



HOPA News

Safe Medication Practices

Helpful DOs and DO NOTs for Writing Chemotherapy Orders

Ray Muller • Memorial Sloan-Kettering Cancer Center

DOs

DO always double-check the dose against the actual drug regimen or protocol.

DO always use the full name (generic preferred over the trade name) of the drug.

DO prescribe all drug doses clearly in terms of dose (eg, micrograms, mg, grams, etc).

DO use a leading zero when the dose is less than 1 unit/mg/gram, etc (ie, an order of .1 mg may be read as 1 mg; write 0.1 mg).

DO avoid excessive attempts at precision and round chemotherapy doses greater than 5 mg to the nearest integer or nearest reasonable amount (ie, for fluorouracil write 525 mg, NOT 521.6 mg; for carboplatin, write 925 mg NOT 919.57 mg; for cisplatin, write 125 mg NOT 126.4 mg).*

DO date all orders with month, day, and year. For inpatient orders, also include time of day.

DO use body surface area (BSA)-based dosing—ie, mg/m² or g/m², or when applicable, mcg/kg—giving the daily dose and the specific number of days it is to be given.

DO list a route of administration and an infusion duration for intravenous solutions (spell out intrathecal, when using that route, as IT may be read as IV).

DO include a current height, weight, and BSA with each chemotherapy order.

DO print critical information such as drug names, doses, etc.

DO double-check all drug names and doses before signing, and verify that they are what you intend the patient to receive.

DO make sure that the medication order sheet has *the correct patient's name* on it, either handwritten or stamped by addressograph plate. NEVER leave orders on a blank order sheet for subsequent stamping by an addressograph plate.

DO NOTs

DO NOT designate drug by brand names, nicknames, company names, or abbreviations. For example, does Paraplatin refer to cisplatin or carboplatin? Does CPT-11 refer to cisplatin or irinotecan? Similarly, “Aredia” (pamidronate) when written, could be misunderstood to be “Adria”† (doxorubicin), or vice versa. Ideally, always use generic names rather than trade names.

DO NOT write the course dose unless the daily dose is written as well. For example, in a patient with a BSA of 1.5 m², cisplatin 20 mg/m²/day for 5 days = 30 mg/day for 5 days = 100 mg/m² per course = 150 mg per course.

DO NOT use a trailing zero when writing an order (eg, an order of 50.0 mg may be read as 500 mg; simply write 50 mg).

DO NOT use a leading decimal. **DO** write 0.1 mg—not .1 mg, which may be misread as 1 mg and cause a 10-fold overdose.

DO NOT use dangerous abbreviations. Using “U” for units may be read as “0” and the patient could receive a 10-fold overdose.

DO NOT refer to drugs by common name of drug class. For example, does “platinum” mean cisplatin, carboplatin, or oxaliplatin?

DO NOT use a soft felt-tip pen. When orders are written on multilayer carbonless paper, copies may be illegible or invisible.

DO NOT sign a blank copy of a medication order for another practitioner—eg, for an RN, RPh, to complete later. Orders should reflect information directly intended and checked by the licensed prescriber.

DO NOT give verbal orders to initiate chemotherapy.

DO NOT abbreviate “daily” as “qd,” which has been mistaken for “qid.” Similarly, **DO NOT** abbreviate “every other day” as “qod.”

HOPA Member Publications

Bob Ignoffo • HOPA Publications Committee

This new column will highlight publications by HOPA members. If you know of articles published by HOPA members within the past 12 months, please send the citation to the Chair of the Publications Committee (see www.hoparx.org/brdsandcmt.aspx) for potential listing in an upcoming newsletter. Thank you.

Recent publications:

1. O'Bryant Cindy L, Crandell Brian C. Community pharmacists' knowledge of and attitudes toward oral chemotherapy. *J Am Pharm Assoc.* 2008;48(5):632-639.
2. Ignoffo Robert J. Current research on PONV/PDNU: Practical implications for today's pharmacist. *Am J Health Syst Pharm.* 2009;66(1 suppl 1):S19-S24.
3. Kloth Dwight D. New pharmacologic findings for the treatment of PONV and PDNU. *Am J Health Syst Pharm.* 2009;66(1 suppl 1):S11-S18.
4. Pruemmer Jane. Epidemiology, pathophysiology, and initial management of chronic immune thrombocytopenic purpura. *Am J Health Syst Pharm.* 2009;66(2 suppl 2):S4-S10.
5. Burzynski Julianna. New options after first-line therapy for chronic immune thrombocytopenic purpura. *Am J Health Syst Pharm.* 2009;66(2 suppl 2):S11-S21.

DO NOT write drug orders in terms of number of ampules or vials. Drugs may come in more than 1 vial or ampule size, leading to administration of doses not intended by the prescriber. For example, both carboplatin and cisplatin come in 3 different vial sizes over a 10-fold size range.

DO NOT use outdated laboratory info when writing orders. Current lab data might indicate a change in renal or hepatic function and a required dose modification might be missed, leading to an incorrect dose. ■

*Rationale: Federal requirements mandate that commercial drug concentrations be between 95% and 105% of labeled strength; in addition, expiration dating procedures are based on ≤10% degradation over time, so for an ordered dose of 127.4 mg, even when Nursing and Pharmacy perform their functions flawlessly, the dose actually received by the patient is somewhere in the range of 114 mg to 134 mg; †Shortened form of Adriamycin.

Adapted from Muller RJ, Kloth DD, Freise C. Designing strategies to prevent cancer chemotherapy errors – Part 1. *Clin Oncol News.* 2006;51-56.

The HOPA Membership Committee Wants a Picture of You!

In an effort to help HOPA members get to know one another better, the Membership Committee is asking members to submit a photo of themselves in the work environment (must be HIPAA compliant, ie, no patients included). These photos will be displayed at the Annual Meeting in Miami.

Please upload your photo at www.hoparx.org/PhotoUpload.aspx or by going to the **Membership** tab, **Upload Your Photo** subtab. Only HOPA members may submit photos, so you will be asked to log in. Thank you for participating!

COMMITTEE UPDATES

Update from the Board

A Start to the New Year: Professionalism in Oncology Pharmacy Practice

*Jane Pruemmer, PharmD, BCOP
At-Large Board Member*

Happy New Year HOPA members! The Executive Board hopes that this year all our members will have the opportunity to log onto the HOPA website (www.hoparx.org) and bring themselves up to date on the latest happenings of the organization. In our ongoing commitment to keep our members informed of the Board's activities, we would like to summarize some of those key events here. The start of a new year always places us in the frame of mind to look at ourselves with thoughts to self-improvement, whether it is regarding our health (diet and exercise) or our professional health. Obviously, we are all looking forward to our next annual meeting in Miami on June 17-20, but now we have additional educational offerings available through HOPA University (HOPA U, www.hopaU.org). Members are encouraged to take advantage of these opportunities to improve their knowledge and skills, and to earn ACPE credits. Why leave the house when you can stay in? HOPA U offers various courses to update you on topics from new drugs to treatment of various oncologic diseases. Go to www.hopaU.org and click on both the "HOPA Activities" and "Additional Activities" links for a complete listing of current offerings.

In addition to working on plans for the Annual Meeting and HOPA U, the Board has worked on revisions to the By-Laws, and would like to thank all members who reviewed the By-Laws and provided comments for further revisions. Other exciting areas of communication to you, our members, include the work of our 11 other standing committees within the organization (BCOP Recertification, CE Accreditation, Education & Standards, Finance, Legislative Affairs, Membership, Nominations & Awards, Professional Affairs, Program, Publications, and Research; see below for selected committee reports). A significant amount of work has been done to keep HOPA moving toward meeting its goals, which are your goals. Additionally, the Board is working together with the committees to develop policies and procedures to facilitate a smooth transition from year to year.

The title of this column, "A Start to the New Year: Professionalism in Oncology Pharmacy Practice," is to remind all of us of our role as health care professionals. We have taken upon ourselves the commitment to provide high-quality pharmaceutical care to our patients. To do this, we must stay on the cutting edge of oncology clinical practice and be knowledgeable of the latest research and technologies available in our field. We have demonstrated our commitment by being active members of HOPA, and by working to keep HOPA the foremost oncology pharmacy organization in the United States. Our ability to obtain quality oncology pharmaceutical education, to participate in presenting well-conducted research, and to network with one another are all tangible values of being a member of HOPA. When I committed to being an oncology pharmacist, I never realized how important this organization would become to me. My professionalism in practice is closely tied to the interactions I have

Reminder: Changes to HOPA By-Laws

Thank you to HOPA members who provided suggestions for revisions to HOPA's By-Laws. We have incorporated many of these changes to create a new version of the By-Laws. As you know, changes to the By-Laws require a vote by the HOPA membership to become final, so members are entitled to review the new proposed revisions and provide comments to the HOPA Board of Directors.

Members received these revisions in an e-mail on January 9. If you haven't already, please take a moment to review the changes and respond with comments if you disagree with these revisions or feel additional revisions need to be made. You have until **Monday, February 23**, to review the By-Laws and respond. Thank you!

The HOPA Board of Directors

with other oncology pharmacy health professionals, and HOPA is a great means to maintain and grow that professionalism.

BCOP Recertification Committee

Fall and winter continue to be very active times of the year for the BCOP Recertification Committee. The committee has identified the 6 presentation topics for the "live" portion of the 2009 recertification cycle and invited the speakers for the 3 meetings. The speakers and topics for this year are as follows:

1. Speaker: John Valgus, PharmD, BCOP
Topic: Update on the Treatment of CNS Malignancies
2. Speaker: John Kuhn, PharmD, FCCP, BCOP
Topic: Application of Pharmacogenomics in Cancer Patients
3. Speaker: Courtney Tsao, PharmD, BCOP
Topic: Update on the Management of Pediatric and Adult ALL
4. Speaker: Dawn Goetz, PharmD, BCOP
Topic: Update on Sarcomas: Soft Tissue, Osteosarcoma, Ewing's & GIST
5. Speaker: Jolynn Sessions, PharmD, BCOP
Topic: Update on the Management of Hepatocellular Carcinoma
6. Speaker: Kristine Crews, PharmD, BCPS
Topic: Update in Statistics for the Hem/Onc Practitioner

The recertification committee is presently responsible for the 6 recertification hours provided at the HOPA Annual Meeting in June, and repeated at the ACCP Annual Meeting in October and the ASHP Midyear Meeting in December.

Members of the HOPA Executive Board and Recertification Committee met with representatives of ACCP and ASHP in December at the 2008 ASHP Midyear meeting to discuss the recertification process and ways to allow HOPA to provide more services for its membership. As a result of the meeting, HOPA is exploring the possibility of using the HOPA U web site to facilitate the provision of the aforementioned 6 hours of recertification credit the HOPA Recertification Committee is responsible for

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COMMITTEE UPDATES

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organizing. In addition, further collaboration with ASHP and ACCP was discussed to create and implement a standard procedure for validating all recertification test questions.

The recertification committee has long seen the need to have a better practice in place for the validation of recertification test questions. Historically, HOPA, ASHP, and ACCP have each used their own individual methods to validate the recertification questions generated from the home syllabus, review course, and “live” content. The goal will be to have the new standard in place for all of the questions used for recertification in 2009.

Lastly, the committee continues to work with DesignWrite to secure financial support for the 2009 programming. As a reminder, in addition to organizing the 6 hours of “live” content provided each year, this committee is responsible for securing the funds that support this endeavor.

Education & Standards Committee

The Education & Standards Committee has been busy this fall and winter developing educational activities for HOPA U. Currently there are 8 educational activities available on HOPA U (7 are activities created by HOPA; see callout box) and we have submitted several other programs for funding. We have numerous other topics in various stages of development as well as two topics in development for Best Practices presentations at the HOPA Annual Meeting. We are working with the Research committee to incorporate a research component into the Best Practices program. The committee has also begun the process of developing HOPA oncology practice standards. Based on your feedback, we will begin developing a technical standard focusing on dosing issues and a clinical standard focusing on competency and training for oncology pharmacists and technicians. Lastly, we are in the early stages of developing regimen-specific patient education materials as a resource for our members. We look forward to continuing to develop educational offerings that meet the diverse needs of our membership, educational resources for our membership, and practice standards.

Education & Standards Committee Survey - Summary

The Education & Standards Committee sent out a survey to the membership in October to ask for input regarding education-related issues. Two hundred and thirteen members (including one technician) from a variety of practice areas completed the survey.

We received several suggestions for educational topics, which are being utilized by the Program and Education & Standards Committees in planning our educational offerings for the annual meeting and HOPA U. The survey revealed that the membership would utilize HOPA U for at least some of their continuing education requirements and would like to see on average 20 hours of online programming offered. The majority of respondents indicated that HOPA should offer some technician CE on HOPA U.

The Committee used feedback from this survey to select which Practice Standards to develop (Dosing Issues and Competency/

Call for Papers and Reviewers — *Journal of Oncology Pharmacy Practice*

The *Journal of Oncology Pharmacy Practice* (JOPP) is the only PubMed-indexed, international pharmacy journal dedicated to the oncology pharmacy practice specialty. It is the official journal of the International Society of Oncology Pharmacy Practice (ISOPP), the organization that participated in the joint HOPA/ISOPP meeting in 2008.

The information included in JOPP provides a unique perspective for oncology pharmacists, nurses, and physicians by balancing clinical and pharmaceutical issues. Its blend of review articles (new drugs, cancer management, and supportive care issues), original research papers, meeting abstracts, and case reports, provides up-to-date information that helps to manage medication therapies for cancer patients and helps to determine best practices for safe-handling of cytotoxic agents.

JOPP is soliciting papers for upcoming issues. JOPP offers online manuscript submission and an author-friendly review process with a publication decision usually made within 4 weeks. At this time, JOPP is particularly interested in reviews of new drugs, cancer management, and supportive care therapies. To submit a paper, please go to <http://mc.manuscriptcentral.com/jopp>. You will be asked to log in or to create a username and password if you are new to JOPP.

To become a reviewer for JOPP, please email me your contact information, focus areas, and your curriculum vitae. If you have any questions about article submission or becoming a reviewer, please contact me.

Barry R. Goldspiel, PharmD, BCOP

Editor, *Journal of Oncology Pharmacy Practice*

E-mail: bgoldspiel@nih.gov

Training for Oncology Pharmacy Staff) and which “Best Practice” topics to develop for the annual meeting (Investigational Drugs and Medication Errors).

A variety of other questions were asked on the survey; in summary, the overwhelming majority of respondents were interested in the availability of the annual meeting online for a fee, the development of web-based training modules, the availability of regional HOPA meetings, journal clubs, the development of a HOPA handbook and/or reference tool, and that BCOP programming at the annual meeting not compete with other clinical programming. The appropriate committees are taking this information into consideration, and along with the Board are looking into these options for the future.

Many thanks to all who completed the survey! The HOPA Committees truly appreciate and value your input!

Professional Affairs Committee

The Professional Affairs Committee (PAC) has been exploring possible relationships with other organizations, such as the American Society of Hematology (ASH), American Pharmaceutical Association (APhA), American Cancer Society (ACS), Multinational

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COMMITTEE UPDATES

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Association of Supportive Care in Cancer (MASCC), and the Oncology Nursing Society (ONS).

We have also been expanding our relationships with our existing partners. The Committee recommended two HOPA members for ASCO's Implementation, Dissemination, and Evaluation (GuIDE) Subcommittee. These pharmacists will be involved with validating ASCO's Guidelines in their practice settings.

The PAC has decided to once again host interest group meetings at the upcoming HOPA Annual Meeting. We are also developing a white paper on chemotherapy dosing in organ dysfunction.

Research Committee

HOPA Research Workshop Grant Award

The HOPA Research Committee would like to congratulate Dr. Patrick Boyle, whose project entitled "A Double-Blind, Randomized, Placebo-Controlled Trial of Carboplatin, Paclitaxel, Bevacizumab and Astragalus versus Carboplatin, Paclitaxel, Bevacizumab and Placebo in Patients with Advanced or Recurrent Non-Small Cell Lung Cancer," was awarded the 2007 HOPA Research Workshop Grant. This \$20,000 grant was developed by the HOPA Research Committee to support the

pharmacy research of investigator(s) with less than 3 years of research experience. Eligible grant applications were those from an investigator who developed his or her proposal at the 2007 Research Workshop.

Reminders

Abstract Deadlines: The practitioner abstract deadline was January 16. The trainee (resident, fellow, student) abstract deadline is **Friday, March 9, 2009** at 11:59 PM (PST). Trainee abstracts may describe ongoing research. Only current trainees may use this deadline. Please see the HOPA website link for **CALL FOR ABSTRACTS** for more information. For questions, please contact Judith Smith at 713-500-6408 or jasmith@mdanderson.org.

Research Network Survey: HOPA members recently received a Research Network survey via e-mail. The survey will help the HOPA Research Committee develop a web-based research resource for our membership. Please take time to fill it out!

Research Workshop: There will be a pre-meeting Research Workshop at the 5th Annual HOPA Annual Meeting this June. Stay tuned for the program announcement and further details.

LOOKING FORWARD TO SEEING YOU AT

SAVE
THE
DATE

HOPA

June 17–20, 2009
Doral Marriott Hotel
4400 NW 87th Avenue
Miami, Florida 33178



2009



Hematology/Oncology
Pharmacy Association

Online registration available at www.hoparx.org.

www.HopaRx.org | www.HopaU.org
175 Wall Street, Princeton, New Jersey 08540
877-467-2791

DRUG UPDATES

Eltrombopag (Promacta®)

Class: Thrombopoietin receptor agonist

Indication: Patients with chronic immune (idiopathic) thrombocytopenic purpura who have had an insufficient response to corticosteroids, immunoglobulins, or splenectomy.

Dose: The starting dose of Promacta is 50 mg once daily; in patients of East Asian ancestry or patients with moderate or severe hepatic insufficiency, the starting dose is 25 mg once daily.

Dose adjustments: Not established in renal/hepatic dysfunction

Adverse effects: Nausea, vomiting, menorrhagia, myalgia, paresthesia, cataract, dyspepsia, ecchymosis, thrombocytopenia, increased ALT/AST, and conjunctival hemorrhage.

Drug interactions: Substrates of OATP1B1 (eg, rosuvastatin) and concomitant use with calcium-rich foods (eg, dairy products and calcium fortified juices), or supplements containing polyvalent cations (antacids and mineral supplements)

Eltrombopag (Promacta®)

*Ali McBride, PharmD, MS
Oncology Pharmacy Resident
H. Lee Moffitt Cancer Center*

Introduction

Immune thrombocytopenic purpura (ITP) is an autoimmune disorder characterized by a low platelet count.¹ ITP can be acute or chronic in nature, defined by the duration of the disorder (acute is 6 months or less in duration, chronic is greater than 6 months).² The majority of acute ITP cases occur in children and are usually self-limiting, resolving within 6 months.² In contrast, ITP in adults typically has an insidious onset, with no preceding viral or other illness, and has a chronic course.² The incidence of ITP is estimated to be 1.6 to 2.68 per 100,000 persons per year. The estimated incidence of diagnosed cases of chronic ITP in the United States is approximately 60,000/year, with the estimated prevalence of diagnosed cases in adults being approximately 53,000.² The incidence of ITP appears to increase with age; adult-onset ITP typically occurs between 18 and 40 years of age and appears to be more common in women.³

Eltrombopag (SB-497115) is an oral, small-molecule, nonpeptide thrombopoietin (TPO)-receptor agonist that was recently approved for adult patients with chronic ITP. The drug initiates thrombopoietin-receptor signaling by binding to the transmembrane domain of the receptor, thereby inducing proliferation and differentiation of cells in the megakaryocytic lineage. In early-phase clinical studies, eltrombopag increased platelet production in volunteers with normal platelet counts.⁴

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ASH 2008 Annual Meeting – Drug Updates for AML & CLL

*Stephen Harnicar, PharmD
Clinical Specialist
Memorial Sloan Kettering Cancer Institute*

The American Society of Hematology (ASH) reached a milestone this past year: as of 2008, ASH is 50 years old. This momentous occasion was celebrated at the ASH Annual Meeting and Exposition held in San Francisco, CA in early December. However, the 50th Annual Meeting was no different from the past in that ASH continued to uphold its mission, to further the understanding, diagnosis, treatment, and prevention of disorders affecting the blood, bone marrow, and the immunologic, hemostatic and vascular systems.¹ With nearly 24,000 attendees, over 500 oral presentations, and about 2,500 poster presentations at the meeting, how could it not? A good many of these presentations focused on hematologic malignancies. Experts presented new data regarding all aspects of leukemias and lymphomas, however, here I will focus on the progress in acute myeloid leukemia (AML) and chronic lymphocytic leukemia (CLL).

The role of molecular markers and mutations and how they relate to prognosis and therapy for AML were hot topics this year. The table below describes the classification of AML mutations.² Recently, Schlenk et al demonstrated that patients <60 years old with a normal karyotype and isolated NPM1 mutations without FLT3-ITD did not benefit from allogeneic stem cell transplantation in first remission. However when these mutations occurred together, survival was significantly improved with transplantation.³ Seeing a benefit in identifying molecular markers, Gaidzik et al at ASH 2008 presented their data aimed to evaluate the incidence and clinical impact of RUNX1 mutations in adult (16-60 years of age) AML patients.⁴ They found that compared to RUNX1 wildtype AML, those with RUNX1 mutations had a significantly higher rate of resistant disease following induction therapy (38% and 20%, respectively; p=0.03), which translated into a significantly inferior event-free survival (p=0.004). There was no difference in relapse-free and overall survival between the two groups. Continued research in this field can further targeted therapy of these mutations and continue to individualize the care that AML patients receive.

Table 1. Classification of Molecular Markers in AML

CLASS	I	II	III
ACTION	Interferes with transcription and leads to a stop in differentiation	Leads to an increase in cell proliferation	Affects genes implicated in cell-cycle regulation or apoptosis

The advancement in induction AML therapy has long been anticipated, since little has changed in our approach since the introduction of cytarabine and anthracyclines. Holowiecki et al presented data on the addition of cladribine or fludarabine to standard 3+7.⁵ Adult patients up to 60 years of age were randomized

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DRUG UPDATES

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Eltrombopag (Promacta®) continued

Eltrombopag was further studied in two separate trials in patients who had completed at least one prior ITP therapy regimen and who had a platelet count $<30 \times 10^9/L$.⁵ Patients were randomized to either daily placebo or eltrombopag administered over a maximum treatment period of 6 weeks, followed by 6 weeks off therapy. During the studies, eltrombopag or placebo was discontinued if the platelet count exceeded $200 \times 10^9/L$. The primary efficacy endpoint was response rate, defined as a change from a baseline platelet count of $<30 \times 10^9/L$ to $\geq 50 \times 10^9/L$ at any time during the treatment period.

The median age of the patients was 50 years and 60% were female. Approximately 70% of the patients had received at least 2 prior ITP therapies (predominantly corticosteroids, immunoglobulins, rituximab, cytotoxic therapies, danazol, or azathioprine) and 40% of the patients had undergone splenectomy. The median baseline platelet counts (approximately $18 \times 10^9/L$) were similar among all treatment groups. The median duration of treatment with the 50 mg dose of eltrombopag in Study 1 was 42 days and Study 2 was 43 days.⁵ The median baseline platelet count was $18 \times 10^9/L$ prior to administration of eltrombopag. Median platelet counts at 3, 6, and 9 months on study were $74 \times 10^9/L$, $67 \times 10^9/L$, and $95 \times 10^9/L$, respectively. The median daily dose of eltrombopag following 6 months of therapy was 50 mg ($n = 53$); the median daily dose was also 50 mg among patients with no change in the dose regimen of eltrombopag over 2 months or more of therapy ($n = 45$).⁵

In clinical studies, hemorrhage was the most common serious adverse reaction and most hemorrhagic reactions followed discontinuation of eltrombopag. Other serious adverse reactions included LFT abnormalities and thrombotic/thromboembolic complications.⁵ A phase III, extended-dosing study (EXTEND) is currently being conducted in adults with chronic idiopathic thrombocytopenic purpura who were previously enrolled in an eltrombopag study.⁶ Further data will study is to evaluate the long-term safety and efficacy of eltrombopag in these patients.

The starting dose of eltrombopag is 50 mg once daily for most patients; however, in patients of East Asian ancestry or those with moderate or severe hepatic insufficiency, the recommendation is 25 mg once daily.⁵ The medication should be given on an empty stomach either 1 hour before or 2 hours after a meal. Patients should also be counseled on allowing a 4-hour interval between eltrombopag and other medications, foods, or supplements containing polyvalent cations (eg, iron, calcium, aluminum, magnesium, selenium, and zinc). The use of supplements with concomitant administration of eltrombopag has been shown to reduce the decreased plasma eltrombopag systemic exposure by approximately 70%.⁵ Furthermore, data from *in vitro* studies demonstrated that eltrombopag is an inhibitor of the organic anion transporting polypeptide OATP1B1 and can increase the systemic exposure of other drugs that are substrates of this transporter. In clinical trials with eltrombopag, a dose reduction of

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ASH 2008 continued

to receive DAC (daunorubicin, cytarabine, cladribine), DAF (fludarabine), or DA alone. The complete response rate after a single induction course was significantly higher in the DAC group compared to DA, whereas there were no differences in DAC vs. DAF. The overall survival at 1 year was significantly higher in the DAC group compared with both the DAF and DA group: 51%, 36%, and 39% respectively.⁵ The authors concluded that the addition of cladribine to standard 3+7 improves the complete response rate and the overall survival in adults up to 60 years old with AML, without additional toxicity, and that this is not seen with DAF.

Developments in relapsed or refractory AML from ASH 2008 include the phase I trial results of a second generation *FLT3* receptor tyrosine kinase inhibitor (AC220) and a phase I/II trial of a XIAP antisense oligonucleotide (AEG35156), both of which show encouraging results with the latter possibly having a role in early reinduction.^{6,7}

Exciting developments in the CLL arena were also presented at ASH 2008. An important part of CLL therapy includes purine analogues. A combination of fludarabine, cyclophosphamide, and rituximab (FCR) and the combination of pentostatin, cyclophosphamide, and rituximab (PCR) have emerged as highly effective therapy.^{8,9} Reynolds et al presented a phase III, multicenter, randomized, community-based trial comparing FCR vs. PCR in untreated or minimally treated (one previous treatment) B-cell CLL. The primary endpoint was infectious complications with efficacy and safety as secondary endpoints. The regimens were 1) PCR (pentostatin 4 mg/m² Day 1, cyclophosphamide 600 mg/m² Day 1, rituximab 375 mg/m² Day 1) (21-day cycles) or 2) FCR (fludarabine 20 mg/m² Day 1–5, cyclophosphamide 600 mg/m² Day 1, rituximab 375 mg/m² Day 1) (28-day cycles).

There were no significant differences in infection rate, infectious events, hospitalization, and days of hospitalization between the two arms, however there was a trend towards less infectious complications with FCR. Patients with a complete response were 17.2% and 7.1% in the FCR and PCR arms respectively, which was significant. However, an overall response rate of 56.3% for FCR and 43.5% for PCR was not. Early follow-up of overall survival was also not significant.¹⁰ Public discussion at ASH about the response rate results included the fact that, overall, the response rates described are lower than that of other studies with FCR and PCR. The authors speculated that this is possibly due to the community-based setting of the trial. Though this trial will shed some light on the two regimens, questions still remain as to which may be superior. For example, a change in the pentostatin dose to 2 mg/m² can help reduce toxicity, but may affect the response rates.

A plethora of exciting data has come out of the ASH 2008 meeting and I advise oncology pharmacy practitioners to view the abstracts online located on the ASH website. I would also recommend

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DRUG UPDATES

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Eltrombopag (Promacta®) continued

rosuvastatin (OATP1B1 substrate) by 50% was recommended for co-administration with eltrombopag.⁵

The treatment goal with eltrombopag is to achieve and maintain a platelet count $\geq 50 \times 10^9/L$ in order to reduce the risk for bleeding. Dosage recommendations are listed in the table below, with recommendations not to exceed a daily dose of 75 mg.⁵ Complete blood counts, platelet counts, peripheral blood smears, and LFTs should be monitored weekly in patients on eltrombopag, until a stable platelet count has been achieved; CBCs that include platelet counts and peripheral blood smears should be obtained monthly thereafter. Eltrombopag should be discontinued if the platelet count does not increase after 4 weeks at the maximum dose or if LFT abnormalities or excessive platelet count responses occur.⁵

Table. Eltrombopag Dose Adjustments Based on Platelet Count Response⁵

Platelet Count	Dose Adjustment
$< 50 \times 10^9/L$ following at least 2 weeks of eltrombopag	Increase daily dose by 25 mg to a maximum of 75 mg/day
$50-199 \times 10^9/L$	Dose unchanged
$200-400 \times 10^9/L$ at any time	Decrease the daily dose by 25 mg. Wait 2 weeks to assess the effects of this and any subsequent dose adjustments.
$> 400 \times 10^9/L$	Stop eltrombopag and increase the frequency of platelet monitoring to twice weekly. Once the platelet count is $< 150 \times 10^9/L$, reinstitute therapy at a daily dosereduced by 25 mg.
$> 400 \times 10^9/L$ after 2 weeks of therapy at lowest dose of eltrombopag	Permanently discontinue eltrombopag

Dispensing of eltrombopag will be authorized through the Promacta® Cares™ program, a patient registry and distribution program. Prescribers, pharmacists, and patients must be enrolled in Promacta Cares in order to prescribe, dispense, or receive Promacta. The program was developed in accordance with the FDA's requirements for appropriate and safe use of eltrombopag while minimizing risks, including the risk of hepatotoxicity. Promacta Cares is part of an ongoing collaboration between GSK and the FDA to provide a format for appropriate additional data collection; baseline and periodic safety information must be reported for all patients. Further information can be found at www.promactacares.com.

In summary, eltrombopag is the first orally bioavailable TPO-receptor agonist that is indicated for patients with ITP who had received one or more prior ITP therapies. In patients refractory to standard therapies, two pivotal studies have shown the drug is effective vs placebo in patients currently on standard therapy.⁶ Patients taking eltrombopag were 8 times more likely to have increased their platelets counts. Side

ASH 2008 continued

attending, if possible, the Highlights of ASH 2008 sessions on February 6-7, 2009 in Miami, Florida or May 15-16, 2009 in Sao Paulo, Brazil.

ASH will hold its 51st Annual Meeting in New Orleans, LA in December 2009. This meeting is expected to herald another 50 years of reporting cutting edge research. ■

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Eltrombopag (Promacta®) continued

effects reported during the clinical studies included headache, upper respiratory tract infection, diarrhea, nasopharyngitis, and arthralgia, with noted laboratory LFT abnormalities. Further studies assessing the risk of thrombosis will be revealed in ongoing clinical studies. The addition of eltrombopag adds yet another medication for the treatment of chronic ITP for use primarily in the outpatient setting. ■

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