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**JULY 2008**
**VOL. 24, NO. 7 • (pages 49-56)**

**Special Report: Medication Reconciliation**

# Joint Commission, pharmacists discuss successful reconciliation practices

*Joint Commission makes new recommendations*

Every pharmacy has a medication reconciliation plan and process, but how many of these are successful? The Joint Commission on Accreditation of Health Care Organizations (JCAHO) of Oakbrook Terrace, IL has made medication reconciliation one of its priorities in 2008, partly because this is such a difficult process for hospitals.

"A national patient safety goal and topic is medication reconciliation," says **Peter Angood**, MD, vice president and chief patient safety officer of JCAHO. "It has been one topic of importance for the field for a couple of years now."

While no one challenges the notion that medication reconciliation should be a priority for hospitals, the actual process of medication reconciliation is very complicated and difficult to do effectively, Angood notes.

"So we held a summit in September, 2007, with 60 organizations who provided feedback and input on the complexity of medication reconciliation," Angood says. "We've since revised our medication reconciliation patient safety goals and are in the final phases of the approval process."

The revised goals were expected to be released in June, 2008, shortly after the deadline for this issue of *Drug Formulary Review*. **(See the August 2008 issue of *Drug Formulary Review* for more information about the revised medication reconciliation goals.)**

Research has shown that most medication errors occur during transitions in care, but errors can be reduced when pharmacists obtain medical histories, says **Joan S. Kramer**, PharmD, BCPS, clinical research and hospital medicine specialist at the Wesley Medical Center in Wichita, KS.

"Patients sometimes don't know what drugs they're taking, and it's

difficult to find the information," Kramer says. "You have to make multiple phone calls."

Also, patients receive medication from multiple pharmacies, and their doctors often are not aware of all of the prescriptions they have, and this can lead to errors.

When pharmacists conduct medication histories, they know precisely which questions to ask to help the patient recall the drug he or she is taking, Kramer says.

If the pharmacist is carrying a portable laptop then he or she can pull up a picture of a drug on the computer and show the patient to verify that this was the medication the patient was taking, she adds.

While medication reconciliation seems like it should be an easy process to accomplish, the reality is the opposite, says **Leslie Eidem**, BSPharm, RPh, pharmacy manager at Wesley Medical Center.

A major obstacle is that there are many health care providers involved with a patient's care both prior to admission and during hospitalization, Eidem says.

"Patients have multiple physicians and use multiple sources for their medications," Eidem says. "The medication history can be asked of the patient several times by different providers and documented in different parts of the medication chart."

So if a reconciliation process isn't defined and formalized within the health record through manual or electronic means, then there is a significant disconnect in the reconciliation and communication at admission, transfer, post-op, and discharge, Eidem adds.

Since it's not practical for many hospitals to involve pharmacists in every medication history, pharmacist researchers and institutions have created and studied some alternative models.

For example, the Wesley Medical Center designed a study intervention that involved a collaboration between pharmacists and nurses, Kramer says.

"We wanted a mechanism to identify the patients that had a high medication utilization and would benefit from a pharmacist intervention versus a patient hospitalized with one medication and where a nurse could take that history," Kramer explains. **(See story about the collaborative pharmacist and nurse medication reconciliation process, p. 54.)**

In other models, pharmacy students are used.

For example, one study shows that pharmacy students trained by a clinical pharmacist could conduct admission medication histories, improving the process. **(See story on using pharmacy students for medication reconciliation, p. 53.)**

"We were looking at what's in the literature to see how medication reconciliation was being done, and I wanted to see if the pharmacy department could enhance the process or provide more accurate histories," says **Rosalyn S. Padiyara**, PharmD, CDE, an assistant professor in the department of pharmacy practice at Midwestern University Chicago College of Pharmacy in Downers Grove, IL.

Where electronic medication data are available, these can contribute greatly to medication reconciliation accuracy, one expert notes.

St. Rita's Medical Center in Lima, OH, receives electronic medication data on about 60% of patients, says **Brian D. Latham**, PharmD,

**Drug Formulary Review** (ISSN#1548-2790), including **Drug Criteria & Outcomes**™, is published monthly by AHC Media LLC, 3525 Piedmont Road, Building Six, Suite 400, Atlanta, GA 30305. Telephone: (404) 262-7436. Periodicals postage paid at Atlanta, GA 30304 and at additional mailing offices. POSTMASTER: Send address changes to **Drug Formulary Review**, P.O. Box 740059, Atlanta, GA 30374.

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a pharmacy operations manager.

The electronic data are collected from prescription purchases made at retail pharmacies, using third-party payers, but excludes pharmacy purchases made with cash, Latham notes. **(See story about electronic medication data capturing, p. 52.)**

"If someone goes to a CVS, Wal-Mart, or somewhere else to get drugs, all of those data are picked up on the electronic report," Latham says. "That gives us baseline data for patients who are unconscious or who don't have all the information they need about drugs."

However institutions handle medication reconciliation, Angood says, there are four areas of focus to consider:

**1. Obtain an accurate list of the patient's current medications.**

"This information is obtained whenever a patient is admitted to the organization," Angood says. "It includes any type of prescribed medications, nutritional support, and includes supplements and alternative medicine."

This list should be generated upon admission and as changes are made to it, he adds.

"These are reconciled as the patient goes through the course of stay in the organization, and those changes are documented," Angood says.

This often is the most challenging part of medication reconciliation for health care organizations, he notes.

"You'll have a Mrs. Jones who shows up with a brown bag of bottles, and she doesn't know what they are, or she left her medications at home," Angood says.

Electronic information typically is limited.

"Electronic health records have only penetrated 12-14% of organizations so far," Angood says. "Also, the electronic interaction between external providers or facilities is in a very early stage."

So a weak link in medication reconciliation is the link to pharmacy providers outside the health care organization, and even the largest chain providers may not have the most sophisticated information systems, Angood explains.

**2. Whenever patients are discharged or transferred, the updated medication reconciliation list is sent to all providers involved.**

"The up-to-date reconciled list is sent to the receiving organization, as well as to the patient's primary care provider or original prescribing physician," Angood says. "So there's continuity to the prescribing list."

This second area has been part of the original medication reconciliation goal, but it turned out to be far more complicated for organizations than anticipated, he notes.

"The issue is they didn't know who the next provider was, and the patient didn't know who the next provider was," Angood says. "We've continued to push that this is part of medication management."

Too often, people go into a facility, get their medications adjusted and are discharged, but nobody remembers their medications, he says.

While the pharmacy can help with this, it's also important that the primary care physician or the original referring physicians or the patient's next known provider receive a copy of the reconciled list, Angood says.

"Patients are not reliable in terms of providing their medication list, so we need organizations to improve their communication," he says. "It's a burden on organizations to make an effort to find out who the providers are, but it's best to send the information to the patient's doctor."

Occasionally, this will not work out.

For example, a patient might be a resident of one state and is seen in the emergency room of another state. So in some settings it might be acceptable to give the medication reconciliation list to the patient, Angood says.

**3. Give the patient an updated list.**

"Make sure the patient or patient's family also receive an up-to-date list of all medications," Angood says. "And make sure they receive education on why the list has changed."

**4. For some short-term medical settings, do a shortened medication reconciliation process.**

"Those types of settings where new medications are not given or that are only temporarily given, you can do a shortened, modified medication reconciliation process," Angood says. "This is when new medications might be ordered for just a short term like one week of an antibiotic."

Such settings might include office-based surgery, outpatient radiology, dialysis, and emergency care.

"These are settings where the patient is in and out and may not receive changes to his meds, but they're being assessed," Angood says. "If you're taking three to five medications and you're going for a radiology procedure and receiving an intravenous contrast, then you want them to assess what medications you're already on.

"If there are significant changes to the patient then the complete medication reconciliation needs to be performed," Angood adds. ■

# Center's electronic process increases satisfaction

*Retail pharmacy data included in process*

Some hospital pharmacists are finding that the best medication reconciliation process involves electronic data and access.

"We've developed a process where we electronically record all of these data into a grid, and the information then is placed on a report," says **Brian D. Latham**, PharmD, a pharmacy operations manager for St. Rita's Medical Center of Lima, OH.

Physicians can check the electronic report to see whether they'd like to continue the patient's medication, hold it, or have a dosage or other change on admission, Latham says.

The electronic system has created a much safer transfer process, and makes data easier to read in the pharmacy. Also, nursing, pharmacy, physician, and patient satisfaction with medication reconciliation has improved since implementation of the electronic form.[1]

Physicians were involved in developing the new process, and so their overall satisfaction with the medication reconciliation process is good, Latham notes.

"We did chart reviews earlier this year, and 95% or more of every patient has had an initial medication reconciliation done within the first 24 hours," Latham says.

For nurses, the new process means that less responsibility is placed on their shoulders for medication changes and re-continuations, he adds.

Since the electronic process was implemented, there have been fewer medication error reports involving communication breakdowns in the hospital.[1]

"We went through a lot of revisions of these forms, and I think we have a good process," Latham says. "It was new to physicians, but it's definitely improved patient safety in the process."

The electronic system includes an electronic report that details prescription information from retail pharmacies about a patient admitted to the hospital, Latham says.

Such information isn't available for 40% of patients, but when it is available it provides baseline data that are particularly useful when patients enter the hospital in an altered mental state or when they don't know what their drugs are, Latham says.

"So right after admission, the medication information goes into a separate computer system, and within five to 10 minutes a report prints out on each nursing unit printer for all patients," Latham explains. "They can take that into the room when they do an assessment."

The retail pharmacy information is available only to medical providers, he notes.

Once the baseline interview is completed and the physician has reviewed and approved it, the information is placed in the chart.

"We don't have physician order entry, so doctors check off manually the home medications they'd like to continue," Latham says. "If they'd like to add any new meds they can do that as well."

The nurse goes through the interview, with a computer that is available at bedside or on a rolling cart, and places all patient information into the computer system. After she's completed the patient interview, she generates a report and prompts it to print, Latham explains.

The hard copy is placed in the chart for the physician to review.

For the minority of cases where the nurse has to rely on the patient interview or family interview to obtain medication information, she might call the patient's pharmacy to fill in missing data, Latham says.

"Occasionally, decentralized pharmacists are called if nurses can't identify a medication that we can identify through our system," he adds. "Typically, the pharmacists don't do that initial interview."

When patients are transferred to another level of care, such as rehabilitation or a psychiatric unit, a new form is developed and printed out.

It includes all of the patient's current medications, and the physician reviews these with another check-box process, Latham says.

"We make sure in every transfer process that the whole list of medications is signed on again," he says.

The same process continues when patients have surgery. This check-box report makes it convenient for surgeons and other health care providers to quickly view all of the medications

a patient has taken prior to surgery, he adds.

At discharge, the original sheet with the home medications is compared with the current inpatient list of medications.

"So a final list before discharge needs to be developed for the patient, comparing the original list and the new list to see what needs to be continued," Latham says. " The nurse takes the information of what the physician selects for the discharge list and places the changes into the computer system.

"Patients see a list that says, 'These are your home medications; these are the medications that were changed while you were in the hospital, and here are the medications you should stop taking,'" Latham explains.

"Patients have a nice list when they leave the hospital, and it has all of their home medications," he adds. "They can take that list to the next provider for a follow-up appointment."

One of the challenges the hospital faced when launching the new electronic medication reconciliation process was obtaining physician buy-in for the checklist part of the process, Latham notes.

Physicians were accustomed to signing off only on the medications they prescribed for patients and were initially reluctant to take responsibility for the entire list of drugs, he says.

Without having one person in charge, it would be difficult to coordinate the entire list of medications, so one physician had to be named the point person on this.

"The attending physician is ultimately responsible," Latham says. "Although the nurses sometimes have to coordinate with some of the other physicians.

"I went to many physician division meetings, and we had physician champions involved who spoke in support of the forms at meetings," Latham says.

It is all a matter of physicians taking time to do the medication reconciliation at transfer.

"I think we had a good buy-in because we made it an easy process for the physician," he says. "The forms are self-explanatory."

### Reference

1. Latham BD. Medication reconciliation: from admission to discharge using electronically generated medication forms from a clinical information system. Abstract presented at the 2006 Mid-Year Clinical Meeting of the American Society of Health-System Pharmacists; Anaheim, CA; Dec. 3-7, 2006. ■



# Students can improve medication reconciliation

*Students found omissions in histories*

Hospitals often lack the time needed to obtain accurate medication histories from newly admitted patients, and this leads to errors.

Having pharmacists obtain medication histories might reduce errors, but it could also increase costs. One solution might be to train pharmacy students to obtain medication histories.

In a study that involved the use of pharmacy students, investigators found that fourth-year pharmacy students could enhance pharmaceutical care in a hospital medication reconciliation program by identifying omissions in original medication histories and notifying pharmacists, nurses, and physicians of problems.[1]

"The students found mistakes when something was improperly documented, such as a patient's prior-to-admission medication or a patient's allergies," says **Rosalyn S. Padiyara**, PharmD, CDE, an assistant professor in the department of pharmacy practice at Midwestern University Chicago's College of Pharmacy in Downers Grove, IL.

Padiyara created the study intervention based on her dual roles as a clinical pharmacist for medication reconciliation at a 300-bed, community hospital and her responsibility as a professor in overseeing pharmacy students.

"To fulfill both responsibilities, I asked myself how I could give the student a beneficial experience and also handle my responsibilities at the hospital," she explains. "I was the primary preceptor for the students, in charge of grading and assessing them, and I was hired to provide medication reconciliation for the hospital, along with another pharmacist, so I combined the two jobs together."

The first step was to find out how the hospital's medication reconciliation worked. Padiyara found that nurses, physicians, and residents were conducting the medication histories.

"I decided to look into the literature to see if there were ways to do it better," she adds. "That was nearly two years ago and although medication reconciliation was a hot topic at the time,

there wasn't a huge amount of available.

Padiyara designed the study for six pharmacy students, who would be working at the hospital for six weeks. "Their rotation involved acute care in a hospital setting, so three would provide medication reconciliation, and three would gain experience in acute care, and then they switched experiences," Padiyara explains.

"Initially, what I'd do is have students go into a patient's room and perform the interview and then present all of the information to me," she says.

"Sometimes we found that getting hold of a patient's physician was difficult, so we developed a form where we could record all of the information gathered," Padiyara says.

The form provided documentation of which medications needed to be started, and it could be inserted in the patient's chart so the physician would see what had not been started and write orders for that, she explains.

Also, the pharmacy students assisted with verifying with the pharmacy, caregiver, or family members which medications the patients were on, Padiyara says, and confirming formulary status.

"In general the interview took about five to seven minutes," she says. "Depending on how many patients they had, they'd either page me or gather all of the information and discuss it all at one time."

Then the students would go back up to the floors to insert the form into the patient's chart that Padiyara had signed off on. These were for physicians to write orders for, if they deemed it necessary, Padiyara adds.

The students found mistakes made in previous medication histories since their own medication histories were used in the study to compare the pharmacy part of the intervention to the usual medication reconciliation process.

"This was something students did after the patient information was already documented in the chart, to assess what was left out and whether there was anything that could be added in order to reduce errors and ultimately enhance the care the patients received," Padiyara says.

## Reference

1. Padiyara RS, Rabi SM. Pharmacy students and reconciliation of medication upon hospital admission. Abstract presented at the 2006 Mid-Year Clinical Meeting of the American Society of Health-System Pharmacists; Anaheim, CA; Dec. 3-7, 2006. ■



# Medication reconciliation process has collaboration

*Key is use of electronic reports*

The key to any intervention to improve medication safety is to achieve the best safety outcomes while using staff time and hospital resources efficiently.

Wesley Medical Center in Wichita, KS, sought to accomplish both of these goals by studying a medication reconciliation process that had nurses and pharmacists collaborate when patients most needed extra attention.

The idea was to have nurses continue to conduct medication histories when patients were admitted to the hospital, but in cases where the patients were taking multiple drugs for multiple conditions, a pharmacist would assist, says **Joan S. Kramer**, PharmD, BCPS, a clinical research and hospital medicine specialist at Wesley Medical Center.

Kramer and co-investigators designed an intervention, using an electronic process that resulted in the medication reconciliation capturing more patient allergies, more prescriptions, and more nonprescription medications.[1]

"We had multiple roundtable discussions with people who became co-authors of our study about what we could study that would benefit patient care the most at the hospital," Kramer says. "We had think-tank meetings to come up with the idea."

A data architect helped the investigators design a computerized report, and after several attempts, the electronic system was developed, Kramer says.

"Our director of pharmacy was instrumental in ensuring we had the resources we needed to accomplish the study and to provide input through crucial meetings when we had trouble with the electronic framework," Kramer says.

As a result of the intervention, the hospital has made some changes to its medication reconciliation process, says **Leslie Eidem**, BSPharm, RPh, a pharmacy manager.

"There are two primary changes that occurred to our medication reconciliation process since the study," Eidem says. "The first is the recognition that automation and the use of the electronic health record were key to improving the process."

This allowed any provider to retrieve data elec-

tronically, and it created automated and standardized reports, Eidem adds.

This electronic record process also expedited the medication history for re-admissions, Eidem says.

Also, the process included development of a side-by-side comparison of reconciliation medications by drug class, she says.

"This allows for recognition of duplication and therapeutic interchanges and the automation of patient education materials at discharge," Eidem says.

"The second change was the incorporation of the review of the home medications at each stage of reconciliation, including admission, transfer, and discharge," she adds.

The intervention worked in this way:

**1. Nurses had 10 questions embedded in their admission report for new patients.** For purposes of the study, the 10 questions were asked both pre-implementation and post-implementation of the medication reconciliation process being studied.

1. Do you take seven or more medications, including prescription, nonprescription, and herbal products?
2. Do you have asthma?
3. Do you have chronic obstructive pulmonary disease?
4. Do you have diabetes?
5. Do you have any cardiac condition (i.e., myocardial infarction, congestive heart failure, arrhythmia, hypertension)?
6. Were you admitted with an adverse drug reaction?
7. Do you need to be vaccinated against pneumococcal disease (never received Pneumovax immunization or received it over five years ago)?
8. Do you need to be vaccinated against influenza (not yet vaccinated this year)?
9. Do you have more than three medication allergies?
10. Do you have medications that need to be identified?[1]

The last question was included partly because patients sometimes think they know which drugs they're taking, but when they are admitted they'll seem unsure, Kramer notes.

"So we need to figure out what they're taking," she says. "Based on those trigger questions developed in the previous pilot study, one 'yes' answer could trigger the pharmacist intervention."

**2. The answers nurses key into an electronic form generate a report to the pharmacy printer.**

The electronic format makes the reports automatic, and a "yes" answer to any of the questions will result in a report that alerts the pharmacy department that a medication history is needed, Kramer explains.

"The pharmacy looks at the report and verifies that the patient meets eligibility for our study, and then the pharmacist talks to the patient and obtains informed consent," Kramer says.

**3. Pharmacists meet with patients.**

Patients who agreed to participate met with a pharmacist who obtained their medication history and compiled that information into the computer system, she says.

"We developed a set of interview questions that should be done when you obtain a medication history, and the pharmacists all felt very comfortable with it," Kramer says.

For instance, when a pharmacist meets with a patient, they ask them about their reactions to taking a medication rather than asking specifically if they had a rash, she explains.

"You ask open-ended questions because you want the patient to tell you what's happened, and you don't want to give them any ideas," Kramer says. "We trained everyone on how to ask these questions."

The average amount of time it took pharmacists to complete the medication history was 12.9 minutes, and the average amount of time it took them to clarify the medications was 5.84 minutes.[1]

Once the interview was completed, the pharmacist would generate a report containing the medication list for prescribers to reconcile on admission, Kramer says.

"Then nurses and pharmacists worked with prescribers to complete the medication reconciliation document," she says.

Either the nurse or the pharmacist would call the physician to go through the list of the medications,

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Kramer says.

"Sometimes prescribers would say, 'I'm going to see this new admit anyway, so just leave that list for me in the chart for when I see the patient,'" Kramer says.

Besides showing that an electronic and collaborative medication reconciliation process could work, the study also demonstrated significant improvement in patient satisfaction, Kramer notes.

Patients were asked both pre- and post-implementation questions about their experience during the medication reconciliation process:

- "When I was discharged from the hospital, I was given clear instructions about which medications I was taking at home."
- "I was given clear directions about how much and how often I am supposed to take my medication."
- "I was given clear directions about how and when to take my medicine."
- "I was given clear information about possible side effects of my medicine."
- "Overall, I feel like I understand my medicine."[1]

On all questions the patients reported a significantly higher rate of satisfaction in the post-implementation phase, Kramer says.

The main drawback to fully implementing the intervention is a staffing issue, Kramer says.

"If we were to continue this process for our hospital we'd need two additional pharmacists solely dedicated to medication reconciliation, and we'd need one to be put in the emergency department and one in the rest of the hospital," Kramer says.

But it could be argued that the benefits would be worth the additional expense, she notes.

Besides the enhanced patient satisfaction, there would be greater efficiency, and presumably improved patient safety — although that wasn't specifically measured, with a more complete medication list being scanned to the pharmacy department, Kramer says.

"In the post-implementation phase, when the pharmacist obtained the medication history, the medication history was printed out, and it was a clean list," Kramer says. "We knew all those dosages existed, the drug names were spelled correctly, and allergies clarified and verified."

There was no need for clarification because the work required to clean up the data had already been done, she adds.

"This saved at least 10 to 15 minutes of phone calls back to nurses and multiple pharmacies to verify the medication history on admission for each patient," Kramer says.

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1. Kramer JS, Hopkins PJ, Rosendale JC, et al. Collaborative pharmacist and nurse before/after study to evaluate patient safety using electronically standardized admission and discharge medication reconciliation in a tertiary care hospital. Abstract presented at 2006 Midyear Clinical Meeting by the American Society of Health-System Pharmacists; Anaheim, CA; Dec. 3-7, 2006. ■

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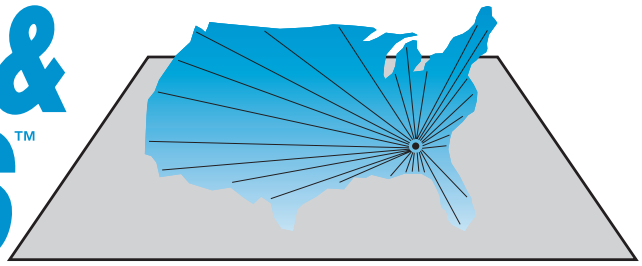

# The Two Faces of ESAs: Beneficial or Detrimental?

By **Kristy Bryant**, PharmD Candidate, Harrison School of Pharmacy, Auburn University

Chemotherapy-induced anemia (CIA) is a very prevalent side effect associated with chemotherapy and affects more than half of all patients with cancer. Patients with CIA endure additional extreme fatigue as well as a decrease in quality of life and worsened long-term outcomes.

Erythropoietin stimulating agents (ESAs) are the current treatment option for CIA, and include epoetin alfa (Epogen®, Procrit®) and darbepoetin alfa (Aranesp®). These agents stimulate the division and differentiation of committed erythroid progenitors in the bone marrow increasing red blood cell production.

The goal of ESA treatment is to avoid blood transfusions by maintaining appropriate Hgb levels between 10 and 12 g/dL. Exceeding Hgb levels of 12 g/dL can lead to serious cardiovascular complications such as myocardial infarction, stroke, and death. ESAs are only indicated for CIA while concomitantly on chemotherapy and these agents should be stopped once chemotherapy has been discontinued.

## *Black box warning*

The FDA recently announced safety concerns associated with ESAs in the treatment of CIA. On Nov. 8, 2007, the black box warning on ESA product labels was strengthened based on adverse safety results from six studies. The black box warning currently addresses the adverse outcomes associated with treatment that include shortened time to tumor progression, shortened overall survival, and increased deaths as a result of disease progression. The FDA revisions state: "Data are not sufficient to exclude the possibility of shortened survival and tumor progression in cancer patients when ESAs are dosed to reach a (Hb) level between 10 and 12 g/dL."

The following is a list of trials whose results have paved the way for this recent ESA safety warning: BEST, ENHANCE, 20010103, 20000161, EPO-CAN-20, DAHANCA 10, PREPARE, and GOG-191. Several of the most relevant trials are summarized below.

## *Trials supporting black box revisions*

The EPO-CAN-20 trial involved patients with non-small-cell lung cancer (NSCLC). The trial was suspended early based on data showing increased mortality in the active treatment arm and negative overall survival results of two additional studies. The authors concluded that this study reaffirms the efficacy of epoetin alfa with regards to increasing Hgb levels. An unplanned safety analysis suggests decreased overall survival in patients with advanced NSCLC treated with epoetin alfa. Concern over the routine use of epoetin alfa for disease-related anemia in patients with NSCLC remains.

The ENHANCE trial involved patients with advanced head and neck cancer. The authors concluded that epoetin corrects anemia but does not improve cancer control or survival, and that disease control may even be impaired.

The BEST trial involved patients with metastatic breast cancer, and was suspended early due to increased mortality in the arm being treated with an ESA. The authors concluded that the use of epoetin alfa to achieve high Hgb targets was associated with increased mortality.

There are currently two ongoing trials that also contributed to the new FDA warnings: the PREPARE study (breast cancer) and the GOG-191 study (cervical cancer). Both of these trials present

higher death rates and/or tumor progression in patients receiving ESAs versus those given placebo.

A review article from the Cochrane database examined safety and efficacy involving multiple types of cancer. The authors concluded that ESAs are effective for prevention or treatment of anemia but are associated with increased risk for thromboembolic events and do not increase survival.

## Clinical practice guidelines

Based on recent literature and FDA label revisions regarding ESA therapy, the American Society of Clinical Oncology (ASCO) along with the American Society of Hematology (ASH) updated their 2007 clinical practice guidelines.

Even though these organizations proceeded with the updates, they made a point to discuss the design flaws of the current literature from which the revisions were derived. Several of the trials contained imbalances of baseline characteristics, which lead to the randomization of "sicker" patients into the active treatment arms. In addition, multiple studies were suspended early due to increased mortality without a definitive cause identified.

ASCO and ASH acknowledged the "difficulty in interpreting their results and applying them to current clinical practice" based on the study weaknesses. The following list includes a brief highlight of the 2007 revisions related to ESA safety concerns:

- With regard to CIA threshold for initiating ESA therapy, epoetin or darbepoetin should be used with a Hgb that is approaching or has fallen below 10 g/dL, to increase Hgb levels and decrease transfusions
- Based on current literature reviews, there is an increased risk of thromboembolic events associated with ESA therapy in this population and extra caution should be taken in patients with an increased risk
- Harm in relation to increased risk of death and serious cardiovascular complications has been linked to treating to a goal Hgb >12 g/dL. Dose modification must be considered once a patient's Hgb nears this level.

## Conclusion

ESA agents have proven to be beneficial and effective in raising Hgb levels and treating CIA in cancer patients. Unfortunately, there are now a total of eight trials that allude to safety concerns for patients being treated for CIA with these agents.

Key recommendations for health care providers include initiating ESA therapy with a Hgb that is near or below 10 g/dL, not to exceed Hgb levels >12 g/dL, as well as communicating to patients the safety concerns regarding tumor progression, shortened overall survival, and increased deaths associated with disease progression. In addition, it is very important to remember that ESAs should be stopped once chemotherapy has been discontinued.

The FDA is conducting an ongoing safety review to evaluate risks and benefits associated with ESA treatment of CIA. In addition, they warn medical professionals to evaluate this risk-to-benefit ratio regarding the best overall care for their patients.

## Resources


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# New FDA Approvals

The FDA has approved Entereg® (alvimopan) to accelerate the **restoration of normal bowel function** in patients 18 years and older who have undergone partial large or small bowel resection

surgery. Alvimopan will be used in hospitalized patients who can receive no more than 15 doses.

"Patients who have undergone abdominal surgery and are on pain medications often experience problems eliminating waste," said **Joyce Korvick**, MD, deputy director, Division of Gastroenterology Products. "Entereg will help accelerate their recovery, improve bowel function, and get these patients back on a normal diet. As with all FDA-approved products, the agency will monitor Entereg throughout its life cycle."

FDA is approving alvimopan with a Risk Evaluation and Mitigation Strategy (REMS) to ensure that the benefits of the drug outweigh the risks. The REMS will include limits on dispensing of the drug.

In approving alvimopan, FDA determined that a REMS is necessary to ensure that the benefits of alvimopan outweigh its risks. The REMS will include restricting alvimopan to inpatient use only, requiring that hospitals be specially certified, distribution of educational materials to health care professionals, and regular assessments of the effectiveness of the REMS.

Following major abdominal surgery, some patients develop a condition known as postoperative ileus (POI). POI is a disorder that causes temporary impairment of the gastrointestinal (GI) tract's motility, or the ability of the intestines to push out waste products (not a complete blockage of the GI tract), following surgery. POI can be a by product of a patient taking opioid pain relievers, like morphine, prescribed after surgery which can slow or inhibit normal motility. Alvimopan works by blocking opioid effects in the bowel.

The recommended dose for alvimopan is one 12 mg capsule given just prior to surgery and then another 12 mg dose administered twice daily for up to 7 days or not to exceed 15 doses. The product will only be available to hospitals and will come in blister packs that are marked "HOSPITAL USE ONLY." Alvimopan is not approved for use in pediatric populations.

The safety and efficacy of alvimopan in postoperative patients were demonstrated in five studies that included 2,177 patients, of whom 1,096 received alvimopan and 1,081 received placebo. Bowel recovery times ranged from 10 to 26 hours shorter for alvimopan-treated patients compared to placebo-treated patients in the five studies. The most common side effects reported were low blood calcium levels, anemia, and gastrointestinal problems, including constipation, dyspepsia (heartburn), and flatulence (excess bowel gas).

FDA has reviewed a 12-month study of alvimopan in patients treated with opioid medications for chronic pain. In this study, there were more reports of myocardial infarctions in patients treated with a 0.5 mg dose of alvimopan twice daily, compared with placebo-treated patients. This imbalance has not been observed in other studies of alvimopan, including studies in patients undergoing bowel resection surgery who took 12 mg of alvimopan, twice daily for up to 7 days. A causal relationship with alvimopan and myocardial infarction has not been established.

Consumers and health care professionals are encouraged to report adverse events to FDA's MedWatch program at (800) FDA-1088 or on-line at: www.fda.gov/medwatch/how.htm.

The FDA has approved Amitiza® (lubiprostone) for the treatment of **irritable bowel syndrome with constipation** (IBS-C) in adult women aged 18 and older. There is currently no prescription drug therapy for IBS-C. With this approval, lubiprostone becomes the only FDA-approved medical treatment for IBS-C available in the United States.

Irritable bowel syndrome is a disorder characterized by cramping, abdominal pain, bloating, constipation, and diarrhea. IBS causes a great deal of discomfort and distress to its sufferers. It affects at least twice as many women as men.

"For some people IBS can be quite disabling, making it difficult for them to fully participate in everyday activities," said **Julie Beitz**, MD, director of the Office of Drug Evaluation III, Center for Drug Evaluation and Research, FDA. "This drug represents an important step in helping to provide medical relief from their symptoms."

The safety and efficacy of lubiprostone was established in two major studies involving 1,154 patients diagnosed with IBS-C. The majority of the patients studied were women (approximately 8% were men). Patients enrolled in the studies were experiencing at least mild abdominal discomfort or pain that was associated with at least two of the following additional symptoms: 1) fewer than three spontaneous bowel movements per week (that did not result from laxative use); 2) hard stools; or 3) moderate or severe straining with bowel movements. In the studies some patients received lubiprostone and others were given a placebo. More patients treated with lubiprostone reported that their IBS symptoms

were moderately or significantly relieved over a 12-week treatment period than patients who received placebo. The safety of long-term treatment was assessed in a study in which all patients were treated with lubiprostone for a duration that ranged 9-13 months. The efficacy of lubiprostone in men was not conclusively demonstrated for IBS-C.

Lubiprostone, like most prescription medications, is accompanied by some side effects. Common side effects of lubiprostone include nausea, diarrhea, and abdominal pain. Other rare side effects include urinary tract infections, dry mouth, syncope (fainting), peripheral edema (swelling of the extremities), dyspnea (difficulty breathing), and heart palpitations.

Lubiprostone should be taken twice daily in 8 mg doses with food and water. Patients and their health care professionals should periodically assess the need for continued therapy.

Lubiprostone is not approved for use in children and men. It is not to be administered to patients suffering from severe diarrhea or patients with known or suspected bowel obstructions. Its safety and efficacy has not been established in patients with renal or hepatic impairment, or in pregnant or nursing mothers.

Lubiprostone is also approved for the treatment of chronic idiopathic constipation (CIC), but the dose for that indication is higher, 24 mg twice a day.

As with all FDA-approved products, the agency will monitor lubiprostone throughout its life cycle. Consumers and health care professionals are encouraged to report adverse events to the FDA's MedWatch program at (800) FDA-1088 or on-line at: www.fda.gov/medwatch/how.htm. ■



## CE *Questions*

Pharmacists participate in this continuing education program by reading the article, using the provided references for further research, and studying the CE questions. Participants should select what they believe to be the correct answers.

Participants must complete a post-test and evaluation form provided at the end of each semester (June and December) and return them in the reply envelopes provided. A statement of credit requires a passing score of 70% or higher. When a passing test and evaluation form are received, a statement of credit and answer guide will be mailed to the participant.

This CE program will improve participants' ability to:

- **Compare** the clinical efficacy and safety of one therapeutic agent over another used in the same setting.
- **Assess** clinical trial data and explain how the results influence formulary decision making.
- **Perform** cost-effectiveness analyses.

1. Patients with chemotherapy-induced anemia endure:
   A. additional extreme fatigue.
   B. decreased quality of life.
   C. worsened long-term outcomes.
   D. All of the above

2. The goal of treatment with erythropoietin stimulating agents (ESAs) is to avoid blood transfusions by maintaining appropriate Hgb levels between:
   A. 6-8 g/dL.
   B. 8-10 g/dL.
   C. 10-12 g/dL.
   D. 12-14 g/dL.

3. ESAs are only indicated for CIA while concomitantly on chemotherapy and these agents should be stopped once chemotherapy has been discontinued.
   A. True
   B. False

4. Which of the following adverse outcomes associated with ESA treatment prompted the FDA to revise the black box warning on ESA product labeling and initiate an ongoing safety review?
   A. Shortened time to tumor progression
   B. Shortened overall survival
   C. Increased deaths associated with disease progression
   D. All of the above