PHARMCON freeCE

Transmission of and Vaccination Against Hepatitis

0.25 CREDIT HOURS

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PHARMACIST OBJECTIVES

1. Recognize first-line treatment options for hepatitis B and hepatitis C in the United States

PHARMACY TECHNICIAN OBJECTIVES

1. Recognize first-line treatment options for hepatitis B and hepatitis C in the United States

OVERVIEW

Micro-learning opportunities were created in response to evidence that learning is maximized when delivered in short and focused 'bursts.' In this session, hepatitis B and hepatitis C treatments will be examined from a broad perspective.

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TARGET AUDIENCE

Pharmacist, Pharmacy Technician

AUTHOR DISCLOSURE

Pete Kreckel reports no financial relationship with the manufacturer(s) or provider(s) of any commercial interest(s) or service(s) that appear in this program.

ACPE UNIVERSAL ACTIVITY NUMBER

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Hepatitis B therapy seems to be improving. Vemlidy® seems to be a game-changer and probably is the most commonly used treatment for hepatitis B.

I did comb through our warehouse's online catalog, and all of the oral drugs mentioned, except Tyzeka™, were available for next-day shipment. The vaccines are so extremely effective, that hopefully these therapies won't be needed in the future.

Drugs to Treat Hepatitis B Infection

- Hepatitis B rates have declined by 82% since 1990
- For the unfortunate remaining 18%, we can discuss drug therapy for treatment of hepatitis B
    - 15-25% of chronically infected people develop chronic liver disease, including cirrhosis, liver failure, or liver cancer

First-line treatments

- Tenofovir disoproxil fumarate (Viread®) is an NRTI for treatment of HIV
    - Dose: 300 mg once daily
    - $1200/month
    - Mechanism: blocks HBV DNA polymerase, the enzyme that is necessary for the virus to replicate in liver cells
    - Available in the United States as a treatment for HIV infection in adults since 2001
    - Approved for hepatitis B in 2008
    - Best option for Lamivudine resistance
    - Resistance has yet to be identified
- Tenofovir alafenamide (Vemlidy®)
    - Approved November 2016
    - Dose: 25 mg once daily
    - $1100.00/month
    - Like Viread®, is also a nucleoside analog reverse transcriptase inhibitor
    - Indicated for the treatment of chronic hepatitis B virus infection in adults with compensated liver disease
    - Alafenamide salt is preferred if pregnant
    - Advantages over Viread®:
        - Fewer adverse effects on bone density and renal function
        - Most patients should be switched from Viread® to Vemlidy® given the most favorable side effect profile
        - Vemlidy® and Viread® are similar in terms of efficacy, however, Vemlidy® achieves similar results to Viread at a dose less than one-tenth that of Viread®
        - Vemlidy® has greater plasma stability, enabling it to deliver tenofovir to hepatocytes more efficiently
        - Renal dosing is not required for Vemlidy®, but is required for all other hepatitis B treatments
- Here's why:
    - Systemic exposure to tenofovir disoproxil fumarate (TDF) can cause nephrotoxicity and a decrease in bone mineral density
    - Unlike TDF, which is converted extensively in plasma to tenofovir, TAF activation occurs intra-cellularly
    - TAF 10 mg once-daily produced circulating tenofovir levels that were 91% lower, BUT the intracellular levels were 4 times higher than a dose of the TDF 300 mg

Treatment duration:

- Hepatitis B e-antigen (HBeAg)-positive chronic hepatitis:
    - Treat ≥1 year until HBeAg seroconversion and undetectable serum HBV DNA; continue therapy for ≥6 months after HBeAg seroconversion
- HBeAg-negative chronic hepatitis: Treat >1 year until hepatitis B surface antigen (HBsAg) clearance
- Decompensated liver disease: Lifelong treatment is recommended

Second-line treatments

- Seldom used; might be considered if cost is a concern
- Entecavir (Baraclude®)
    - Bristol Myers Squibb
    - Approved December 2005
    - Indication:
        - Nucleoside analogue approved for chronic Hepatitis B infection
        - Treatment of adults with evidence of active viral replication and either evidence of persistent elevations in ALT or AST or histologically active disease
        - Has no activity against HIV.
    - Entecavir should not be used for patients with lamivudine-resistant HBV, since resistance has been observed in up to 50% of lamivudine-refractory patients after five years of treatment
    - Dosage is 0.5 mg daily
        - Give 1 mg daily if lamivudine-resistant
    - NOTE: Generic is available
        - Cost is $400/month
        - Brand – $1,400/month
    - Adverse reactions:
        - Black box:
            - Lactic acidosis
            - Hepatomegaly with steatosis
        - Neurological: Headache
        - Gastrointestinal: diarrhea and indigestion as well as fatigue
- Lamivudine (Epivir HBV®) 100 mg tablets
    - Approved December 1998
    - Indication: Hepatitis B infection and HIV infection
    - Mechanism:
        - Inhibits both HBV DNA polymerase and HIV reverse transcriptase
        - Completely inhibits HBV polymerase at concentrations that have negligible effects on host DNA polymerase
        - Has intracellular half-life many hours longer than plasma half-life, which allows for infrequent dosing
    - Warnings/Precautions/Adverse Effects:
        - Black Box Warning: Lactic acidosis, hepatomegaly with steatosis
        - Neurological: Headache, insomnia, depressive disorders
        - Gastrointestinal: Nausea, vomiting, diarrhea, anorexia
        - Respiratory: Cough, nasal signs and symptoms
        - General: Malaise and fatigue, fever, and rash

- Drug Interactions:
  - Trimeth/Sulfa: increases Lamivudine AUC by approximately 44%
    - No change in dose of either drug is recommended.
- Patient Information:
  - Must be followed under care of physician while on medication
  - Not a cure for the disease, does not reduce transmission risk to other partners
  - Compliance is a must—do not miss doses
  - May see redistribution of body fat
- NOTE: dosage for HBV is 100 mg/day
  - Dosage for HIV is: 300 mg/day, either 150 mg BID or 300 mg QD
  - This drug is well-tolerated, but drug resistant mutations do occur
    - After 1 year, 15%; 2 years, 38%; 3 years, 56%; 4 years, 67% resistance
- Lamivudine is also used for prevention of re-infection after transplantation for hepatitis B-induced cirrhosis
  - Dose: 100 mg daily
  - Begin 4 weeks before transplant and continue for at least 12 months post-transplant

- Adefovir (Hepsera®)
  - Approved September 2002
  - Indication:
    - For HBV, typically not recommended due to weak anti-viral activity
  - Mechanism:
    - Inhibits HBV DNA polymerase by competing with natural substrate deoxyadenosine triphosphate and causing DNA chain termination, after incorporation into viral DNA
  - Warnings/Precautions/Adverse Effects:
    - Use with caution in patients with renal dysfunction
    - Clearance is influenced by renal fx
    - 25% show exacerbation of hepatitis upon discontinuation
    - Black box: lactic acidosis, hepatomegaly with steatosis,
    - Neurological: Headache
    - Gastrointestinal: Nausea, vomiting, diarrhea, anorexia
    - General: Malaise and fatigue, fever, and rash
- Telbivudine (Tyzeka™) by Idenix
  - Approved October 2006
  - Only available through specialty pharmacies
  - Mechanism of Action: Telbivudine is a synthetic thymidine nucleoside analogue with activity against HBV DNA polymerase
  - In practice:
    - Telbivudine appears to have slightly more potent antiviral effects compared with lamivudine and adefovir
    - Adverse events (myopathy and peripheral neuropathy) make it a seldom-used choice, compared with alternative antiviral agents
  - Dosage (Adults and Adolescents [16 years of age]): 600 mg once daily, taken orally, with or without food
    - Renal adjustment (30-49 ml/min): 600 mg every other day
    - Renal adjustment (<30 ml/min): 600 mg every 72 hours

    - Warnings:
        - Lactic acidosis and severe hepatomegaly with steatosis, including fatal cases, have been reported with the use of nucleoside analogues alone or in combination with antiretrovirals
        - Pregnancy Category B
        - Do not breastfeed while taking Tyzeka™
- Pegylated interferon-alpha-2a (Pegasys®)
    - Dosed at 180 mcg given sub-q for 48 weeks
    - May exacerbate auto immune diseases, thyroid diseases, infectious diseases
    - Causes flu like symptoms, headache, bone marrow suppression and fatigue.

Treatment-naïve patients with chronic positive HBV

Name	Pegylated Interferon alpha-2a	Lamivudine	Adefovir	Entecavir	Telbivudine	Tenofovir (Viread®) (Vemlidy®)
Brand	Pegasys®	Epivir®	Hepsera®	Baraclude®	Tyzeka™	Viread® Vemlidy® 25 mg
Dose	180 mcg/wk	100 mg/day	10 mg/day	0.5 mg/day	600 mg	300 mg/ 25 mg
Route	SC	oral	oral	oral	oral	oral
Duration	48wk	>48wk	>48wk	48wk	>52	>48
Viral resistance (1-year)	none	15-30%	none	none	6%	none
Histologic improvement	38% at week 72	49-62%	53-68%	72%	35%	74%

- Best treatment options: Tenofovir (Viread or Vemlidy)
    - Ideal for treatment-naïve
    - Most treatment failures are due to poor adherence
- Best reference: https://www.aafp.org/pubs/afp/issues/2019/0301/p314.html

--Have a great day on the bench!!

Activity Test

Transmission of and Vaccination Against Hepatitis

Activity tests must be completed online at www.freeCE.com.
A passing grade of 70 or higher and completion of an online activity evaluation are required to earn credit.

1. **Which of the following medications is the best option to treat lamivudine-resistant hepatitis B?**
   A. Tenofovir disoproxil (Viread®)
   B. Tenofovir alafenamide (Vemlidy®)
   C. Entecavir (Baraclude®)
   D. Adefovir (Hepsera®)

2. **This hepatitis C combination therapy is approved for an 8-week regimen compared to the other combination regiments which all have a 12-week regimen:**
   A. Sofosbuvir/velpatasvir (Epclusa®)
   B. Glecaprevir/pibrentasvir (Mavyret®)
   C. Ledipasvir/sofosbuvir (Harvoni®)
   D. Elbasvir/grazoprevir (Zepatier®)