification of HZV.
- Incorporate new data on prevention and treatment for a practical approach to treating patients with HZV.

A 40-year-old woman presented to a primary care clinic with 3 days of facial pain and rash. She had no past medical, surgical, social, or family history that was significant for this presentation. She described the rash as painful blisters located near her left temple and extending to the top of her left eyelid (**Figure 1**). She tried over-the-counter (OTC) topical anti-itch and steroid creams, which did not help. OTC analgesics and anti-inflammatories also failed to relieve her pain, which progressed from a 2 on the first day of the rash to a current rating of 7 on a 0-to-10 pain intensity rating scale.

Angela Kelley is director of didactic education and an assistant professor in the PA program at Gannon University's Ruskin (Fla.) Campus. The author has disclosed no potential conflicts of interest, financial or otherwise.

DOI:10.1097/01.JAA.0000892712.73041.ae



© TRYBEX/SHUTTERSTOCK.COM

The patient's vital signs were within normal limits. Her physical examination revealed no abnormalities except for vesicular lesions that followed a dermatomal pattern on her left temple, forehead, into her left upper eyelid with an additional vesicle below the left lower eyelid. She had a slight decrease in movement upon opening her mouth on the left side, secondary to pain approaching her temple.

Laboratory results from a physical she had 3 weeks earlier showed no significant abnormalities in her complete blood cell count, comprehensive metabolic panel, lipid panel, and thyroid-stimulating hormone level. Because psychologic stress is a precursor to herpes zoster outbreaks, a Generalized Anxiety Disorder (GAD)-7 anxiety scale was performed in the office and revealed that the patient was suffering from moderate anxiety. When asked for more details, she reported that her stress had escalated over the past month because of a looming deadline affecting a possible job promotion.

Because of the dermatomal pattern and clinical manifestation of the rash, the patient was diagnosed with herpes zoster, also known as shingles. She recalled that she had chickenpox as a child in 1983, and had not received the varicella vaccination. Because she only had allergies to macrolides, the patient was started on valacyclovir 1,000 mg three times a day for 7 days and gabapentin 300 mg once daily for 1 day, then tapered up to three times a day for pain over the next 2 days. She was instructed about potential adverse reactions to these medications and advised to return in 4 weeks to discuss

Key points

- Herpes zoster, or shingles, is caused by a reactivation of the chickenpox virus. It can occur in patients of any age, but is more common in older adults.
- Patient history is critical to effectively managing the outbreak and to prevent severe complications such as HZO and PHN.
- Treatment with antivirals and medications for pain control only appear to be effective if taken within the first 72 hours of symptom onset.
- Varicella vaccination is recommended for nonpregnant adults who do not have evidence to support immunity to the varicella virus.

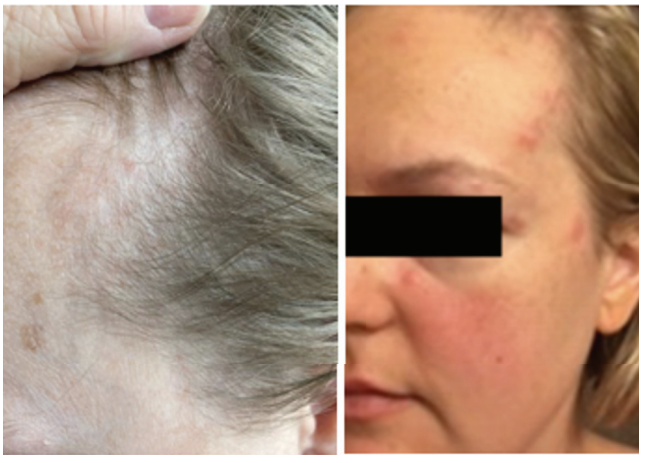


FIGURE 1. The patient's rash

weaning from the gabapentin based on her pain level. She was referred to an ophthalmologist because of her risk for herpes zoster ophthalmicus (HZO).

ABOUT HERPES ZOSTER

Herpes zoster, or shingles, is a common diagnosis that is well known not only to medical professionals, but also to patients because of the significant amount of pain that the condition can cause. Fortunately, clinicians can use preventive and therapeutic measures to control the frequency and complications of outbreaks. Although most cases occur in patients over age 50 years, many younger patients can develop this painful condition.

In a patient who has had an initial varicella zoster virus (VZV) infection, the virus remains in a latent state in the patient's dorsal root ganglia, and can reactivate later to cause herpes zoster.[1] According to the CDC, an estimated one out of three people in the United States develops herpes zoster at some point during their lifespan, which leads to an estimated 1 million cases per year.[2] A retrospective study found that herpes zoster incidence in patients ages 35 years and older increased from 2.5 patients per 1,000 in 1993 to 6.1 in 2006 and 7.2 in 2016.[3] The same researchers evaluated the data in younger patients from 1998 to 2016, with one analysis occurring in patients under age 18 years and one in patients under age 35 years. They found that 0.22 of 1,000 children in the youngest age ranges (ages 3 to 5 years and under age 3 years) had a herpes zoster incidence during the time of the study. As the age of the study population increased, incidences in the study also increased, with more than 4 out of 1,000 incidences occurring at age 34 years.[4]

Fully determining epidemiologic data for herpes zoster is challenging for multiple reasons. For example, clinicians often associate this condition with patients over age 50 years; however, as with the case patient, those infected with the varicella virus as young children may present with shingles in their younger years. Others who may present to clinicians with herpes zoster are patients who were born before the development and administration of the varicella vaccine in 1996, but who were not old enough to receive the shingles vaccine, which is recommended for patients age 50 years and older, although patients age 18 years and older may be given the vaccine if they are at increased risk for herpes zoster.[5] Beginning in 1996, the varicella vaccine was initially given in one dose; however, due to continued breakthrough infections, a second dose was recommended in 2006.[4] The CDC reports that the one-dose varicella vaccine is 85% effective against multiple forms of varicella, as well as close to 100% effective against severe cases of varicella.[6] The newer two-dose vaccine was shown to be 88% to 98% effective against all forms of varicella in postlicensure clinical trials, and 100% effective against severe cases of varicella.[6] Also, many children are exposed to VZV due to not being administered vaccines for multiple reasons, such as parental preference to withhold vaccines, socioeconomic factors due to cost, and lack of health insurance. Occasionally, children who were vaccinated against varicella present to clinics with the clinical manifestations and laboratory titers of core antibodies of varicella. Breakthrough infections of varicella led to the recommendation of adding a second dose of the varicella vaccine to children.[4]

PATHOPHYSIOLOGY AND RISK FACTORS

As mentioned, herpes zoster is a reactivation of previous VZV infection.[7] Advancing age is the most common risk factor for herpes zoster. Other risk factors include exposure to VZV in utero or before age 1 year, patients with immunocompromised states or who take immunosuppressants, and other conditions that can lower a patient's immunity, such as being a recipient of hematopoietic stem-cell transplants or organ transplants, psychological stress, and physical trauma.[7,8]

CLINICAL PRESENTATION

The most common presentation of herpes zoster is a vesicular rash that presents on the body in a dermatomal pattern. Dermatomes, which are patterns of sensory nerves

that originate from a single spinal nerve or cranial nerve root, can be located easily by clinicians according to **Figure 2**. The herpes zoster rash pattern usually only affects one to two adjacent dermatomal regions as a manifestation of cutaneous herpes zoster. However, the dermatomal rash can involve three or more dermatomes and is then considered to be disseminated zoster.[2,7] The rash associated with herpes zoster commonly appears on the trunk and does not cross the body's midline unless it is widespread.

A painful, tingly, or itchy sensation is noted with the rash, which could begin several days after a prodromal period of sensitivity. Herpes zoster also can manifest on the trigeminal nerve (cranial nerve [CN] V), and commonly appears on the ophthalmic branch, which is the first branch of the trigeminal nerve (**Figure 3**). If not diagnosed promptly, ophthalmic branch involvement can lead to complications, such as dissemination of the virus into the central nervous system (CNS).[7]

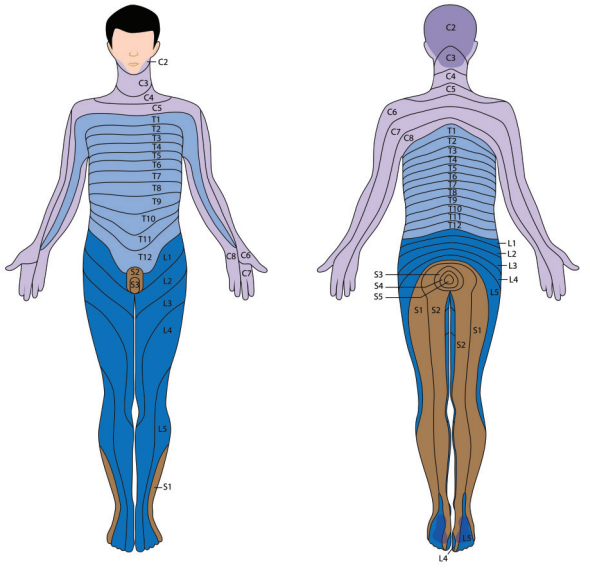


FIGURE 2. Dermatomes

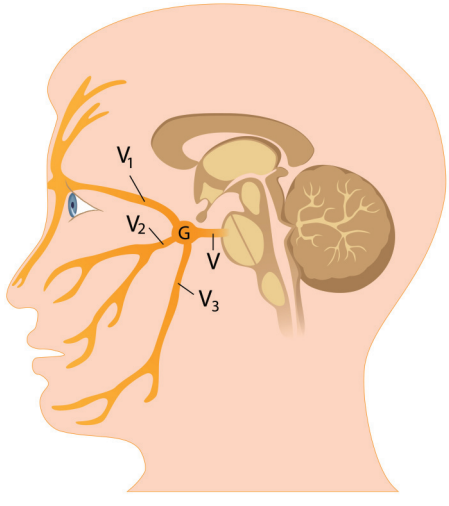


FIGURE 3. Trigeminal nerve

DIFFERENTIAL DIAGNOSES

The differential diagnosis for herpes zoster depends on the anatomical location of the vesicular rash as well as the stage of presentation. Herpes simplex virus (HSV) can cause a vesicular rash, but a dermatomal pattern is less common unless the HSV infection is recurrent.[7] When taking the patient's history, ask about previous chickenpox infection or if the patient has been vaccinated against the varicella virus. If neither are confirmed, consider primary VZV (chickenpox) in the differential. Other differentials include impetigo, insect bites, medication reactions, cellulitis, and smallpox.[7] For patients presenting with pain similarly to the case patient, consider trigeminal neuralgia; however, pain in only the ophthalmic branch of CN V is rare. Most often in patients with trigeminal neuralgia, the second and/or third branches of CN V (maxillary and mandibular nerves) have the associated pain and patients are less likely to present with a vesicular rash.[9] Other possible diagnoses for pain in the trigeminal nerve include atypical face pain, or trigeminal neuropathies caused by autoimmune disorders such as scleroderma, systemic lupus erythematosus, and Sjögren syndrome.[9]

DIAGNOSTIC TESTING AND DIAGNOSIS

Diagnosis of herpes zoster most commonly is made clinically based on patient presentation. However, numerous methods for confirmation are available if needed in atypical cases.[2] Polymerase chain reaction (PCR) testing has the most sensitivity and specificity for detecting herpes zoster, and can be performed using vesicle fluid, cerebrospinal fluid (CSF), corneal swabs, or blood. Other diagnostic testing includes viral culture, saliva testing, direct fluorescent antibody testing (DFA), Tzanck smear, and serology. The serologic tests include laboratory tests such as VZV immunoglobulin G and M (IgG and IgM). Although DFA, viral cultures, and PCR have higher specificity, serology testing is used infrequently due to its lower sensitivity and specificity, because patients often have positive IgG results at the onset of the cutaneous reaction.[2] CSF testing is rarely used because it requires invasive techniques usually reserved for patients with CNS presentation of the virus, such as in disseminated complicated cases.[7]

COMPLICATIONS

Postherpetic neuralgia (PHN) is a chronic debilitating condition that can last long after the acute viral phase of herpes zoster, and which occurs in 9% to 34% of patients.[10] Diagnosis is made clinically; however, clinicians must be mindful of PHN if a patient presents with pain along dermatomes before presence of a rash. Antibody testing for herpes zoster can be helpful to test in these precipitating situations if zoster is in the differential.

TABLE 1. Oral antiviral treatment for adults[7,12]

	Dosage	Route	Recommended length of therapy
Valtrex/valcyclovir	1 g three times/day	Oral	7 days
Famvir/famciclovir	500 mg three times/day	Oral	7 days
Zovirax/acyclovir	800 mg five times/day	Oral	7-10 days
Acyclovir	10 mg/kg three times/day	IV	5-10 days or until resolved clinically

Between 8% and 20% of patients with herpes zoster develop HZO, which affects the first (ophthalmic) branch of CN V and can lead to vision loss if not treated promptly.[11] In addition to the vesicular presentation and pain, patients with HZO may have fever, headache, fatigue, and the Hutchinson sign--vesicular lesions around the tip of the nose, indicating involvement of the nasociliary branch and a much higher risk for ocular involvement.[11] A patient with HZO also may present with signs of blepharitis, keratitis episcleritis, and conjunctivitis of the eyelid.[11] A thorough examination of the eye includes recommendations for fundoscopic examination, visual acuity testing, slit-lamp examination including fluorescein staining, and ocular tonometry to evaluate for elevated intraocular pressure (IOP). Prompt referral to ophthalmology is warranted for any positive finding.[11]

Ramsay Hunt syndrome, also known as herpes zoster oticus, affects the facial and auditory nerves. This is a rare complication, characterized by severe ear pain, facial muscle weakness, numbness of the anterior tongue, hearing impairment, vertigo, and tinnitus. These symptoms and physical examination findings can mislead clinicians to mistake this complicated presentation as a stroke.[7]

TREATMENT

Herpes zoster is treated with antivirals and medications for pain control (Table 1), but medications only appear to be effective if taken within the first 72 hours of symptom onset.[7] Systemic IV treatment is reserved for immunocompetent patients with moderate or severe pain, nontruncal involvement, severe rash, and age over 50 years, as well as patients with immunocompromise and those with CNS, visceral, or disseminated infection.[7]

Because no antivirals are FDA-approved for herpes zoster in children, dosages occasionally are based on dosing for chickenpox.[7] Antiviral treatment should begin within 48 hours of rash onset, although it can begin within 72 hours for all patients.[7] Most adverse reactions to antivirals are headache and gastrointestinal symptoms.

Table 2 gives examples of medications used to control pain in patients with herpes zoster. In patients with mild to moderate pain levels, acetaminophen and NSAIDs typically

TABLE 2. Treatments for pain control[7,10,12,20]

	Level/type of pain	Dosage	Route	Recommended length of therapy	Maximum dosage/day	Schedule of medication
Acetaminophen	Mild to moderate	325-1,000 mg every 4-6 hours	Oral	As needed for pain	4,000 mg/day	N/A
NSAIDs	Mild to moderate	400 mg every 4-6 hours	Oral	As needed for pain	Ibuprofen, 2,400 mg/day	N/A
Oxycodone	Moderate to severe	Titrate every 2 days from 5 mg to 30 mg every 4-6 hours	Oral	As needed for pain	120 mg/day	Schedule II
Tramadol	Moderate to severe	Titrate from 50 mg to 100 mg once to twice daily	Oral	As needed for pain	• 300 mg/day if patient is over age 75 years • 400 mg/day otherwise	Schedule IV
Gabapentin	PHN	Titrate 100-300 mg three times/day	Oral	As needed for pain	3,600 mg/day	Varies by state: OTC, prescription, schedule II-V
Pregabalin	PHN	75 mg once to twice daily	Oral	As needed for pain	600 mg/day	Schedule V
Nortriptyline	PHN	25 mg at bedtime	Oral	As needed for pain	150 mg/day	N/A
Lidocaine patch 5%	PHN	1 patch applied every 12 hours	Transdermal		3 patches at a time	N/A

are used. Oxycodone and tramadol have been approved for patients with moderate to severe pain.[12,13] Some of the most common adverse reactions to oxycodone and tramadol are constipation, nausea, somnolence, and dizziness.[12,13]

Some notable changes in pain control are the new classifications of schedules for tramadol and gabapentin, used in patients with PHN, due to concern for abuse and misuse.[13] Because of the potential for harm when gabapentin is combined with opioids, as well as the abuse potential of gabapentin alone, many states have instituted reporting to the prescription drug monitoring program (PDMP), and many states have classified this medication as a scheduled substance.[14] Clinicians are encouraged to seek information based on their prescribing authority in each state as to whether a DEA license is required to prescribe these medications.

First-line options for PHN are gabapentin, pregabalin, or tricyclic antidepressants. Gabapentin and pregabalin are FDA-approved for PHN in adults.[10] Some of the most common adverse reactions to these medications are peripheral edema, fatigue, and nausea. Tricyclic antidepressants can be titrated for pain control for PHN. If a clinician has a concern with prescribing medications that might alter the CNS in older adults, topical lidocaine in various forms can be prescribed as first-line treatment.

HZO typically is treated with oral antivirals and prompt referral to an ophthalmologist. **Table 3** lists other treatments and preventive measures for complications such as keratitis, glaucoma, and scarring of the pupil. These additional options are considered by clinicians in managing complications from iritis to retinal necrosis. Topical and/or systemic corticosteroids also have been used, but data are conflicting about the use of corticosteroids in patients with viral infections, so patient cases should be considered individually.[7] On occasion, topical antibiotics such as erythromycin ointment are used to prevent secondary bacterial infections, and ophthalmologists may consider debridement if a patient presents with epithelial keratitis.[11]

TABLE 3. Additional treatments[7]

- Topical or systemic corticosteroids to treat or prevent iritis, episcleritis, or keratitis (data conflict)
- Mydriatic eyedrops to reduce pupil scarring
- IV acyclovir for severe cases of HZV
- Medications to lower ocular pressure in patients with glaucoma
- Intravitreal antiviral therapy for retinal necrosis in patients with immunocompromise

PROGNOSIS

In nonophthalmic herpes zoster in immunocompetent patients, skin lesions tend to resolve in 2 to 4 weeks although complete resolution may take longer than 4 weeks.[7] In patients with a more severe presentation of the virus, older adults, and those with immunocompromise, healing may take longer.[7] The prognosis for HZO varies depending on patient risk factors, the timing of diagnosis and treatment, and how advanced the infection is at presentation. If an immunocompetent patient receives treatment early on in the infection, the vesicles usually resolve within 4 weeks.[11]

PREVENTION AND PATIENT EDUCATION

VZV can be transmitted to infants and small children who have not yet received the varicella vaccine, and pregnant and immunocompromised patients. Therefore, contact precautions should be used to prevent this spread until vesicular lesions have crusted completely.[7]

Shingrix The two-shot recombinant zoster vaccine (Shingrix) is FDA-approved for patients age 50 years and older as well as immunocompromised adults and patients over age 18 years with immunodeficiencies.[1,15] Patients should postpone the Shingrix vaccination until after pregnancy to prevent any potential complications in utero.[16] The live herpes zoster vaccine, Zostavax, is no longer available in the United States.[2,16]

VZV vaccine Because exposure to VZV is the cause of herpes zoster, varicella vaccination is recommended for nonpregnant adults who do not have evidence to support immunity to the varicella virus.[16] The varicella vaccine is contraindicated in pregnant patients because of unknown risks to the fetus.[17] The CDC also recommends that nonpregnant patients who have received the varicella vaccine should refrain from becoming pregnant for 1 month after vaccination.[17]

VARIZIG Pregnant patients, infants, and patients with immunocompromise are at a high risk for severe varicella.[18] If someone in this group has been exposed to varicella, postexposure prophylaxis with varicella zoster immune globulin (VARIZIG) might be considered.[18] VARIZIG is indicated in immunocompromised adults, immunocompromised children, adults who do not show evidence of immunity to varicella, pregnant patients, newborns whose mothers become infected with varicella just before or just after delivery, premature infants, and infants under age 1 year.[19] As postexposure prophylaxis, VARIZIG can reduce the severity of varicella.[19] Headache, chills, nausea, rash, fatigue, and pain at the injection site are the most common adverse reactions to this vaccine.[19]

CASE CONCLUSION

The case patient reported at her follow-up appointment that the ophthalmologist performed a thorough evaluation and determined that she had not yet developed HZO. She was advised by her ophthalmologist to continue the medications she was prescribed at her primary care visit, and she also was prescribed ciprofloxacin ophthalmic drops to treat any potential corneal ulceration and to prevent a secondary bacterial infection. The patient was followed very closely by her specialist to determine if mydriatic eyedrops or other treatments would be needed to prevent

further complications. She was started on medications to help with her anxiety and stress level and also was advised to use other stress-reduction methods. On her physical examination, the vesicles had crusted and she stated that her pain level was improving. She was advised to begin tapering the gabapentin to twice a day and if that controlled her pain, she could taper to once a day and discontinue the medication after 7 days of tapering.[20] **JAAPA**

Earn Category I CME Credit by reading both CME articles in this issue, reviewing the post-test, then taking the online test at http://cme.aapa.org. Successful completion is defined as a cumulative score of at least 70% correct. This material has been reviewed and is approved for 1 hour of clinical Category I (Preapproved) CME credit by the AAPA. The term of approval is for 1 year from the publication date of December 2022.

REFERENCES

1. Tseng HF, Bruxvoort K, Ackerson B, et al. The epidemiology of herpes zoster in immunocompetent, unvaccinated adults ≥50 years old: incidence, complications, hospitalization, mortality, and recurrence. *J Infect Dis*. 2020;222(5):798-806.
2. Centers for Disease Control and Prevention. Shingles (herpes zoster). www.cdc.gov/shingles/hcp/clinical-overview.html. Accessed September 14, 2022.
3. Harpaz R, Leung JW. The epidemiology of herpes zoster in the United States during the era of varicella and herpes zoster vaccines: changing patterns among older adults. *Clin Infect Dis*. 2019;69(2):341-344.
4. Harpaz R, Leung JW. The epidemiology of herpes zoster in the United States during the era of varicella and herpes zoster vaccines: changing patterns among children. *Clin Infect Dis*. 2019;69(2):345-347.
5. US Food and Drug Administration. Shingrix prescribing information. www.fda.gov/vaccines-blood-biologics/vaccines/shingrix. Accessed August 17, 2022.
6. Centers for Disease Control and Prevention. Varicella vaccine effectiveness and duration of protection. www.cdc.gov/vaccines/vpd-vac/varicella/hcp-effective-duration.htm. Accessed September 22, 2022.
7. Ridzon R, Fedorowicz Z, Iacoviello V. Herpes zoster. www.dynamed.com/condition/herpes-zoster. Accessed August 17, 2022.
8. Srivastava RM, Katiyar V, Agrawal S. Posttraumatic maxillary and ophthalmic herpes zoster in an immune-competent female--a unique presentation. *Oman J Ophthalmol*. 2020;13(1):46-47.
9. Callaghan BC, van Zuuren EJ, Rae-Grant A. Cranial neuropathies. www.dynamed.com/condition/cranial-neuropathies. Accessed August 17, 2022.
10. Schwartz HB, Fedorowicz Z, Rae-Grant A. *Postherpetic neuralgia*. www.dynamed.com/condition/postherpetic-neuralgia. Accessed September 22, 2022.
11. Minor M, Payne E. Herpes zoster ophthalmicus. Treasure Island, FL: StatPearls Publishing. https://pubmed.ncbi.nlm.nih.gov/32491711. Accessed August 17, 2022.
12. US Drug Enforcement Agency. Diversion Control Division. Oxycodone (trade names: Tylox, Percodan, OxyContin). www.deadiversion.usdoj.gov/drug_chem_info/oxycodone/oxycodone.pdf. Accessed September 22, 2022.
13. US Drug Enforcement Agency. Diversion Control Division. Tramadol (trade names: Ultram, Ultracet). www.deadiversion.usdoj.gov/drug_chem_info/tramadol.pdf. Accessed August 17, 2022.
14. Peckham AM, Ananickal MJ, Sclar DA. Gabapentin use, abuse, and the US opioid epidemic: the case for reclassification as a controlled substance and the need for pharmacovigilance. *Risk Manag Healthc Policy*. 2018;11:109-116.
15. Anderson TC, Masters NB, Guo A, et al. Use of recombinant zoster vaccine in immunocompromised adults aged ≥19 years: recommendations of the Advisory Committee on Immunization Practices--United States, 2022. *MMWR Morb Mortal Wkly Rep*. 2022;71(3):80-84.
16. Ostrovsky D, Fedorowicz Z, Randall D. Immunizations in adults. www.dynamed.com/prevention/immunizations-in-adults. Accessed September 22, 2022.
17. Centers for Disease Control and Prevention. Guidelines for vaccinating pregnant women. www.cdc.gov/vaccines/pregnancy/hcp-toolkit/guidelines.html. Accessed August 17, 2022.
18. Levin MJ, Duchon JM, Swamy GK, Gershon AA. Varicella zoster immune globulin (VARIZIG) administration up to 10 days after varicella exposure in pregnant women, immunocompromised participants, and infants: varicella outcomes and safety results from a large, open-label, expanded-access program. *PLoS One*. 2019;14(7):e0217749.
19. VARIZIG prescribing information. Saol Therapeutics. https://varizig.com/liquid-product_info.html. Accessed September 22, 2022.
20. US Food and Drug Administration. Neurontin (gabapentin) prescribing information. www.accessdata.fda.gov/drugsatfda_docs/label/2017/020235s064_020882s047_021129s046lbl.pdf. Accessed September 22, 2022.