Chronic Hepatitis C Virus (HCV) Genotype 1 Guidelines

American Association for the Study of Liver Diseases (AASLD) has released practice guidelines for the management of chronic hepatitis C in patients with genotype 1. Medical literature has been reviewed through June 2011 for the development of these guidelines. Peginterferon alpha plus ribavirin has been the standard of care. In genotype 1 chronic hepatitis C, dual therapy is given for 48 weeks. Sustained virologic response (SVR) is typically 40–50 percent. The new oral NS3/4A serine protease inhibitors, boceprevir (Victrelis®) and telaprevir (Incivek®), have demonstrated potent inhibition of HCV genotype 1 replication and a markedly improved SVR.

SVR rates with boceprevir in clinical trials were 63–66 percent. SVR rates with telaprevir in clinical trials were 69–75 percent. Some of the highlights include

- Treatment recommendation for all patients:
  - Boceprevir or telaprevir should be used in combination with peginterferon and ribavirin (Class 1; level A). Boceprevir and telaprevir should not be used as monotherapy due to the risk of development of viral resistance (Class 1; level A).
  - Treatment recommendation for treatment-naïve patients:
    - Boceprevir 800 mg with food given 3 times daily (every 7–9 hours) in addition to peginterferon and weight-based ribavirin for 24–44 weeks. Patients received peginterferon alfa and ribavirin for 4 weeks as lead-in treatment before boceprevir is initiated (Class 1; level A).
      - In patients without cirrhosis treated with boceprevir, HCV RNA level at weeks 8 and 24 are undetectable, shortened course of therapy may be considered for a total of 28 weeks (4 weeks of lead-in peginterferon alfa/ribavirin followed by 24 weeks of triple therapy) (Class 2a, level B).
      - Treatment with triple drug therapy should be stopped if HCV RNA level is > 100 IU/mL at treatment week 12 or detectable at treatment week 24 (Class 2a, level B).
    - Telaprevir 750 mg should be given with food 3 times daily (every 9 hours) with peginterferon alfa and weight-based ribavirin for 12 weeks followed by an additional 12–36 weeks of peginterferon alfa and ribavirin (Class 1, level A).
      - In patients without cirrhosis treated with telaprevir, HCV RNA level at weeks 4 and 24 are undetectable, shortened course of therapy may be considered for a total of 24 weeks (Class 2a, level A).
      - Telaprevir with peginterferon alfa and ribavirin should be discontinued if HCV RNA is > 1,000 IU/mL at treatment weeks 4 or 12 and/or detectable at treatment week 24 (Class 2a, level B).
    - Patients with cirrhosis treated with boceprevir or telaprevir in combination with peginterferon alfa and ribavirin should receive therapy for 48 weeks (Class 2b, level B).
- Treatment recommendation for treatment-experienced patients:
  - Re-treatment with boceprevir or telaprevir in combination with peginterferon alfa and weight-based ribavirin can be recommended for patients who had virologic relapse or were partial responders after a prior course of treatment with standard interferon alfa or peginterferon alfa and/or ribavirin (Class I, level A).
  - Re-treatment with telaprevir in combination with peginterferon alfa and weight-based ribavirin may be considered for prior null responders to a course of standard interferon alfa or peginterferon alfa and/or ribavirin (Class 2b, level B).
  - Response-guided therapy of treatment-experienced patients with either boceprevir or telaprevir regimens may be considered for relapers (boceprevir: Class 2a, level B; telaprevir: Class 2b, level C).
  - Response-guided therapy of treatment-experienced patients with either boceprevir or telaprevir regimens may be considered for partial responders (boceprevir: Class 2b, level B; telaprevir: Class 3, level C).
  - Null responders should not be treated with response-guided therapy to shorten the course of treatment (Class 3, level C).
  - Patients being re-treated with boceprevir with peginterferon alfa and ribavirin who have detectable HCV RNA > 100 IU at week 12 should be discontinued from all therapy, as there is a high likelihood of developing antiviral resistance (Class 1, level B).
  - Patients being re-treated with telaprevir with peginterferon alfa and ribavirin who have detectable HCV RNA > 1,000 IU at weeks 4 or 12 should be discontinued from all therapy, as there is a high likelihood of developing antiviral resistance (Class 1, level B).

Sources:
www.aasld.org
www.ashp.org
www.fda.gov
www.medscape.com
www.ashp.org
www.PTCommunity.com
www.pubmed.gov

Editorial Staff:
Executive Editor: Maryam Tabatabai, PharmD
Deputy Editors: Kris Rawlings, PharmD
Carole Kerzic, RPh

Contact Information:
Maryam Tabatabai, PharmD
(513) 794-5265 or www.MagellanMedicaid.com
<table>
<thead>
<tr>
<th>Generic Name</th>
<th>Trade Name</th>
<th>Description</th>
<th>Applicant</th>
<th>FDA Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>ipratropium bromide/albuterol sulfate</td>
<td>Combivent® Respimat®</td>
<td>Ipratropium bromide / albuterol sulfate (Combivent Respimat) is indicated for chronic obstructive pulmonary disease (COPD) for patients who require a second bronchodilator. Combivent Respimat, a propellant-free inhaler, is a suitable alternative for patients who are currently using Combivent® (ipratropium bromide and albuterol sulfate) Inhalation Aerosol. Combivent Inhalation Aerosol is being phased out because it contains chlorofluorocarbons (CFCs), chemical compounds that decrease the ozone layer. Combivent Respimat will be available in mid-2012. Combivent Respimat is given as 1 inhalation 4 times a day, not to exceed 6 inhalations in 24 hours.</td>
<td>Boehringer Ingelheim</td>
<td>FDA NDA Approval 10/07/2011</td>
</tr>
<tr>
<td>tadalafil</td>
<td>Cialis®</td>
<td>Tadalafil (Cialis) is now indicated for the treatment of the signs and symptoms of benign prostatic hyperplasia (BPH) and for the treatment of erectile dysfunction and the signs and symptoms of BPH. Tadalafil is given as 5 mg once daily for BPH without regard to food or to timing of sexual activity. Tadalafil should not be used in combination with alpha blockers for the treatment of BPH. Tadalafil is available in 2.5 mg, 5 mg, 10 mg, and 20 mg tablets.</td>
<td>Lilly</td>
<td>FDA New Indication Approval 10/07/2011</td>
</tr>
<tr>
<td>sitagliptin/simvastatin</td>
<td>Juvisync™</td>
<td>Sitagliptin/simvastatin (Juvisync) is indicated in patients for whom treatment with both sitagliptin and simvastatin is appropriate. Sitagliptin is a dipeptidyl peptidase-4 (DPP-4) inhibitor indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus. Simvastatin is an HMG-CoA reductase inhibitor (statin) indicated as an adjunctive therapy to diet to (1) reduce the risk of total mortality by reducing CHD deaths and reduce the risk of non-fatal myocardial infarction, stroke, and the need for revascularization procedures in patients at high risk of coronary events; (2) reduce elevated total-C, LDL-C, Apo B, TG and increase HDL-C in patients with primary hyperlipidemia (heterozygous familial and nonfamilial) and mixed dyslipidemia; (3) reduce elevated TG in patients with hypertriglyceridemia and reduce TG and VLDL-C in patients with primary dysbetalipoproteinemia; (4) reduce total-C and LDL-C in adult patients with homozygous familial hypercholesterolemia. Sitagliptin/simvastatin should not be used in patients with type 1 diabetes or for the treatment of diabetic ketoacidosis. Juvisync will be available in the following combinations: 100 mg/10 mg, 100 mg/20 mg, and 100 mg/40 mg per day. The recommended usual starting dose is 100 mg/40 mg once a day in the evening.</td>
<td>Merck</td>
<td>FDA NDA Approval 10/07/2011</td>
</tr>
<tr>
<td>deferiprone</td>
<td>Ferriprox®</td>
<td>Deferiprone (Ferriprox) is an iron chelator indicated for the treatment of patients with transfusional iron overload due to thalassemia syndromes when current chelation therapy is inadequate. Safety and effectiveness have not been established for the treatment of transfusional iron overload in patients with other chronic anemias. Approval is based on a reduction in serum ferritin levels. There are no controlled trials demonstrating a direct treatment benefit, such as improvement in disease-related symptoms, functioning, or increased survival. Warnings for deferiprone include neutropenia and agranulocytosis and require weekly monitoring of absolute neutrophil count. Dosing is weight-based and administered orally three times daily. Deferiprone will be available as a 500 mg tablet.</td>
<td>ApoPharma</td>
<td>FDA NDA Approval 10/14/2011</td>
</tr>
<tr>
<td>exenatide</td>
<td>Byetta®</td>
<td>Exenatide (Byetta) is now indicated for add-on therapy to insulin glargine, with or without metformin and/or a TZD, in conjunction with diet/exercise for adults with type 2 diabetes who are not achieving adequate glycemic control on insulin glargine alone. The risk of hypoglycemia is increased when exenatide is used in combination with a sulfonylurea. When using exenatide in combination with insulin, the dose of insulin should be evaluated. In patients at increased risk of hypoglycemia consider reducing the dose of insulin. Previously, exenatide was approved as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.</td>
<td>Amylin</td>
<td>FDA New Indication Approval 10/19/2011</td>
</tr>
<tr>
<td>clobazam</td>
<td>Onfi™</td>
<td>Clobazam (Onfi), a benzodiazepine, is approved as an adjunctive (add-on) treatment for seizures associated with Lennox-Gastaut syndrome in adults and children two years of age and older. Clobazam is generally administered twice daily and is dosed based on body weight. Clobazam is a Schedule IV drug under the Controlled Substances Act. Onfi will be available as 5 mg, 10 mg, and 20 mg tablets in January 2012.</td>
<td>Lundbeck</td>
<td>FDA NDA Approval 10/21/2011</td>
</tr>
</tbody>
</table>