Complete Summary

GUIDELINE TITLE

Diagnosis, management, and treatment of hepatitis C.

BIBLIOGRAPHIC SOURCE(S)

Strader DB, Wright T, Thomas DL, Seeff LB. Diagnosis, management, and treatment of hepatitis C. Hepatology 2004 Apr;39(4):1147-71. [213 references] PubMed

GUIDELINE STATUS

This is the current release of the guideline.

**** REGULATORY ALERT ****

FDA WARNING/REGULATORY ALERT

Note from the National Guideline Clearinghouse: This guideline references a drug(s) for which important revised regulatory and/or warning information has been released.

- July 31, 2008, Erythropoiesis Stimulating Agents (ESAs): Amgen and the U.S. Food and Drug Administration (FDA) informed healthcare professionals of modifications to certain sections of the Boxed Warnings, Indications and Usage, and Dosage and Administration sections of prescribing information for Erythropoiesis Stimulating Agents (ESAs). The changes clarify the FDA-approved conditions for use of ESAs in patients with cancer and revise directions for dosing to state the hemoglobin level at which treatment with an ESA should be initiated.
- January 24, 2008, Leukine (sargramostim): Voluntary market suspension of the current liquid formulation of sargramostim, a granulocyte-macrophage colony-stimulating factor (GM-CSF), because of an upward trend in spontaneous reports of adverse reactions, including syncope (fainting). The lyophilized form of the drug is not affected. See the U.S. Food and Drug Administration (FDA) web site for more information.
- November 8, 2007 and January 3, 2008 Update, Erythropoiesis Stimulating Agents (ESAs): The U.S. Food and Drug Administration (FDA) notified healthcare professionals of revised boxed warnings and other safety-related product labeling changes for erythropoiesis-stimulating agents (ESAs) stating serious adverse events, such as tumor growth and shortened survival in patients with advanced cancer and chronic kidney failure.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Hepatitis C

GUIDELINE CATEGORY

Diagnosis
Evaluation
Management
Treatment

CLINICAL SPECIALTY

Family Practice
Gastroenterology
Infectious Diseases
Internal Medicine
Preventive Medicine

INTENDED USERS

Advanced Practice Nurses
Health Care Providers
Nurses
Physician Assistants
Physicians

GUIDELINE OBJECTIVE(S)

To provide clinicians with approaches to the diagnosis, management, and prevention of hepatitis C virus (HCV) infection

TARGET POPULATION

Screening

- Persons who have injected illicit drugs in the recent and remote past, including those who injected only once and do not consider themselves to be drug users
- Persons with conditions associated with a high prevalence of hepatitis C virus (HCV) infection, including:
    - Persons with human immunodeficiency virus (HIV) infection
    - Persons with hemophilia who received clotting factor concentrates before 1987
    - Persons who were ever on hemodialysis
    - Persons with unexplained abnormal aminotransferase levels
- Prior recipients of transfusions or organ transplants, including:
    - Persons who were notified that they had received blood from a donor who later tested positive for HCV infection
    - Persons who received a transfusion of blood or blood products before July 1992
    - Persons who received an organ transplant before July 1992
- Children born to HCV-infected mothers
- Health care, emergency medical, and public safety workers after a needle stick injury or mucosal exposure to HCV-positive blood
- Current sexual partners of HCV-infected persons

Counseling/Treatment

- Hepatitis C virus-infected adults and children

INTERVENTIONS AND PRACTICES CONSIDERED

Diagnosis

1. Testing for hepatitis C virus (HCV) infection
2. Counseling on how to avoid HCV
3. Laboratory testing including testing for HCV antibodies, HCV ribonucleic acid (RNA), HCV genotyping, liver biopsy

Initial Treatment

1. Pegylated interferon (peginterferon) alfa and ribavirin
2. 48-week treatment for persons with genotype-1 HCV infection and 24-week treatment for persons with genotype-2 or 3 HCV infection
3. Acetaminophen, nonsteroidal anti-inflammatory drugs, antidepressants, and, occasionally, growth factors for management of adverse events

Note: Routine use of growth factors, such as epoetin and granulocyte colony-stimulating factor (G-CSF) was considered but not recommended

Retreatment of Persons Who Failed to Respond to Previous Treatment

1. Peginterferon plus ribavirin for persons who have undergone previous regimens of treatment using non-pegylated interferon

Diagnosis and Treatment of HCV-Infected Children

1. Testing (including liver biopsy) as in adults
2. Interferon alfa-2b and ribavirin for children aged 3 to 17 years

Diagnosis and Treatment of Persons with Human Immunodeficiency Virus (HIV) Coinfection

1. Anti-HCV testing
2. HCV RNA testing
3. Peginterferon alfa plus ribavirin
4. Substituting didanosine by an equivalent before beginning ribavirin
5. Liver transplantation

Treatment of Persons with Renal Disease

1. Liver biopsy
2. Interferon
3. Peginterferon monotherapy (awaiting results of ongoing controlled trials)

Treatment of Persons with Decompensated Cirrhosis

1. Considering referral for liver transplantation
2. Antiviral therapy with close monitoring of adverse events
3. Growth factors for treatment-associated anemia (epoetin) and leukopenia (G-CSF, and granulocyte-macrophage CSF [GM-SCF])

Treatment of Patients after Solid Organ Transplantation

1. Treatment of liver transplant recipients with caution and close monitoring of adverse events
2. Treatment is generally contraindicated in other solid organ transplant (heart, lung, kidney)

Treatment of Persons with Acute Hepatitis C

1. Confirmation of the diagnosis by HCV RNA measuring in serum
2. Interferon or peginterferon
3. Delay treatment for 2 to 4 months for spontaneous resolution

Treatment of Active Injection Drug Users

1. Individualized decisions to treat persons who currently use illicit drugs or who are on methadone maintenance program
2. Continued support from drug abuse and psychiatric counseling services

MAJOR OUTCOMES CONSIDERED

- Risk factors for hepatitis C virus infection transmission
- Predictors of treatment response
- Efficacy and safety of treatment

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

A formal review and analysis of the recently published world literature on the topic (Medline search)

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Grade I: Randomized controlled trials

Grade II-1: Controlled trials without randomization

Grade II-2: Cohort or case-control analytic studies

Grade II-3: Multiple time series, dramatic uncontrolled experiments

Grade III: Opinions of respected authorities, descriptive epidemiology

METHODS USED TO ANALYZE THE EVIDENCE

Review of Published Meta-Analyses
Systematic Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus
Informal Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

Not stated

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

The guideline developers reviewed published cost analyses.

METHOD OF GUIDELINE VALIDATION

Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Not stated

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Recommendations are followed by quality of evidence ratings (Grades I, II-1, II-2, II-3, III), which are defined at the end of the "Major Recommendations" field.

Testing and Counseling

Testing

1. Persons who should be tested for HCV infection **(Grade III)**:
    - Persons who have injected illicit drugs in the recent and remote past, including those who injected only once and do not consider themselves to be drug users
    - Persons with conditions associated with a high prevalence of hepatitis C virus (HCV) infection, including:
        - Persons with human immunodeficiency virus (HIV) infection
        - Persons with hemophilia who received clotting factor concentrates before 1987
        - Persons who were ever on hemodialysis
        - Persons with unexplained abnormal aminotransferase levels
    - Prior recipients of transfusions or organ transplants, including:
        - Persons who were notified that they had received blood from a donor who later tested positive for HCV infection
        - Persons who received a transfusion of blood or blood products before July 1992
        - Persons who received an organ transplant before July 1992
    - Children born to HCV-infected mothers
    - Health care, emergency medical, and public safety workers after a needle stick injury or mucosal exposure to HCV-positive blood
    - Current sexual partners of HCV-infected persons*

NOTE: Adapted from Recommendations for prevention and control of hepatitis C virus (HCV) infection and HCV-related chronic disease. Centers for Disease Control and Prevention MMWR Recomm Rep 1998;47(RR-19):1–39.

*Although the prevalence of infection is low, a negative test in the partner provides reassurance, making testing of sexual partners of benefit in clinical practice.

Counseling

2. Persons infected with HCV should be counseled on how to avoid HCV transmission to others (refer to Table 3 in the original guideline document for more information) **(Grade III)**.

Laboratory Testing

3. Patients suspected of having chronic HCV infection should be tested for HCV antibodies **(Grade II-2)**.
4. HCV ribonucleic acid (RNA) testing should be performed in (a) patients with a positive anti-HCV test **(Grade II-2)**; (b) patients for whom antiviral treatment is being considered, using a quantitative assay **(Grade II-2)**; and (c) patients with unexplained liver disease whose anti-HCV test is negative and who are immune-compromised or suspected of having acute HCV infection **(Grade II-2)**.
5. HCV genotype should be determined in all HCV-infected persons prior to treatment in order to determine the duration of therapy and likelihood of response **(Grade I)**.
6. Regardless of the level of alanine aminotransferase (ALT), a liver biopsy should be done when the results will influence whether treatment is recommended, but a biopsy is not mandatory in order to initiate therapy **(Grade III)**.
7. A liver biopsy may be obtained to provide information on prognosis **(Grade III)**.

Initial Treatment of HCV Infection

8. The treatment of choice is pegylated interferon (peginterferon) plus ribavirin **(Grade I)**.
9. For patients for whom liver histology is available, treatment is indicated in those with more-than-portal fibrosis **(Grade III)**.
10. Treatment decisions should be individualized based on the severity of liver disease, the potential of serious side effects, the likelihood of treatment response, and the presence of comorbid conditions **(Grade III)**.

Genotype-1 HCV Infection

11. Treatment with peginterferon plus ribavirin should be planned for 48 weeks, using ribavirin doses of 1,000 mg for those $\leq$75 kg in weight and 1,200 mg for those more than 75 kg **(Grade I)**.
12. Quantitative serum HCV RNA should be performed at the initiation of, or shortly before, treatment and at week 12 of therapy **(Grade I)**.
13. Treatment may be discontinued in patients who do not achieve an early virologic response (EVR) at 12 weeks, although the decision should be

individualized according to the tolerability of therapy, severity of underlying liver disease, and demonstration of some degree of biochemical and/or virologic response **(Grades I, III)**.

14. Persons whose treatment continues through 48 weeks, and whose qualitative measurement of HCV RNA at that time is negative, should be retested for HCV RNA 24 weeks later to document a sustained virologic response (SVR) **(Grade II-1)**.

Genotype-2 or Genotype-3 HCV Infection

15. Treatment with peginterferon plus ribavirin should be administered for 24 weeks, using a ribavirin dose of 800 mg **(Grade I)**.
16. Persons whose treatment continues for the full 24 weeks, and whose qualitative measurement of HCV RNA at that time is negative, should be retested for HCV RNA 24 weeks later to document an SVR **(Grade II-1)**.

Retreatment of Persons Who Failed to Respond to Previous Treatment

17. Retreatment with peginterferon plus ribavirin should be considered for nonresponders or relapsers who have significant fibrosis or cirrhosis and who have undergone previous regimens of treatment using nonpegylated interferon **(Grade II-3)**.
18. Retreatment with peginterferon plus ribavirin with the aim of eradicating HCV is not indicated in patients who have failed to respond to a prior course of peginterferon plus ribavirin, even if a different type of peginterferon is administered **(Grade III)**.

Special Patient Groups

19. Regardless of the serum aminotransferase levels, the decision to initiate therapy with interferon and ribavirin should be individualized based on the severity of liver disease by liver biopsy, the potential of serious side effects, the likelihood of response, and the presence of comorbid conditions **(Grade III)**.

Diagnosis and Treatment of HCV-Infected Children

20. Diagnosis and testing (including liver biopsy) of children suspected of having chronic HCV should proceed as with adults **(Grade II-2)**.
21. Because of the high rate of clearance of the HCV virus within the first year of life and the level of anxiety that may be caused by an early positive test, routine testing for HCV RNA in infants born to HCV-infected mothers is not recommended. Testing with anti-HCV may be performed at 18 months or later. If an earlier diagnosis is desired, PCR for HCV RNA may be performed at or after the infant's first well-child visit at 1 to 2 months **(Grade I)**.
22. Children aged 3-17 who are infected with hepatitis C and are considered appropriate candidates for treatment may receive therapy with interferon alfa-2b and ribavirin, administered by those experienced in treating children **(Grades I, III)**.
23. Treatment of children under the age of 3 years is contraindicated **(Grade III)**.

Diagnosis, Natural History, and Treatment of Persons With HIV Coinfection

24. Anti-HCV testing should be performed in all HIV-infected persons **(Grade III)**.
25. HCV RNA testing should be performed to confirm HCV infection in HIV-infected persons who are positive for anti-HCV, as well as in those who are negative and have evidence of unexplained liver disease **(Grade III)**.
26. Hepatitis C should be treated in the HIV/HCV-coinfected person in whom the likelihood of serious liver disease and a treatment response are judged to outweigh the risk of morbidity from the adverse effects of therapy **(Grade III)**.
27. Initial treatment of hepatitis C in most HIV-infected persons is peginterferon alfa plus ribavirin for 48 weeks **(Grade III)**.
28. Given the high likelihood of adverse events, HIV/HCV-coinfected patients on HCV treatment should be monitored closely **(Grade III)**.
29. Ribavirin should be used with caution in persons with limited myeloid reserves and in those taking zidovudine and stavudine. When possible, patients receiving didanosine should be switched to an equivalent antiretroviral before beginning therapy with ribavirin **(Grade III)**.
30. HIV-infected patients with decompensated liver disease may be candidates for orthotopic liver transplantation **(Grade III)**.

Treatment of Persons With Renal Disease

31. The decision to perform a liver biopsy in patients with renal disease should be individualized based on the clinical assessment of the need for therapy and the need to establish the severity of liver disease **(Grade III)**.
32. Eligible patients with renal insufficiency or end-stage renal disease and HCV may be treated with interferon **(Grade II-2)**.
33. Treatment with peginterferon alfa-2a monotherapy at a dose of 135 micrograms subcutaneously (SQ)/wk for patients on hemodialysis may be considered, with close monitoring for interferon toxicity. However, a firm recommendation regarding the use of peginterferon monotherapy must await results of ongoing controlled trials **(Grade III)**.
34. Patients with renal failure should not be treated with ribavirin **(Grade II-2)**.

Treatment of Persons With Decompensated Cirrhosis

35. Patients with clinically decompensated cirrhosis should be referred for consideration of liver transplantation **(Grades I, III)**.
36. Antiviral therapy may be initiated at a low dose in patients with mild degrees of hepatic compromise, as long as treatment is administered by experienced clinicians, with vigilant monitoring for adverse events, preferably in patients who have already been accepted as candidates for liver transplantation **(Grade II-3)**.
37. Growth factors can be used for treatment-associated anemia (epoetin) and leukopenia (G-CSF, GM-CSF) and may limit the need for antiviral dose reductions in patients with decompensated cirrhosis **(Grade III)**.

Treatment of Patients After Solid Organ Transplantation

38. Treatment of HCV-related disease following liver transplantation should be undertaken with caution because of the increased risk of adverse events and should be performed under the supervision of a physician experienced in transplantation **(Grade II-2)**.
39. Antiviral therapy is generally contraindicated in recipients of heart, lung, and kidney grafts **(Grade III)**.

Treatment of Persons With Acute Hepatitis C

40. The diagnosis of acute hepatitis C in patients with new-onset, unexplained liver disease should be confirmed by measuring HCV RNA in serum **(Grade II-2)**.
41. Although excellent results were achieved in reported uncontrolled studies using standard interferon monotherapy, it is appropriate to consider the use of peginterferon because of its improved ease of administration **(Grade III)**.
42. No recommendation can be made about the addition of ribavirin, and the decision will therefore need to be considered on a case-by-case basis **(Grade III)**.
43. In the absence of controlled study data, no definitive recommendations can be made about the timing of treatment initiation; however, it seems reasonable to delay treatment for 2 to 4 months after acute onset to allow for spontaneous resolution **(Grade II-3)**.
44. No definitive recommendation can be made about the duration of treatment needed to treat acute hepatitis C; however, it seems reasonable to continue treatment for at least 6 months **(Grade II-3)**.

Treatment of Active Injection Drug Users

45. Treatment of HCV infection should not be withheld from persons who currently use illicit drugs or who are on a methadone maintenance program, provided they wish to take HCV treatment and are able and willing to maintain close monitoring and practice contraception **(Grade III)**.
46. The decision of whether to treat should be made considering the anticipated risks and benefits for the individual **(Grade III)**.
47. Continued support from drug abuse and psychiatric counseling services is an important adjunct to treatment of HCV infection in persons who use illicit drugs **(Grade III)**.

Definitions:

Quality of Evidence

Grade I: Randomized controlled trials

Grade II-1: Controlled trials without randomization

Grade II-2: Cohort or case-control analytic studies

Grade II-3: Multiple time series, dramatic uncontrolled experiments

Grade III: Opinions of respected authorities, descriptive epidemiology

CLINICAL ALGORITHM(S)

Two algorithms are provided in the original guideline document for:

1. Managing and Treating Patients with Chronic Hepatitis C Virus (HCV) Infection, Genotype 1.
2. Managing and Treating Patients with Chronic HCV Infection, Genotype 2 or 3.

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of evidence is specifically stated for each recommendation (see the "Major Recommendations" field).

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Improved diagnosis and treatment of hepatitis C virus (HCV) infection and prevention of HCV infection complications

POTENTIAL HARMS

Adverse events of medication

In general, the incidence and types of side effects of peginterferon alfa plus ribavirin are similar to those identified for interferon plus ribavirin. Approximately 75% of those treated experience 1 or more of the following systemic side effects:

1. Those typically associated with interferon alfa, such as neutropenia, thrombocytopenia, depression, hypothyroidism and hyperthyroidism, irritability, concentration and memory disturbances, visual disturbances, fatigue, muscle aches, headaches, nausea and vomiting, skin irritation, low-grade fever, weight loss, insomnia, hearing loss, tinnitus, interstitial fibrosis and hair thinning. "Flu-like" symptoms and depression appeared to occur significantly less frequently with peginterferon alfa-2a plus ribavirin than with interferon alfa-2b plus ribavirin.
2. Those typically associated with ribavirin, such as hemolytic anemia, fatigue, itching, rash, sinusitis, birth defects, or gout. Because of the concern of birth defects from the use of ribavirin, it is imperative that persons who receive the drug use strict contraception methods both during treatment and for a period of 6 months after treatment.

Deaths reported in association with the use of interferon alfa and ribavirin include suicide, myocardial infarction, sepsis, and stroke.

Adverse events tend to be more severe in the initial weeks of treatment.

CONTRAINDICATIONS

CONTRAINDICATIONS

Characteristics of persons for whom therapy is currently contraindicated:

- Major, uncontrolled depressive illness
- Renal, heart, or lung transplantation recipient
- Autoimmune hepatitis or other condition known to be exacerbated by interferon and ribavirin
- Untreated hyperthyroidism
- Pregnant or unwilling/unable to comply with adequate contraception
- Severe concurrent disease such as severe hypertension, heart failure, significant coronary artery disease, poorly controlled diabetes, obstructive pulmonary disease
- Under 3 years of age
- Known hypersensitivity to drugs used to treat hepatitis C virus (HCV)

Note: All patients have detectable hepatitis C virus ribonucleic acid (RNA).

QUALIFYING STATEMENTS

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- These recommendations suggest preferred approaches to the diagnostic, therapeutic, and preventive aspects of care. They are intended to be flexible, in contrast to standards of care, which are inflexible policies to be followed in every case.
- This guideline represents currently acceptable recommendations; it is recognized that reasonable physicians may deviate from the strategy and remain within acceptable standards of treatment. The issue of treatment of chronic hepatitis C is in constant flux. There is highly active clinical research in this area, and new information appears with increasing frequency. Presented here is the current state of the art for management and treatment of persons with chronic hepatitis C. However, these recommendations will need to be revised and updated in the future as additional critical and pivotal information becomes available.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

IMPLEMENTATION TOOLS

Clinical Algorithm
Personal Digital Assistant (PDA) Downloads

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Living with Illness

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Strader DB, Wright T, Thomas DL, Seeff LB. Diagnosis, management, and treatment of hepatitis C. Hepatology 2004 Apr;39(4):1147-71. [213 references] PubMed

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2004 Apr

GUIDELINE DEVELOPER(S)

American Association for the Study of Liver Diseases - Private Nonprofit Research Organization

SOURCE(S) OF FUNDING

American Association for the Study of Liver Diseases

GUIDELINE COMMITTEE

Practice Guidelines Committee

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

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FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Dr. Thomas serves on the advisory board for Roche Pharmaceuticals.

Dr. Wright serves on the advisory boards of Hoffmann-La Roche and Amgen, receives research support from Hoffmann-La Roche, Orthobiotec, and Schering Plough Research Institute, and is on the Hoffmann-La Roche Speakers Bureau.

ENDORSER(S)

American College of Gastroenterology - Medical Specialty Society
Infectious Diseases Society of America - Medical Specialty Society

GUIDELINE STATUS

This is the current release of the guideline.

GUIDELINE AVAILABILITY

Electronic copies: Available from the American Association for the Study of Liver Diseases Web site.

Print copies: Available from the American Association for the Study of Liver Diseases, 1729 King Street, Suite 200; Alexandria, VA 22314; Phone: 703-299-9766; Web site: www.aasld.org; e-mail: aasld@aasld.org.

AVAILABILITY OF COMPANION DOCUMENTS

This guideline is available as a Personal Digital Assistant (PDA) download via the APPRISOR™ Document Viewer from www.apprisor.com.

PATIENT RESOURCES

None available

NGC STATUS

This NGC summary was completed by ECRI on July 27, 2004. The information was verified by the guideline developer as of August 25, 2004. This summary was updated on May 3, 2005 following the withdrawal of Bextra (valdecoxib) from the

market and the release of heightened warnings for Celebrex (celecoxib) and other nonselective nonsteroidal anti-inflammatory drugs (NSAIDs). This summary was updated by ECRI on June 16, 2005, following the U.S. Food and Drug Administration advisory on COX-2 selective and non-selective non-steroidal anti-inflammatory drugs (NSAIDs). This summary was updated by ECRI on December 5, 2005, following the U.S. Food and Drug Administration advisory on Aranesp, Epogen, and Procrit. This summary was updated by ECRI on January 29, 2007, following the U.S. Food and Drug Administration advisory on erythropoiesis stimulating agents. This summary was updated by ECRI Institute on July 9, 2007, following the FDA advisory on erythropoiesis stimulating agents. This summary was updated by ECRI Institute on November 6, 2007, following the U.S. Food and Drug Administration advisory on Antidepressant drugs. This summary was updated by ECRI Institute on February 26, 2008 following the U.S. Food and Drug Administration advisory/voluntary market withdrawal of the liquid formulation of Leukine (sargramostim). This summary was updated by ECRI Institute on March 21, 2008 following the FDA advisory on Erythropoiesis Stimulating Agents. This summary was updated by ECRI Institute on August 15, 2008 following the U.S. Food and Drug Administration advisory on Erythropoiesis Stimulating Agents (ESAs).

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Readers with questions regarding guideline content are directed to contact the guideline developer.

Date Modified: 11/3/2008