Expert and Consumer Evaluation of Consumer Medication Information-2008

Final Report to the
U.S. Department of Health and Human Services and
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INTRODUCTION

Background

In 1995, the United States Food and Drug Administration (FDA) proposed a regulation to set specific goals regarding the distribution and quality of medication information provided to consumers (60 FR 44182; August 24, 1995). Specific goals of the regulation included a target that by the year 2000, 75% and by 2006, 95% of new prescriptions dispensed would include useful written information for patients. Before the regulation could go into effect, Public Law 104-180 was enacted.[1] While the law adopted the goals of the 1995 proposed rule, it prohibited the FDA from taking regulatory steps specifying uniform content under the assumption that private-sector initiatives were able to meet the goals, which FDA was charged with evaluating. A Steering Committee was created and developed the *Action Plan for the Provision of Useful Prescription Medicine Information,* which described criteria for evaluating the "usefulness" of written medication information for consumers.[2] The FDA contracted a study to determine progress toward meeting the goals of Public Law 104-180. This study, finished in 2001, evaluated consumer medication information (CMI) obtained from pharmacies for four commonly prescribed medications.[3] The study found great variability in the quality of the consumer medication information provided by pharmacies. In 2002, the FDA Drug Safety and Risk Management Advisory Committee recommended that FDA take a more active role in advising and encouraging the private sector to meet the next target goal set for year 2006.[4] In response to that recommendation, the FDA developed a Guidance document for the private sector describing criteria for content and formatting of consumer medication information.[5] The research reported here serves as a follow-up to the 2001 evaluation of the quality of consumer medication information dispensed in community pharmacies using criteria contained in the 2006 Guidance document. The study was conducted by the National Association of Boards of Pharmacy (NABP) through a subcontract with the University of Florida, College of Pharmacy.

RESEARCH QUESTIONS

The 2008 study addressed the following specific research questions:

1. What percentage of shoppers getting prescriptions filled for lisinopril and metformin in community pharmacy settings was given *any* written Consumer Medication Information (CMI) beyond label directions?

2. What percentage of shoppers was given written CMI that adhered to criteria as defined by the FDA Guidance document, developed for two specific study drugs, and applied by a panel of experts to evaluate the quality of CMI leaflets?

3. What percentage of CMI leaflets adhered to criteria consumers were asked to use to evaluate quality of the leaflets?

4. How did expert and consumer evaluations of the quality of CMI differ in the 2001 and 2008 studies?

METHODS

Study methods followed closely the previously conducted study on the quality on consumer information conducted by Drs. Svarstad and Mount at the University of Wisconsin.[3] The 2001 study evaluated written consumer information dispensed by a random sample of 384 community pharmacies from throughout the continental United States for four newly prescribed medications used to treat prevalent medical conditions. The 2001 study sought the assistance of a pharmacist clinical consultant to help develop and refine expert evaluation forms using explicit criteria for each study drug. These forms were then reviewed by a national expert panel and applied by the panel to derive a quality score for each of the dispensed CMI leaflets. The current 2008 study utilized a similar approach. Two medications that were not included in the 2001 research, metformin and lisinopril, were used which required adjustments in the evaluation subcriteria. In addition to the necessary drug-specific adjustments, the 2008 criteria incorporated information in the FDA Guidance document on useful written CMI[5], which had not been released when the 2001 study was conducted. Applying the specific advice contained in the Guidance document resulted in an expanded list of subcriteria for many of the standards used in 2001 for defining useful CMI. For the 2008 study, a panel of two pharmacist and two physician experts developed the expert evaluation forms which were then reviewed and applied by a national panel of pharmacy experts.

The 2001 study also developed a set of evaluation criteria to assist consumers in evaluating the usefulness of CMI. These criteria were utilized unaltered in this 2008 study by a national convenience sample of consumers who were convened in local group sessions.

Selection of Pharmacies

As in the 2001 study CMI leaflets were obtained by professional shoppers from a national representative sample of pharmacies. Shoppers utilized prescriptions solicited by the FDA from physicians located in the same geographic area as selected pharmacies. The target sample size was set at 384 to mirror the sample size of the 2001 study. The sample size requirements for both studies were calculated to power the analysis to determine the percentage of pharmacies dispensing *any* written information to professional shoppers, with 95% confidence interval limits not larger than ± 5% of the true population value under the worst-case scenario assumption that there would be only 50% of pharmacies providing written information. The same sample size would be

required under the same assumptions and with the same confidence limits to detect the percentage of pharmacy-provided CMI that met target thresholds established by expert judges. The National Association of Boards of Pharmacy (NABP) took responsibility for sampling. Specifically, NABP purchased from Medical Marketing Service, Inc (MMS; Wood Dale, IL) a list of 420 pharmacies selected by randomized procedures from a national electronic list of retail pharmacies certified by the National Council for Prescription Drug Programs (NCPDP). The list included each pharmacy's name, address, and telephone number. Pharmacies on the list included those identified as: independent, chain, or franchise pharmacies within any retail, grocery, or department store setting. The list did *not* include pharmacies identified as hospital, clinic, long-term care, mail order, IV infusion, dispensing physicians, Indian Health Service, Veterans Administration Hospital, or other government/federal setting. The list also did not include pharmacies located in Alaska, Hawaii, Puerto Rico, the US possessions, or in Ohio, Oregon, or Georgia, the latter three of which prohibit the filling of prescriptions for research purposes.

The final universe from which the list of 420 pharmacies was selected included 55,513 pharmacies meeting the above mentioned criteria. To select the random list of pharmacies visited during the study, MMS performed an n^{th} name select; i.e., the firm selected every 134^{th} record to reach the desired quantity of 420 pharmacies.

Procedures for Collecting Consumer Medication Information (CMI)

To collect the CMI leaflets from the selected pharmacies, the NABP subcontractor Second to None (STN; Ann Arbor, MI) hired professional shoppers to pose as patients and visit each pharmacy location to fill prescriptions written by FDA-recruited physicians for the two study drugs. Upon visiting the pharmacies and having the prescriptions for the two drugs filled, the shoppers collected but did not open or write on any information received from the pharmacies. Following the pharmacy visit, each shopper sent the two filled prescription containers and any written materials provided by the pharmacy staff with the medication to STN. All pharmacy visits were conducted between January 28 and March 31, 2008.

Second to None ensured that all materials were received from the shoppers after each assignment was completed. Upon receipt of materials from shoppers, STN separated the CMI from the medication and placed the two medication bottles into Ziploc bags labeled with the location number, the shopper initials, and the visit date. Second to None labeled each CMI leaflet with the location number, removed any pharmacy identifiers (e.g., name, address, city, state, and zip), placed the CMI into an envelope labeled with the location number, and stored all materials collected in a locked office. The CMI was sent by STN in three separate batches to the University of Florida. At study completion, STN shipped all of the medications, along with copies of the prescriptions and an Excel file listing location number, visit date and pharmacy name and address, to FDA.

Training of Professional Shoppers

Before professional shoppers were assigned to pharmacies, each individual underwent training to be able to play the role of a person recently diagnosed with diabetes and high blood pressure and to answer questions from pharmacy staff according to a standard patient role. Shoppers were referred to as Patient-Observers in the shopper training program. Shoppers had to pass an online exam developed by the University of Florida to test understanding of the patient role they were assuming. The role that was developed by the University of Florida included the patient name and address, his or her reason for filling a prescription in the area of the pharmacy, and health and medication history. A standard scenario of a patient filling a prescription for metformin and lisinopril was developed incorporating key aspects of the patient role as follows:

> Patient-Observers are from (Patient-Observer's own city and state). If asked why they are getting their prescriptions filled at this particular pharmacy, they should say that they went past the pharmacy while visiting the area and remembered that they needed to get the prescriptions filled. They have no regular pharmacy that they use. They received two prescriptions from their doctor but forgot to fill the prescriptions immediately. They were told by their doctor that they have high blood pressure and diabetes. They have no other medical conditions. They take no other medications and have no drug allergies. They have not taken these medications before. They don't have insurance for medication and therefore will pay with cash.
>
> The reason Patient-Observers have these two new prescriptions is that they went to their doctor to find out the results of some blood tests they had taken the preceding week. For the blood tests, they went in early in the morning before they had anything to eat so the lab people could take their blood. When they saw their doctor, they were told that their blood sugar was too high and that their blood pressure was also a little high. The doctor prescribed medications for the high blood pressure (lisinopril) and diabetes (metformin). The doctor was busy and did not give any other information. The doctor said the directions would be on the prescription bottles. Patient-Observers have a follow-up appointment with the doctor in two weeks.
>
> If pharmacy personnel discuss getting refills or suggest follow-up contact with the pharmacy, the Patient-Observer should say "There is a pharmacy near my house that I will probably use".

After reading through the training materials, professional shoppers were instructed to:

- Memorize the standard patient-observer role according to the scenario presented above.

- Review Questions Commonly Asked in the Pharmacy Setting and Patient-Observer Answers (Appendix A).
- Complete an online exam to test understanding of (a) study protocol and (b) standard responses to pharmacist questions. A passing grade of 90% was required before shoppers were sent out on the assignment.

Training materials included a videotape of three scenarios developed by the University of Florida in their model pharmacy teaching laboratory where shoppers were able to observe actors presenting prescriptions to pharmacists and responding to questions according to the scripted or suggested responses the patient-observers were being instructed to use. Each Patient-Observer was asked to practice his or her scenario with someone acting as a pharmacist. They were asked to become comfortable with the standard scenario and be able to follow the study protocol in order to avoid problems in collecting CMI. All materials were provided by the University of Florida to the shopper research firm for distribution to patient-observers.

When shoppers presented the prescriptions to pharmacy personnel, they were instructed to ask, "How long will it be before the prescriptions are ready?" The shopper could then decide to wait or return later. The return was to be as soon as possible after the pick-up time provided by the pharmacy personnel. Shoppers were instructed to ask no other questions of pharmacy personnel. They were told to avoid initiating conversation and to volunteer no information other than that required to address specific questions from pharmacy personnel. If shoppers recognized any individual in the pharmacy, they were advised to exit the pharmacy prior to presenting the prescription.

Immediately prior to being sent on assigned pharmacy visits, shoppers were provided with study prescriptions and the name and address of their assigned pharmacy. They traveled to the pharmacy, presented the prescriptions to be filled, picked up and paid for the prescriptions with cash, answered any questions according to the standard scenario, accepted any written information materials that were offered, and exited the pharmacy.

Expert Evaluations

Table 1 contains the standards (general criteria) outlined in the 1999 action plan[2] that were operationalized for the 2001 evaluation of written prescription information by the University of Wisconsin.[3] These criteria were further defined by the FDA in the 2006 Guidance Document on Useful Written Consumer Medication Information.[5] Expert panel members for the 2008 evaluation used these general criteria to define explicit subcriteria for the two study medications, lisinopril and metofrmin.

Table 1. Standards/Criteria for Consumer Medication Information

Standard/ Criterion	Information must:
1	Include drug names and indications for use
2	Include contraindications and what to do if applicable
3	Include specific directions about how to use, monitor, and get most benefit
4	Include specific precautions and how to avoid harm while using it
5	Include symptoms of serious or frequent adverse reactions and what to do
6	Include general information and encouragement to ask questions
7	Be scientifically accurate, unbiased, and up-to-date
8	Be readily comprehensible and legible

Development of Expert Evaluation Tool

A panel of four clinical experts, who were approved by NABP and FDA, (one internist, one endocrinologist, one drug information pharmacist, and one community pharmacist) developed the initial set of study drug-specific evaluation subcriteria to guide expert evaluation of the CMI. Appendix B lists the members of this development expert panel. Three meetings were held with the development panel (8 hours total) to develop the subcriteria and numerous electronic exchanges were used to refine the subcriteria definitions after the initial group meetings. In order to identify the specific content relevant to the study drugs (standards 1 to 6) as identified in the FDA guidance document the research team developed a master drug information repository from the following sources and compendia: the FDA approved labeling[6,7], Clinical Pharmacology Online[8], Micromedex[9], Drug Facts and Comparisons[10], American Hospital Formulary System[11] and Lexi-Comp.[12] Information was organized in a spreadsheet that allowed comparisons across references and printed on poster-size displays that were taped to the conference room walls for quick retrieval of information. Internet access was also available during meetings for review of primary literature. In addition, panelists considered consumer information made available inClinical Pharmacology Drug Information online[13], and American Hospital Formulary System Drug Information.[14] Each information source was the most current version available in October, 2008. Finally, the panel reviewed current examples of medication leaflets obtained from local pharmacies for selection of content, wording and general presentation of information.

Each item of content identified by the development panel as critical for good-quality consumer information relevant to Standards 1 to 6 in the FDA guidance document for a study drug was phrased as a single subcriterion. The development panel had several in-depth discussions about the purpose and effectiveness of consumer medication

information. Critical discussion points included the challenge to balance comprehensiveness against information overload and confusion, and the degree to which information can facilitate patient autonomy in monitoring drug therapy. Specifically, the panel stressed the importance of explicit recommendations for patient action when serious side effects or contraindications were noted and explicit guidance on monitoring procedures relevant to drug safety and effectiveness. In order to maintain comparability with the 2001 criteria no attempt was made to reward conciseness or to penalize for information overload, even though comprehension and recollection of information may be affected.

There was some controversy about the inclusion of off-label indications in patient information, which is considered inappropriate practice in the FDA guidance document. Both study drugs, lisinopril and metformin, have significant evidence for the effectiveness of specific off-label indications and are widely used for these purposes. Thus, consumer understanding that valid indications exist for these drugs in addition to the FDA approved indications may help avoid patient confusion. A similar controversy surfaced about the use of these drugs in young children, which is not approved but is common in medical practice. The panel decided to collect information on these two types of off-label use for descriptive purposes, but to suspend inclusion in the aggregate quality scores.

For Standards 7 and 8 the development panel reviewed the subcriteria utilized in the 2001 report and made minor modifications. Standard 7 specified that the information that was included in the leaflet was scientifically accurate, unbiased, and up-to-date. The operational definition used for accuracy addressed only presence of incorrect information but not absence of correct information as penalties for missing information would be reflected in reduced scores for Criteria 1-6. Thus, failure to meet this criterion reflects errors of commission and not errors of omission. For Standard 8 additional items were included based on formatting advice contained in the 2006 guidance document and observations put forward by the development expert panel. Six subcriteria were added to the original 2001 version which were: use of short paragraphs with a single topic in situations where bullet points were not used, limited use of medical or technical terms that were not defined, adequate white space around text (≥.5 inch), use of fonts with serifs, and short line length (≤6 inches). In order to address the issue of information overload, the word count of the CMI was also obtained, but not included in the quality score for reasons of consistency with the FDA guidance document. The word count included only the text that provided medication information. Additional text on the leaflets such as advertisements, general information about the disease state, or coupons was excluded.

For analytic purposes subcriteria were aggregated within each criterion or standard as well as in an overall quality score.

Finally, the development expert panelists suggested defining subcriteria such that they could be assessed as being either met or not met. Thus, for the 2008 evaluation, the category of "partially met" was not used, which resulted in a modification of the 2001 scoring system. All other summative statistics were the same as for the 2001 study.

National Validation Expert Panel

A national panel of eight experts was nominated by the investigators and approved by NABP and FDA (see Appendix C). The expert panelists included pharmacy practitioners, drug information specialists, and pharmacy educators with expertise in pharmacotherapy and patient education and communication. Four panelists were assigned to review lisinopril CMI and four were assigned to metformin. Each panelist was asked to review the FDA Guidance document and the draft Expert Evaluation Form prepared by the Development Expert Panel. Recommendations for adjustments of the Forms were reviewed by the Development Expert Panel and incorporated into revised drafts . These forms were then used to evaluate a random sample of 40 CMI leaflets by the National Expert Panel members. In order to determine inter-rater reliability each CMI leaflet was evaluated by two panelists independently. Final revisions of the form addressed subcriteria that were scored differently by the two judges. Reliability checks of expert evaluations continued during the study period with 20% of CMI leaflets being double scored, but no further adjustments were made to the final Evaluation Forms.

Expert Evaluation Forms

The final Expert Evaluation Forms are included as Appendices D and E. The general criteria mirror those in the 1996 action plan, the 2001 evaluation, and the 2006 FDA Guidance document on useful CMI. Two subcriteria (the possibility of use for off-label indications and use in children) were reported for descriptive purposes but were not included in the summated scoring. Several additional subcriteria were excluded from the final total score because of low inter-rater reliability during the study. An example of a low reliability subcriterion was the distinction between recommendations for the consumer to *not* use a medication versus advice to contact the provider when serious side effects occurred or contraindications were present. Statements like "contact your provider before use" were interpreted differently by different raters. Another example was disagreement on whether the CMI provided information on the route of administration. This information was often included in the personalized label directions that were separate from the main body of drug information and thus not counted by some raters. These items are highlighted in the appended evaluation forms. The final number of subcriteria included in each overall quality score was 77 for lisinopril and 78 for metformin.

Inter-rater Reliability of Revised Expert Evaluation Forms

The percent agreement between raters for the final set of subcriteria for lisinopril ranged from 72.0% to 100% with a mean of 92.5% (±6.6). Respective values for metformin were 80.9% to 100% with a mean of 93.4% (±5.3).

Staff Assessments of Comprehensibility/Readability

Eleven subcriteria for Criterion 8 (comprehensibility/readability) that involved explicit objective assessments were determined by research staff. These assessments included such subcriteria as font size, amount of space between lines and around text, line length, use of bullets, and other formatting suggestions contained in the FDA guidance document. The staff assessment form is included as Appendix F. Total word count and word count of longest paragraph (if bulleting was not used) are included for descriptive purposes only. The remaining subcriteria are included in summary scores for Criterion 8, with reading levels over 8 defining the threshold for the subcriterion on reading difficulty .

Each CMI leaflet was scanned into a pdf file, which was converted to a Word document. The length of the document was determined by word count and reading difficulty was determined by the Flesch-Kincaid Grade Level Index.[15] This index gives information about the grade level that would typically be required to read and comprehend written text.

The formula for the Flesch-Kincaid Grade Level score is:

$$(.39 \times ASL) + (11.8 \times ASW) - 15.59$$

where:

ASL = average sentence length (number of words divided by number of sentences)

ASW = average number of syllables per word (the number of syllables divided by the number of words)

Space between lines of text and amount of white space around text were measured with calipers. Font size was determined with an "E-scale" (AccuSpec II©, transparent type gauge and specifier set, The C-Thru Ruler Company©) using a template with a capital 'E' as the standard to which the same capital letter in each leaflet was compared. These assessments were limited to the main body of the text that provided medication information. Advertisements for other products, store coupons, or Health Insurance Portability and Accountability Act (HIPAA) statements, which were often included on the leaflets, were not considered.

Scoring Procedures

For each subcriterion in the Sections for Criteria 1-6, national expert panel raters indicated whether the information was present or not. Criterion 7 asked experts to indicate that the information that was provided was scientifically accurate, unbiased, and up-to-date and Criterion 8 had subcriteria that operationalized the criterion "Information is readily comprehensible and legible". Seven subcriteria in Criterion 8 were evaluated by national expert panel members and an additional eleven subcriteria, which involved explicit objective assessments, were determined by research staff.

The percent adherence was reported as an overall aggregate score across all subcriteria, for each individual general criterion (1-8), and for each individual subcriterion. The percent adherence for the total score and the eight general criteria were summarized as the mean and standard deviation (sd) for each study drug. In addition, frequency distributions were reported, reflecting six levels of adherence that that were used to summarize findings in the 2001 study. They were:

- Level 0: no written information provided
- Level 1: information included 0-19% of subcriteria
- Level 2: information included 20-39% of subcriteria
- Level 3: information included 40-59% of subcriteria
- Level 4: information included 60-79% of subcriteria
- Level 5: information included 80-100% of subcriteria

For comparability with 2001 results the percent leaflets meeting level 4 or 5 (representing the 60% threshold) is reported as well.

It should be noted that percentages become increasingly imprecise as the number of items that are summarized decreases. For example, for a criterion with only four subcriteria, a difference in only one subcriterion will result in a 25% crude difference in the score and a change in the above described levels. Averages are expected to be somewhat more robust than frequency distributions.

Consumer Evaluation Procedures

Consumer Evaluation Form and Scoring Procedures

The Consumer Evaluation Form (CEF) developed and validated by Svarstad and Mount [3] and used in the 2001 study evaluating CMI was used to obtain consumers' perceptions of the quality of the CMI leaflets. A copy of the CEF is included as Appendix G. For each item, consumers were asked to circle the one number on a semantic differential scale with opposite adjectives that might describe the leaflet (e.g., scores could range from 1 [adjective describing poor quality] to 5 [adjective describing good quality]). The first

nine items asked the consumers how they would feel if they were taking the medicine for the first time and received the information sheet from the pharmacy. The remaining three items asked for an overall opinion about the readability, comprehensibility and usefulness of the leaflet. Responses for all items were summated and reported as the average (mean) percentage and standard deviation (sd) of all possible points. As with the expert rating frequency distributions, consumer ratings were reported as follows:

- Level 1: 0-19% of possible points
- Level 2: 20-39% of possible points
- Level 3: 40-59% of possible points
- Level 4: 60-79% of possible points
- Level 5: 80-100% of possible points

Missing items on the CEF would be imputed with the person average if there were ≤ 3 questions left unanswered.

Internal Consistency Reliability

Svarstad and Mount[3] had established the test-retest reliability of the Consumer Evaluation Form, indicating that consumer ratings were stable over time. Before item scores were summated in the current investigation, the internal consistency of the summated scale was determined using Cronbach's coefficient alpha. An alpha of .70 was set as the lower limit for reliability. In addition, item analysis was planned and items that had an item-corrected total score correlation of <.30 or which reduced coefficient alpha were to be targeted for possible exclusion from the summated scales.

Recruitment of Consumer Evaluators

Fourteen site coordinators from 14 different cities in 13 states were identified to recruit consumers and gather data on consumer evaluations of CMI leaflets. Site coordinators were each asked to recruit approximately 12 consumers willing to spend two hours evaluating a sample of 6 CMI leaflets. All materials used in recruiting consumers, all forms used in data gathering, and informed consent forms for participants were approved first by the University of Florida Institutional Review Board (IRB) and then by the local IRBs for every site requiring separate approval. Site coordinators were sent IRB-approved posters they could use as recruitment materials as well as guidelines for recruiting consumers and gathering evaluation data. Site coordinators recruited consumers from church groups, clinic populations, members of organizations, and apartment buildings using "snowball" recruitment techniques. Site coordinators were encouraged to recruit a diverse group of consumers, able to read CMI written in English, who had no training as a health professional, who did not have diabetes or hypertension and who had not taken either of the study drugs or drugs in the same class (e.g. ACE-inhibitors).

Data Entry and Processing

All expert and consumer evaluation forms were entered into a Microsoft® Access 2008 database. Data entry was performed by two individuals simultaneously to reduce entry errors. Frequency tables and descriptive analyses were generated in Microsoft Excel and data analysis was conducted using SPSS Version 16, Chicago, IL.

RESULTS

A total of 55 pharmacies of the 420 sampled were excluded from the study, mainly because shoppers were unable to fill the prescriptions because they were asked for identification or the location was no longer in business. Shoppers obtained new prescriptions for lisinopril at 365 and for metformin at 364 community pharmacies in 41 states.[1] Twenty-two pharmacies (6%) did not provide any written information beyond the directions on the prescription vials. The remaining 94% (95% confidence interval 91.5, 96.4) provided printed CMI for filled prescriptions for lisinopril (n=343) and metformin (n=342). These 685 leaflets were rated by the national expert panel on content and format. They were also evaluated by consumer evaluators. The leaflets ranged from 33 words to 2,482 words. No publisher was identified for 43% of CMI. For those CMI with information on the publisher, First Databank (56%) and Wolters Kluwer Health, Inc. (42%) were most common.

Expert Evaluations

Overall quality of written consumer information

Including all prescriptions that were filled in pharmacies (with or without dispensing of written information) the overall quality of written information was as follows: 22 (6.0%) of prescriptions for both lisinopril and metformin were dispensed without written medication information, indicating the lowest quality of written information provision. A total of 274 (75%) of prescriptions for lisinopril and 233 (64%) for metformin met 60% or more of all subcriteria (Table 2). The 60% threshold matched the level set in the 2001 evaluation for the minimum acceptable level in defining useful written information. Fourteen percent of lisinopril and 16% of metformin CMI leaflets had very low levels of quality with adherence scores of less than 40%. The mean percent of subcriteria provided was 62% for lisinopril and 59% for metformin.

[1] One CMI for metformin was missing because one pharmacy was only presented a prescription for lisinopril by the professional shopper.

Table 2. Quality of patient written information including prescriptions dispensed without written information

		Level of adherence to subcriteria					
Drug	Mean % of subcriteria (SD)	Level 0: no written CMI % (n)	Level 1: 0-19% % (n)	Level 2: 20-39% % (n)	Level 3: 40-59% % (n)	Level 4: 60-79% % (n)	Level 5: 80-100% % (n)
Lisinopril N=365	61.9 (21.0)	6.0 (22)	0 (0)	8.0 (29)	11.0 (40)	68.0 (248)	7.1 (26)
Metformin N=364	58.5 (20.5)	6.0 (22)	0.8 (3)	9.6 (35)	19.5 (71)	63.5 (231)	0.6 (2)

When limited to those pharmacies where written consumer medication information was actually dispensed, the mean adherence with all subcriteria was 66% for lisinopril and 62% for metformin (Table 3). Twenty-nine (9%) of leaflets met less than 40% of all subcriteria and 274 (80%) met 60% or more for lisinopril. For metformin, 38 (11%) met less than 40% of all subcriteria and 233 (68%) met 60% or more.

Table 3. Quality of Consumer Medication Information (CMI) for criteria 1-8 for those prescriptions dispensed along **with** written information

		Level of adherence to subcriteria				
Drug	Mean % of subcriteria (SD)	Level 1: 1-19% % (n)	Level 2: 20-39% % (n)	Level 3: 40-59% % (n)	Level 4: 60-79% % (n)	Level 5: 80-100% % (n)
Lisinopril N=343	65.9 (14.4)	0 (0)	8.5 (29)	11.7 (40)	72.3 (248)	7.6 (26)
Metformin N=342	62.2 (14.5)	0.9 (3)	10.2 (35)	20.8 (71)	67.5 (231)	0.6 (2)

Expert Evaluations by Criterion

Table 4 shows the distribution of expert panelists' ratings of patient information leaflets by criterion. The percentage of prescriptions dispensed without CMI is omitted from these tables. Level of adherence varied across the eight criteria, with the highest means obtained on Criterion 7 (scientific accuracy). The mean percentage of points on Criterion 7 was over 97% for both study drugs. The mean percentage points for the remaining criteria varied with the lowest adherence in Criterion 3 (directions) and 8 (comprehensibility/legibility).

Table 4. Adherence to criteria of dispensed CMI as rated by expert panel (n=342 for metformin, n=343 for lisinopril)

Criterion Drug (number of subcriteria)	Mean % of subcriteria (SD)	Level of adherence to subcriteria				
		Level 1: 0-19% of points	Level 2: 20-39% of points	Level 3: 40-59% of points	Level 4: 60-79% of points	Level 5: 80-100% of points
		% (n)	% (n)	% (n)	% (n)	% (n)
1. Drug name & indications						
Lisinopril (6)	74.6 (25.5)	7.0 (24)	2.3 (8)	5.2 (18)	28.9 (99)	56.6 (194)
Metformin (5)	69.8 (21.3)	5.6 (19)	5.8 (20)	37.1 (127)	35.4 (121)	16.1 (55)
2. Contraindications						
Lisinopril (5)	72.9 (20.0)	6.7 (23)	3.8 (13)	5.8 (20)	81.3 (279)	2.3 (8)
Metformin (10)	76.0 (32.7)	14.9 (51)	4.4 (15)	0.3 (1)	5.6 (19)	74.9 (256)
3. Directions						
Lisinopril (17)	53.9 (23.9)	13.7 (47)	9.6 (33)	34.1 (117)	28.9 (99)	13.7 (47)
Metformin (16)	45.6 (18.3)	15.5 (53)	15.8 (54)	50.0 (171)	17.0 (58)	1.8 (6)
4. Precautions						
Lisinopril (12)	80.9 (26.0)	5.5 (19)	3.2 (11)	13.1 (45)	6.7 (23)	71.4 (245)
Metformin (11)	76.7 (27.1)	8.8 (30)	2.6 (9)	6.1 (21)	15.2 (52)	67.3 (230)
5. Adverse Reactions						
Lisinopril (10)	80.8 (20.8)	4.4 (15)	2.9 (10)	2.6 (9)	13.4 (46)	76.7 (263)
Metformin (9)	69.3 (20.5)	4.4 (15)	3.8 (13)	14.6 (50)	48.5 (166)	28.6 (98)
6. General information						
Lisinopril (6)	65.8 (31.1)	11.7 (40)	7.0 (24)	19.5 (67)	23.0 (79)	38.8 (133)
Metformin (6)	63.3 (31.1)	14.3 (49)	10.5 (36)	14.3 (49)	23.1 (79)	37.7 (129)
7. Accuracy						
Lisinopril (5)	97.3 (14.0)	2.3 (8)	0.6 (2)	0.3 (1)	1.5 (5)	95.3 (327)
Metformin (5)	97.4 (14.3)	1.8 (6)	0.6 (2)	0.6 (2)	1.5 (5)	95.6 (327)
8. Legibility / Comprehensibility						
Lisinopril (16)	43.8 (11.1)	0.3 (1)	44.3 (152)	46.7 (160)	7.9 (27)	0.9 (3)
Metformin (16)	42.6 (10.8)	0.6 (2)	46.5 (159)	45.0 (154)	7.6 (26)	0.3 (1)

Scores for each criterion were similar between lisinopril and metformin with the largest discrepancies in criteria 3 (directions) and 5 (adverse reactions). Metformin scored consistently lower than lisinopril.

Tables 5 and 6 provide detailed information on each subcriterion and highlight differences in scoring between lisinopril and metformin. Criterion 1 requires inclusion of generic and brand names, phonetic spelling of generic names, and information about indications for use. Most leaflets for both lisinopril and metformin included generic names and indications for use. Brand names and physical description of the medication were each provided for less than half of the CMI leaflets. The possibility of off-label use was mentioned on 84% of leaflets for lisinopril but only 26% of CMI for metformin (not

included in summated quality scores). Specific off-label indications were provided on 22% of leaflets for lisinopril and 12% for metformin. When specific off-label indications were identified, prevention of diabetic nephropathy and polycystic ovarian syndrome were the main indications for lisinopril and metformin, respectively.

Criterion 2 requires specific information about contraindications and what to do if applicable. For lisinopril, leaflets identified between 86% (angioedema) and 95% (pregnancy) of the contraindications identified in package information. However, only 2% mentioned that angioedema can be fatal. Ten percent of leaflets failed to mention allergic reactions to ACE-inhibitors as a contraindication for use. For metformin, appropriate listing of contraindications ranged from 40% for x-ray contrast agents to 89% hypersensitivity or allergic reaction to metformin . Serious conditions such as heart attack, dehydration, or hypoxemia were listed by approximately 80% of the leaflets.

Criterion 3 requires specific directions about how to use, monitor, and get the most benefit from the medication. Over 90% of instructions for both lisinopril and metformin mentioned administration with regard to meals. Usual dosing information was included in slightly over one-third of leaflets for both medications and actual personal dosing instructions were appended to the leaflet for 60% of leaflets for both medication. While slightly over 70% of leaflets mentioned that monitoring was needed, detail on monitoring parameters was provided in approximately 70% of leaflets (1% for vitamin B12 and 54% for CBC), and the recommended frequency of such tests or the actions patients could take to assure appropriate monitoring (e.g. ask your doctor about tests) were rarely (<20%) mentioned.

Criterion 4 requires specific precautions and information about how to avoid harm while using the medication. For metformin, 88-90% of leaflets identified lactic acidosis, alcohol use, and pregnancy as precautions with the use of the medication. Only 69% of metformin leaflets mentioned drug-drug interactions as a possible concern and 71% advised consumers to tell healthcare providers about all medications being taken. For lisinopril, most leaflets described the precaution about use of potassium supplements and salt substitutes. Consumers were told to tell providers about all medications being taken in 80% of the lisinopril CMI leaflets. Breast feeding was a precaution for 91% of lisinopril leaflets dispensed. Bone marrow disease was only mentioned by approximately 40% of lisinopril leaflets. Information on the use in children, specifically the lack of approval, was mentioned by less than half of the leaflets.

Criterion 5 requires information about the symptoms of serious or frequent adverse reactions and what to do. At least 90% of leaflets identified all of the serious side effects for both lisinopril and metformin. However, only 3% (lisinopril) to 18% (metformin) of leaflets advised to discontinue the medication immediately although most advised contacting physicians when a serious side effect occurred. The vast majority of lisinopril leaflets identified all of the most common side effects. For metformin, most of the common side effects except flatulence and headache were

identified by the majority of CMI leaflets, resulting lower scores than lisinopril. Over 80% of leaflets for metformin and lisinopril advised consumers to contact their doctor or pharmacist if the common side effects did not go away or were bothersome.

Criterion 6 requires several items of general information and encouragement to ask questions. The majority of leaflets advised consumers to ask their doctor or pharmacist if they had any questions. Advice to keep out of the reach of children and not share medications was provided in 52-67% of leaflets. Approximately half had the name of the publisher and half had the date of publication for both medications.

Criterion 7 requires that the information that is presented be scientifically accurate, unbiased, and up-to-date. Nearly all CMI adhered to each of the subcriteria in this category.

Criterion 8 requires that information be readily comprehensible and legible. Formatting and legibility criteria identified as deficiencies in the 2001 report were defined more specifically in the 2006 Guidance document resulting in a more elaborate set of subcriteria. For example, the 2001 study, before specific FDA guidance was available, specified a 12-point font as fully meeting the criterion and 10-point font partially meeting the criterion for adequate print size. The 2006 Guidance document specified that print size should use at least 10-point font. This study finds that only 29% met the Guidance criterion of 10-point or larger. Font sizes ranged from 5 point to 12 point with nearly 30% being less than 8 point and an additional 42% being 8 point.

Only 15% of leaflets for either medication met the criterion for space between lines of ≥2.2mm. CMI leaflets also had very little white space around text with only 26% meeting the criterion of margins ≥.5 inches. Only 7% used bullets when listing key points and this was most likely to be seen in very short leaflets. Bolded text was rarely used for emphasis (6%) and less than 3% of CMI for either medication used bolded text or boxes around black box warning information. Most common for providing emphasis was use of all caps, which has been shown to be more difficult to read.[16] Headings were seldom placed on separate lines (22%) and paragraphs tended to be long and not use bullets to separate items of information (23% met criteria of being short with a single topic). The word count for the longest paragraphs in each leaflet found a range of from 5 to 892 words in one paragraph.

Reading level analysis found that only 10% of lisinopril and 6% of metformin leaflets were written at ≤ 8th grade reading level. The mean reading level (F-K Score) for lisinopril was 9.40 ± 1.31 and for metformin 9.94 ±1.33.

Formatting criteria that were generally met included presence of a good ink-paper contrast, use of both upper and lower case lettering for most of the text, and minimal use of italics or ornate typeface (97-99% of leaflets). This was consistent with findings from the 2001 study.

Table 5. Percent of leaflets with adherence to subcriteria for lisinopril (n= 343)

Adherence %	Criteria 1-6: Information is sufficiently specific and comprehensive
	1. Drug names and indications for use
97	1.1 Generic name (lisinopril)
85	1.2 Phonetic spelling of generic name (lyse-IN-oh-pril)
39	1.3 Brand names (e.g., Prinivil®, Zestril®)
91	1.4 Drug class (ACE-I)
92	1.5 Indication: hypertension, congestive heart failure, acute MI
45	1.6 Physical description of the drug or FDA imprint code is mentioned
84*	1.7 Off-label use possibility is mentioned*
	2. Contraindications and what to do if applicable
86	2.1 Angioedema history or history of similar symptoms
02	2.2 Angioedema can be fatal
90	2.3 Hypersensitivity to lisinopril or other ACE-I
95	2.4 Pregnancy or planning to become pregnant
91	2.5 Teratogenic / can cause birth defects/ fetal harm
	3. Specific directions about how to use, monitor, and get most benefit
91	3. 1 Administration: with or without food
38	3. 2 Usual Dosing
71	3. 3 Recommendation to follow individual dosing instructions
59	3. 4 Personal dosing instructions are inserted in leaflet
76	3. 5 Missed dose – action to take: reasonable recommendation
71	3. 6 Overdose – action to take: contact poison control center or emergency services
32	3. 7 Phone number for poison control center provided
32	3. 8 Overdose symptoms
70	3.9 Safety monitoring (general statement that monitoring is needed)
71	3.10 Renal function monitoring
70	3.11 Potassium / electrolytes monitoring
54	3.12 CBC monitoring
13	3.13 Frequency of tests
08	3.14 Action to take: ask about lab tests
71	3.15 Effectiveness monitoring (general statement that monitoring is needed)
72	3.16 Blood pressure monitoring needed
18	3.17 Action to take: ask about blood pressure readings / tests or self-monitor
	4. Specific precautions and how to avoid harm while using it
76	4. 1 Drug-drug interactions: Diuretics
94	4. 2 Drug-drug interactions: Potassium supplements
86	4. 3 Action to take if patient is taking potassium supplements
95	4. 4 Drug-drug interactions: Salt substitutes
87	4. 5 Action to take if the patient is taking salt supplements
80	4. 6 Inform healthcare provider about all medications you take
78	4. 7 Other: Aortic Stenosis/Hypertrophic cardiomyopathy/heart problems
80	4. 8 Other precautions: Impaired Renal Function / renal artery stenosis
79	4. 9 Other precautions: Hyperkalemia / electrolyte problems

41	4.10 Other precautions: Leucopenia/neutropenia / bone marrow disease
84	4.11 Other precautions: Upcoming surgery or anesthesia
91	4.12 Other precautions: Breast feeding
01*	4.13 Children < 6 years of age: Has not been tested*
47*	4.14 Children < 6 years of age: Should not be used / not recommended*
	5. Symptoms of serious or frequent adverse reactions and what to do
93	5.1 Serious side effects: Angioedema
90	5.2 Serious side effects: Fainting
91	5.3 Serious side effects: Infection symptoms
03	5.4 Action to take for serious side effects: don't take drug
80	5.5 Action to take for serious side effects: contact provider
93	5.7 Common side effects: Headache
96	5.8 Common side effects: Dizziness
94	5.9 Common side effects: Cough
86	5.10 Action: Tell doctor/pharmacist if side effects do not go away or bother you
	6. General information and encouragement to ask questions
64	6.1 Sharing medication: do not give this medicine to others
67	6.2 Out of reach of children
76	6.3 Storage directions
63	6.4 Name of publisher
51	6.5 Date of publication / most recent revision / expiration date
74	6.6 Ask doctor or pharmacist if you have any questions or concerns
	7. Information is scientifically accurate, unbiased, up-to-date
98	7.1 Information is neutral in content and tone
97	7.2 No promotional messages about brand, manufacturer, or distributor
96	7.3 No inaccurate or outdated claims about benefits of the product
99	7.4 No inaccurate or outdated claims about risks of product
97	7.5 No other inaccurate or outdated information was found
	8. Information is readily comprehensible and legible
31	8.1 Short paragraphs with a single topic
94	8.2 Limited use of medical / technical terms
03	8.3 Black box warning is printed in bold-face or box
87	8.4 No ads or coupons for other products or non-pharmacy services
15	8.5 Space between lines ≥2.2 mm
26	8.6 Adequate white space around text (≥.5 inch)
29	8.7 Font size ≥10 pt
97	8.8 Good ink-paper contrast
25	8.9 Fonts with Serifs
49	8.10 Line length ≤ 6"
99	8.11 Minimal use of italics or ornate typeface
99	8.12 Upper and lower case lettering
05	8.13 Bolded text used for emphasis
22	8.14 Headings placed on separate lines
07	8.15 Bullets used to enhance readability
10	8.16 Written at ≤8th grade level

*For descriptive purposes reported only; not counted in summated scores.

Table 6. Percent of leaflets with adherence to subcriteria for metformin (n= 342)

Adherence %	Criteria 1-6: Information is sufficiently specific and comprehensive
	1. Drug names and indications for use
96	1.1 Generic name (metformin)
87	1.2 Phonetic spelling of generic name (met-FOR-min)
37	1.3 Brand names (e.g., Fortamet™, Glucophage®, Glucophage® XR)
93	1.4 Indication: Diabetes, type 2
39	1.5 Physical description of the drug or FDA imprint code is mention
25*	1.6 Off-label use possibility is mentioned*
	2. Contraindications
63	2.1 80 years or older and no test for kidney function
85	2.2 Renal or kidney disease
80	2.3 Liver problems
80	2.4 Serious dehydration
40	2.5 X-ray/ contrast agent
81	2.6 Planned surgery
81	2.7 Serious condition, such as heart attack, severe infection, or stroke
84	2.8 Metabolic acidosis: acute or chronic
79	2.9 Hypoxemia
89	2.10 Hypersensitivity to metformin
	3. Specific directions about how to use, monitor, and get most benefit
91	3.1 Administration: with meals
34	3.2 Usual Dosing (e.g., "the regular tablet is usually taken 1-3 times a day")
90	3.3 Recommendation to follow individual dosing instructions
60	3.4 Personal dosing instructions are inserted in leaflet
75	3.5 Missed dose – action to take: reasonable recommendation
64	3.6 Overdose – action to take: contact poison center or emergency services
17	3.7 Phone number for poison control center provided
71	3.8 Safety monitoring (general statement that monitoring is needed)
68	3.9 Renal function
01	3.10 Vitamin B12
05	3.11 Frequency of tests (e.g., "renal function at initiation and annually")
01	3.12 Action to take: ask about lab tests
72	3.13 Effectiveness monitoring (general statement that monitoring needed)
69	3.14 Glycosylated hemoglobin (HbA1c or A1c)
09	3.15 Monitoring schedule (e.g., "HbA1c at least every six months")
00	3.16 Action to take: Ask about lab tests
	4. Specific precautions and how to avoid harm while using it
88	4.1 Lactic acidosis
78	4.2 Frequency of lactic acidosis ("rare" or numeric estimate)
78	4.3 Case fatality rate or statement that it can be fatal
88	4.4 Symptoms of lactic acidosis described (e.g., "tired, muscle/stomach pain, cold, dizzy, tachycardia")
81	4.5 Actions to take: Contact provider immediately
33	4.6 Actions to take: Don't take medication
90	4.7 Alcohol use
88	4.8 Pregnancy

81	4.9 Action to take: Tell your doctor if you are pregnant or breast feeding
69	4.10 Drug-drug interactions identified
71	4.11 Action to take: Inform provider about all medications you take
02*	4.12 Children under 10: Has not been tested in children under 10*
40*	4.13 Should not be used / is not recommended in children under 10*
	5. Symptoms of serious or frequent adverse reactions and what to do
92	5.1 Serious side effects: Hypoglycemia or symptoms
70	5.2 Action to take: contact provider
18	5.3 Action to take: don't take drug
93	5.4 Common side effects: Diarrhea, Indigestion, Abdominal Discomfort
91	5.5 Common side effects: Nausea/Vomiting
57	5.6 Common side effects: Flatulence
53	5.7 Common side effects: Headache
87	5.8 Common side effects: Metallic taste in mouth
81	5.9 Action to take: Tell your doctor or pharmacist if any of the common side effects do not go away or bother you
	6. General information and encouragement to ask questions
52	6.1 Sharing medication: do not give this medicine to others
62	6.2 Out of reach of children
75	6.3 Storage directions
55	6.4 Name of publisher
48	6.5 Date of publication / most recent revision / expiration date
87	6.6 Ask doctor or pharmacist if you have any questions or concerns
	7. Information is scientifically accurate, unbiased, up-to-date
98	7.1 Information is neutral in content and tone
98	7.2 No promotional messages about a brand, manufacturer, or distributor
98	7.3 No inaccurate or outdated claims about benefits of the product
98	7.4 No inaccurate or outdated claims about risks of product
97	7.5 No other inaccurate or outdated information was found
	8. Information is readily comprehensible and legible
14	8.1 Short paragraphs with a single topic
93	8.2 Limited use of medical / technical terms
01	8.3 Black box warning is printed in bold-face or box
91	8.4 No ads or coupons for other products or non-pharmacy services
15	8.5 Space between lines ≥2.2 mm
26	8.6 Adequate white space around text (≥.5 inch)
28	8.7 Font size ≥ 10 pt
97	8.8 Good ink-paper contrast
25	8.9 Fonts with Serifs
49	8.10 Line length ≤ 6"
99	8.11 Minimal use of italics or ornate typeface
99	8.12 Upper and lower case lettering
06	8.13 Bolded text used for emphasis
22	8.14 Headings placed on separate lines
07	8.15 Bullets used to enhance readability
06	8.16 Written at ≤8th grade level

*For descriptive purposes only. Scores are not counted in quality summated scores.

Factors related to expert rated quality criteria

Pharmacies dispensing medications to shoppers included 87 independent pharmacies, 252 chain outlets, and 4 franchise stores. All instances where prescriptions were dispensed without any CMI occurred in independent pharmacies. Various quality criteria and leaflet characteristics were significantly different between chain and independent pharmacies (Table 7). Chain pharmacies dispensed longer CMIs, which met a larger percent of the expert-required content (criterion 1-6) for the two medications (70-75%) than did independent pharmacies (49-53%), with a mean difference of 22.1% (95% CI 15.8, 28.4) and 21.1% (14.9, 27.3) for lisinopril and metformin, respectively. For the formatting criterion (criterion 8), independent pharmacies generated slightly higher quality scores, with a mean difference of 7.8% (5.2, 10.4) and 9.3% (6.9, 11.7) for lisinopril and metformin, respectively.

Table 7. Association between Expert-rated Quality Criteria and Pharmacy Type

Overall Quality					
		Lisinopril		**Metformin**	
	N	Mean	95% CI of Difference	Mean	95% CI of Difference
Independent	87	55.1 ±20.3	10.0 – 19.0	52.1 ±20.1	9.2 – 18.1
Chain	252	70.0 ±9.3		65.8 ±9.9	

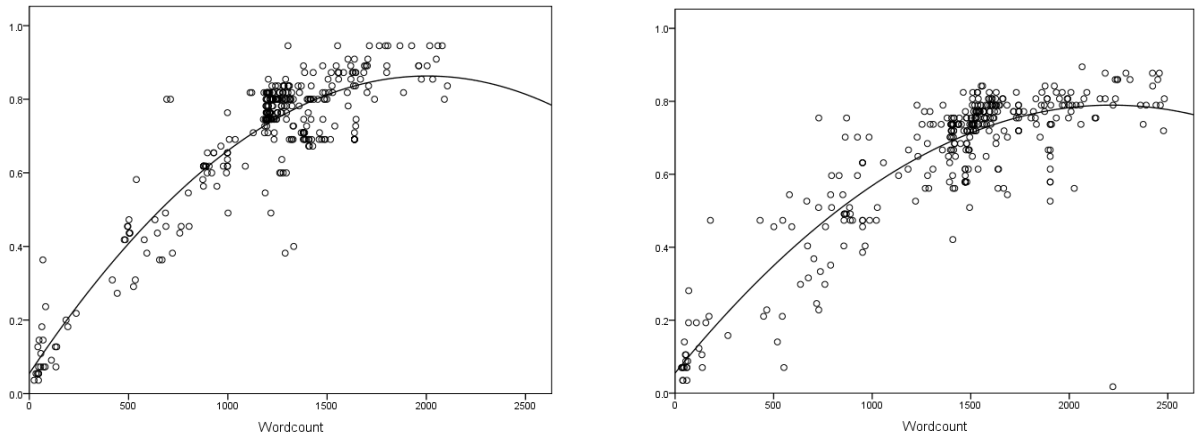
Content (Criterion 1-6)					
		Lisinopril		**Metformin**	
	N	Mean	95% CI of Difference	Mean	95% CI of Difference
Independent	87	53.0 ±28.7	15.8 – 28.4	49.0 ±28.1	14.9 – 27.3
Chain	252	75.1 ±12.4		70.1 ±12.8	

Format (Criterion 8)					
		Lisinopril		**Metformin**	
	N	**Mean**	95% CI of Difference	**Mean**	95% CI of Difference
Independent	87	49.6 ±10.1	5.2 – 10.4	49.5 ±10.5	6.9 – 11.7
Chain	252	41.8 ±10.8		40.2 ±9.7	

Word Count					
		Lisinopril		**Metformin**	
	N	Mean	95% CI of Difference	Mean	95% CI of Difference
Independent	87	856 ±546	336 – 581	978 ±677	423 - 728
Chain	252	1314 ±316		1553 ±401	

While longer leaflets had higher levels of adherence to content criteria, exploratory analysis of the length of leaflets and adherence to criteria indicate that, at a certain point there may be minimal gain in comprehensive coverage of content with substantially increased leaflet length (Figure 1). Specifically, for the 92 lisinopril leaflets that met more than 80% of content quality criteria the average word count was 1523 with a minimum of 1112 and a maximum of 2106 words (inter-quartile range 1280, 1700). Respective values for the 47 metformin leaflets were 1918 with a minimum of 1462, a maximum of 2482 and an inter-quartile range of 1604 to 2182.

Figure 1. Distribution of content quality scores versus word count for lisinopril and metformin (quadratic curve estimation with R^2>0.75)



Comparison of 2001 and 2008 expert evaluation data

In 2008, 6% of pharmacies failed to dispense written patient information whereas in 2001 approximately 11% had failed to dispense any CMI. Including the pharmacies that failed to dispense written information and using the 60% or more level of adherence as the threshold for acceptable quality, data indicate some improvement in overall quality between 2001 and 2008. The mean quality score in 2008 was 62% (95% CI 57.0, 67.0) for lisinopril and 59% (54.0, 65.1) for metformin while in 2001 the means ranged from 51% (46.0, 56.0) to 55% (50.0, 60.0) for the four study medications. Data on individual

criteria comparing 2001 and 2008 and including only pharmacies that did dispense leaflets are presented in Table 8. These data indicate an improvement in criterion 1 "drug names and indications". However, in the 2001 study, three out of the four drugs had averages for this criterion of between 50% and 54% while one outlier scored only 14%, which lowered the overall average considerably. There were also improvements in 2008 in provision of information on contraindications, precautions, and adverse drug reactions. One area that went against this trend was the criterion "specific directions about how to use, monitor, and get the most benefit", which had lower adherence to criteria in 2008 than in 2001, largely due to increased emphasis in 2008 on providing information on safety and effectiveness monitoring. Specifically, the 2008 evaluation included a large number of subcriteria that listed parameters, frequencies, and action steps for patients related to safety and effectiveness monitoring.

It is particularly noteworthy that for Criterion 8 ("Information is readily comprehensible and legible"), the percent of leaflets meeting the 60% threshold was lower in 2008 than in 2001. Only 8% of leaflets met the 60% threshold in the 2008 evaluation whereas in 2001, 18% met the threshold. The data for the percent of CMI meeting the 60% threshold in 2001 were highly skewed for the different medications, with 3%, 9%, 12% and 47% of the four drugs meeting threshold. Omitting the latter value pertaining to nitroglycerin sublingual CMI, the percent meeting the threshold would be virtually unchanged from 2001 to 2008.

Table 8. Comparison of 2001 and 2008 expert evaluation of CMI: Percent of leaflets meeting 60% threshold adherence levels across all study drugs.

Criterion	Level of adherence to criteria	
	≥60% of points	
Year	**2001**	**2008**
1. Drug name and indications	43	68
2. Contraindications	33	82
3. Directions	67	31
4. Precautions	21	80
5. Adverse Reactions	27	84
6. General information	18	61
7. Accuracy	98	97
8. Legibility/ Comprehensibility	18	08

Consumer Evaluations of CMI

Descriptive data on consumers

A total of 212 consumers evaluated six CMI leaflets each. Of these 66% were female while 34% were male. Consumer age ranged from 19 to 78 years, with a mean of 40.2 (±14.7, median=37.5). About 1.4% had less than a high school degree, 10% were high school graduates, 35% had some college, and 54% were college graduates. For race/ethnicity 67% were white, 13% were Asian, 9% were Hispanic/Latino, 9% were African-American, and 2% listed "other" (including three who were Native-American).

Consumer ratings of CMI

Each Consumer Medication Information leaflet was assessed by at least one consumer. A total of 22 consumer evaluations included imputation for 1-3 missing items. When multiple consumers evaluated the same leaflet, the mean scores for each item were used to generate the total score. Cronbach's coefficient alpha for the summated scale of the 12 items used in the 2001 evaluation indicated that the scale had high internal consistency reliability (α=.95). All item-corrected total correlations were greater than r=.55 and no item deletion would raise alpha. Therefore, no items were eliminated, making the scale the same as that in the 2001 study.

Table 9 summarizes the consumer summated score ratings of the CMI leaflets divided into 5 levels indicating the percent of possible points for each study drug. The level 5 threshold was reached by approximately 26% of lisinopril and 21% of metformin leaflets. Over 75% scored 60% or higher for lisinopril and 66.9% scores 60% or higher for metformin.

Table 9. Consumer overall ratings of patient information leaflets using 5-point method of assessment by drug

Drug	Mean Rating (SD)	Level of information quality				
		Level 1: 0-19% of points	Level 2: 20-39% of points	Level 3: 40-59% of points	Level 4: 60-79% of points	Level 5: 80-100% of points
		% (n)	% (n)	% (n)	% (n)	% (n)
Lisinopril	69.6 (15.2)	0 (0)	2.9 (10)	21.9 (75)	48.5 (166)	26.9 (92)
Metformin	65.8 (15.9)	0 (0)	4.7 (16)	28.4 (97)	45.6 (156)	21.3 (73)
Total	--	0 (0)	3.8 (26)	25.1 (172)	47.0 (322)	24.1 (165)

Table 10 summarizes consumer evaluations by specific subcriteria included on the Consumer Evaluation Form. The items were identical to those included in the 2001 evaluation of written prescription information.[3] Consumers were most critical of print size, line spacing, and ease of reading. For lisinopril, 35% of consumers gave a rating of 1 or 2 (lowest ratings) on print size, 37% gave low ratings for line spacing, and 24% for ease of reading. For metformin, 41% gave the two lowest ratings for print size, 43% for line spacing, and 33% for ease of reading. Consumers tended to be most positive about helpfulness, completeness, and usefulness of the CMI with mean ratings ranging from 3.6-3.8 on these items across both medications.

Table 10. Distribution of consumer ratings of patient information leaflets using 5-point scales by subcriterion

		Distribution of scores (1=poor; 5=good)									
Drug Criterion	**Mean rating (SD)**	**Rating score = 1**		**Rating score = 2**		**Rating score = 3**		**Rating score = 4**		**Rating score = 5**	
		%	**(n)**	**%**	**(n)**	**%**	**(n)**	**%**	**(n)**	**%**	**(n)**
Lisinopril (N = 343)											
Print size	3.1 (1.4)	12.5	(43)	22.7	(78)	23.0	(79)	25.4	(87)	16.3	(56)
Print quality	3.4 (1.3)	5.5	(19)	14.0	(48)	30.0	(103)	33.8	(116)	16.6	(57)
Line spacing	3.1 (1.4)	12.2	(42)	23.6	(81)	27.1	(93)	24.8	(85)	12.2	(42)
Organization	3.6 (1.2)	1.5	(5)	12.5	(43)	26.0	(89)	38.8	(133)	21.3	(73)
Length	3.5 (1.1)	2.3	(8)	11.7	(40)	31.8	(109)	41.1	(141)	13.1	(45)
Clarity	3.6 (0.9)	2.3	(8)	8.2	(28)	25.4	(87)	46.1	(158)	18.1	(62)
Helpfulness	3.8 (1.1)	1.5	(5)	5.8	(20)	19.5	(67)	49.0	(168)	24.2	(83)
Completeness	3.7 (1.2)	2.3	(8)	8.2	(28)	21.6	(74)	41.1	(141)	26.8	(92)
Ease of finding info	3.5 (1.2)	4.1	(14)	11.7	(40)	27.4	(94)	37.3	(128)	19.5	(67)
Ease of reading	3.3 (1.4)	9.3	(32)	14.9	(51)	27.1	(93)	35.6	(122)	13.1	(45)
Ease of understanding	3.7 (1.1)	2.0	(7)	5.5	(19)	27.7	(95)	49.0	(158)	15.7	(54)
Usefulness	3.8 (1.1)	2.3	(8)	4.4	(15)	22.4	(77)	47.5	(163)	23.3	(80)
Metformin (N = **342)**											
Print size	3.0 (1.5)	19.0	(65)	21.6	(74)	20.2	(69)	24.0	(82)	15.2	(52)
Print quality	3.3 (1.3)	8.8	(30)	18.7	(54)	25.7	(88)	31.3	(107)	15.5	(53)
Line spacing	2.9 (1.4)	20.0	(67)	23.4	(80)	24.6	(84)	20.8	(71)	11.7	(40)
Organization	3.5 (1.1)	3.2	(11)	9.9	(34)	35.4	(121)	36.5	(125)	15.0	(51)
Length	3.2 (1.2)	6.1	(21)	16.7	(57)	33.0	(113)	31.6	(108)	12.6	(43)
Clarity	3.5 (1.1)	2.9	(10)	11.7	(40)	30.1	(103)	43.3	(148)	12.0	(41)
Helpfulness	3.7 (1.1)	1.5	(5)	6.7	(23)	24.9	(85)	47.1	(161)	19.9	(68)
Completeness	3.7 (1.2)	3.5	(12)	7.3	(25)	21.1	(72)	46.8	(160)	21.3	(73)
Ease of finding info	3.2 (1.3)	5.6	(19)	18.7	(64)	30.7	(105)	33.0	(113)	12.0	(41)
Ease of reading	3.1 (1.2)	15.8	(54)	17.5	(60)	28.4	(97)	27.0	(92)	11.4	(39)
Ease of understanding	3.5 (1.1)	5.3	(18)	11.1	(38)	28.4	(97)	43.9	(150)	11.4	(39)
Usefulness	3.7 (1.1)	2.6	(9)	7.9	(27)	25.1	(86)	45.6	(156)	18.7	(64)

Comparison of consumer evaluations for 2001 and 2008

Comparison of the 2001 and 2008 consumer evaluations indicates improvement in the percent of points obtained in 2008 as compared to 2001 (Table 11). In 2001, 23% received scores in the lowest two categories while only 4% scored in the lowest categories in 2008. Nearly equal percents were in the highest level (Level 5) in 2001 and 2008. In all, 56% of 2001 leaflets and 71% of 2008 leaflets had over 60% of total points allocated. Of concern is that the items that were most negatively scored in the 2001 study (print size, line spacing, and ease of reading) continued to be scored lowest with mean scores that are nearly identical in the two studies.

Table 11. Consumer evaluations of CMI leaflets for 2001 (N= 1,236) and 2008 (N=685)

Study	Level of information quality				
	Level 1: 0-19% points	**Level 2: 20-39% points**	**Level 3: 40-59% points**	**Level 4: 60-79% points**	**Level 5: 80-100% points**
	% (95% CI)	**% (95% CI)**	**% (95% CI)**	**% (95% CI)**	**% (95% CI)**
2001	7.9 (6.4, 9.4)	14.8 (12.8, 16.8)	21.0 (18.7, 23.3)	30.9 (28.3, 33.5)	25.4 (23.0, 27.8)
2008	0 (0)	3.8 (2.4, 5.2)	25.1 (21.9, 28.4)	47.0 (43.3, 50.8)	24.1 (20.9, 27.3)

Limitations

The 2008 study was designed to parallel the 2001 evaluation conducted by University of Wisconsin investigators.[3] The same limitations apply as those identified in 2001, including the inability to generalize to excluded settings such as mail order outlets and to a general population of consumers because of the non-representative sampling procedures. The consumers who participated in the CMI evaluation were all English-speaking and were more highly educated than would be found in the general population. In order to assure comparability with 2001 findings no further psychometric testing or adjustments were made in the consumer evaluation criteria. Likewise, expert ratings were mirrored to the 2001 study in that each subcriterion was given equal weight and quality was defined as the aggregate percent of subcriteria that was met. The weight or importance of each content item remains undefined and should be the focus of further research, especially in light of concerns about information overload.

Discussion

The study did find that the majority of community pharmacies provided computer generated CMI. However, the length and format of the CMI and the percent of critical content items covered continued to vary considerably from pharmacy to pharmacy. While a larger percentage of critical content was met in this 2008 study when compared to the 2001 study, certain criteria indicated substandard quality. This was true especially with directions on monitoring medications and actions to take when side effects or other problems occurred, which were only met by half of the CMI, reflecting a lack of specific instructions to patients on how to monitor and manage their drug therapy. This is particularly important as patient involvement in drug therapy decisions and management is emphasized as an effective patient safety strategy.

While the percent of content criteria met by leaflets has increased over that found in 2001, adherence to formatting, which is crucial to making information to consumers comprehensible and readable, has not improved. The high reading level required to comprehend CMI, the small font sizes used, the lack of use of bullets or headings on separate lines, the narrow spacing between lines of text all continue to be problematic. Black box warnings were more likely to use all capital letters rather than the bold-face type or boxed text that are recommended. Many of the new criteria contained in the 2006 Guidance document, including use of fonts with serifs, bolding rather than all caps for emphasis, and adequate white space around text, had very low adherence.

Consumer Medication Information (CMI) leaflets provided in pharmacies are primarily generated electronically as part of the dispensing process. The CMI content is determined by a small number of private vendors who sell drug information materials to pharmacy outlets through their pharmacy software vendors. The formatting of the CMI is then determined by pharmacies and/or their software vendors. As a result, there can be CMI leaflets with the same publisher and date of publication but with very different content and appearance. For example, examination of two metformin leaflets, both

from chain outlets, indicated that First Databank was the publisher for both, 2008 the date of publication, yet one leaflet had 760 words and 30% adherence to content criteria (Criteria 1-6) while the other had 2,457 words and 88% adherence to content criteria (see Appendix H). In the shorter leaflet, the Side Effects section began with the statement "See also Warning Section," but the warning section had been eliminated in the abbreviated CMI. Also omitted were the sections on brand names, warnings, precautions, drug interactions, overdose, missed dose and storage. In examining two leaflets by Wolters Kluwer and with February 27, 2008 or March, 2008 expiration of information dates, it was found that one had 136 words and 11% adherence to content while the other had 2,156 words and 81% adherence to content criteria (Appendix H). Thus, direct quality comparisons of the publishing houses were impossible in this study. In examining standard drug monographs it was unclear to us, whether and, if so, what criteria are used to select information provided to consumers.

Another area of concern in examining individual CMI was the amount of information provided in addition to information on the medication dispensed, which could cause distraction for consumers and make it difficult to determine the most important information to read. An example of the front and back of a CMI leaflet with possibly distracting information is shown in Appendix I. Leaflets often included all of the HIPAA disclosure information on the reverse side of the medication information.

While the longer the leaflet, the more the content criteria were met, exploratory analysis seems to suggest that the longer CMI meet more of the content criteria at the potential cost of "information overload" and possible redundancy in the information provided. More than 1000 word differences were found between leaflets with similar content quality scores which suggest a significant difference in conciseness. The efficiency and conciseness with which content is presented is an important issue given concerns about the danger of overloading consumers with so much information that CMI materials are not read and warning information not retained. The amount of redundant information in CMI leaflets should be an area of examination in future research.

It should be noted in this context that content quality was largely defined by presence of certain information, resulting in better scores for high-volume leaflets. However, considering information overload and the potential of misinforming patients, the presence of critical information might need to be weighed against redundant or clinically meaningless items. Leaflets that "cover all the bases" to protect against potential litigation may fail to meet their primary purpose in instructing patients on how to derive the most benefit from drug therapy.

Conclusion and Recommendations

While the CMI distribution method through pharmacies appears effective, the content and format of this information remains concerning. We identified various shortcomings in the provision of written medication information to consumers, including lack of

critical information about the management of medications, significant redundancy of information resulting in excessively long leaflets, poor formatting, and inadequate legibility and reading level. These important findings and the resulting agenda for improvement notwithstanding, it should be noted that other issues remain under-researched and unaddressed. Most importantly, while the FDA guidance document has successfully defined critical components of CMI, it is unclear what quantity, presentation, and format of CMI will result in adequate patient comprehension and ultimately, appropriate actions to improve patient safety. It is furthermore unclear whether drug information is selected according to the greatest applicability to patient concerns and the need to support patients' ability to monitor and manage drug therapy. Finally, adequate pharmacepidemiological data would aid in discerning theoretical concerns about drug safety and effectiveness (such as potential drug-drug interactions that lack evidence of clinical relevance) from information truly critical for drug therapy management.

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Appendix A: Questions Commonly Asked in the Pharmacy and Patient-Observer Answers

Questions	Answers
Hello, may I help you?	Yes, would you fill these prescriptions for me?
Have you filled prescriptions here before?	No.
What is your name?	(assigned name)
What is your birth date?	(your modified birth date)
What is your address?	(your modified address)
Why are you getting the prescriptions filled here?	I was visiting in the area and went by your pharmacy. This reminded me that I had prescriptions that needed to be filled.
What is your telephone number?	(your modified telephone number)
How will you pay for the prescriptions?	I will pay with cash.
Do you have prescription insurance?	No.
Do you have any other medical conditions?	No.
Do you take any other prescription medications?	No, I am not taking any other medications.
Do you have any allergies to medications?	No, none that I know of.
Have you been taking any over-the-counter or non-prescription medications?	No, I haven't been taking any medications.
Is this the first time you have taken any of these medications?	Yes, it's the first time I've taken any of these.
What did the doctor tell you about the medications?	Just that the directions would be on the label.
When are you talking with the doctor next?	I will be seeing my doctor in two weeks.
What will you do if you have any problems with the medication?	I will call my doctor.
What will you do if your health does not improve?	I will call my doctor.
For what reason did your doctor prescribe metformin?	My diabetes (If pressed say: the doctor said my blood sugar was up)
For what reason did doctor prescribe the lisinopril?	My doctor said I had some high blood pressure (If pressed say: That's about all I know)
Did your doctor tell you to check your blood sugar at home?	No. He said we would talk about that at my next visit in two weeks.

Do you follow any special diet?	Yes. (If asked, it is low fat and low salt. Your doctor gave you a brochure and said to read it and you would discuss it next visit).
Do you exercise?	Yes, I walk 20-30 minutes a day.
Did the doctor tell you to take aspirin?	No, we didn't discuss that.
Have you had any other symptoms?	No, I just get thirsty a lot.
Did the doctor give you any "samples" of the medication?	No.
Do you have any questions for the pharmacist?	No
Would you like written information about the medication?	Sure
Do you have any questions about your medicines?	No

Appendix B: Development Expert Panel to Develop Expert Evaluation Form
Consumer Medication Information (CMI) Evaluation Project, 2008

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Appendix D: Consumer Medication Information (CMI) Evaluation Form – Lisinopril

NOTE: Highlighting indicates items not included in summated scores

A. Drug names and indications for use

- ❒ 1. **Generic** name (lisinopril)
- ❒ 2. **Phonetic spelling** of generic name (lyse-IN-oh-pril)
- ❒ 3. **Brand** names (e.g., Prinivil®, Zestril®)
- ❒ 4. **Drug class** (ACE-I)
- ❒ 5. Indication: **hypertension** or high blood pressure
- ❒ 6. Indication: Congestive **heart failure**
- ❒ 7. Indication: after acute **myocardial infarction** or heart attack
- ❒ 8. Physical **description** of the drug or FDA **imprint** code is mentioned
- ❒ 9. **Off-label use** mentioned (e.g., "this drug can be prescribed for other uses" or reference to specific off-label indications)
  If specific off-label indications are mentioned, please specify: ……

B. Specific directions about how to use, monitor, and get most benefit

- ❒ 1. Administration: **by mouth**
- ❒ 2. Administration: with or without **food**
- ❒ 3. **Usual Dosing** (e.g., "usually taken once or twice a day")
- ❒ 4. Recommendation to follow **individual dosing** instructions
  - ❒ Personal dosing instructions are inserted in leaflet
- ❒ 5. **Missed dose** – action to take: reasonable recommendation (e.g., "Take a missed dose as soon as you remember it. If it is almost time for the next dose, skip the missed dose. Do not take a double dose to make up for a missed one.")
- ❒ 6. **Overdose** – action to take: contact poison control center or emergency services
  - ❒ **Phone** number for poison control center provided
  - ❒ Overdose **symptoms** (e.g., "low blood pressure, light-headedness")
- ❒ 7. **Safety monitoring** (general statement that monitoring is needed)
  - ❒ **Renal** function
  - ❒ **Potassium / electrolytes**
  - ❒ **CBC**
  - ❒ **Frequency** of tests (e.g., "K shortly after initiation and periodically")
  - ❒ Action to take: **ask about lab tests** ……..
- ❒ 8. **Effectiveness monitoring** (general statement that monitoring is needed)
  - ❒ Blood pressure
  - ❒ Lab / other tests
  - ❒ Action to take: **ask about blood pressure readings / tests or self-monitor** ……..

C. Contraindications **Action to take**: "do not use"

- ❒ 1. **Angioedema** history or history of similar symptoms ❒
  - ❒ Angioedema can be **fatal**
- ❒ 2. **Hypersensitivity** to lisinopril or other ACE-I ❒
- ❒ 3. **Pregnancy** or planning to become pregnant ❒
  - ❒ **teratogenic** / can cause birth defects / fetal harm

D. Specific precautions and how to avoid harm while using it

1. **Drug-drug interactions** **Action to take:** "do not take until you have talked to your doctor"

- ❒ **Diuretics** ❒
- ❒ **Potassium** supplements ❒
- ❒ **Salt** substitutes ❒
- ❒ Statement that drugs **other** than those listed may interact (list drugs additional to those above is not sufficient)
- ❒ **Inform** healthcare provider about all medications you take

Action to take: "do not take until you have talked to your doctor"

2. **Other precautions**

- ❒ **Aortic Stenosis**/Hypertrophic **cardiomyopathy/**heart problems ❒
- ❒ Impaired **Renal** Function / renal artery stenosis ❒
- ❒ **Hyperkalemia** / electrolyte problems ❒
- ❒ Symptomatic **Hypotension** ❒
- ❒ **Leucopenia/Neutropenia** / bone marrow disease ❒
- ❒ **Hypoglycemia** or low blood sugar/glucose ❒
- ❒ Upcoming surgery or **anesthesia** ❒
- ❒ **Breast feeding** ❒

3. **Children** under 6 years of age

- ❑ Has not been tested in children under 6
- ❑ Should not be used / is not recommended in children under 6

E. Symptoms* of s*erious or frequent adverse reactions and what to do

1. **Serious side effects** **Action to take:** Don't take medication Contact provider immediately

- ❑ **Angioedema** (e.g., "swelling of face") ❒ ❒
- ❒ **Fainting** ❒ ❒
- ❒ **Infection symptoms** ❒ ❒

2. **Common side effects** **Action to take:** Tell your doctor/pharmacist if any of these do not go away or bother you

- ❑ **Headache** ❒
- ❑ **Dizziness** ❒
- ❑ **Cough** ❒

❒ 3. Statement that **list** of side effects is **not complete** (specific statement in side effect section required)

F. General information and encouragement to ask questions

❒ 1. **Sharing medication:** do not give this medicine to others
❒ 2. **Out of reach of children**
❒ 3. **Storage directions** (e.g., "at room temperature and away from light, excess heat, and moisture")
❒ 4. **Leaflet does not include all** information (uses, precautions, interactions, adverse reactions, or side effects).
❒ 5. Name of **publisher**
❒ 6. **Date of publication** / most recent revision / expiration date
❒ 7. **Ask doctor or pharmacist** if you have any questions or concerns
❒ 8. More **detailed written information** is available from pharmacist or physician (PI)

G. Information is scientifically accurate, unbiased, up-to-date

❒ 1. Information is **neutral** in content and tone

❒ 2. **No promotional** messages about a specific brand, manufacturer, or distributor (may compare chemical entities)

❒ 3. No inaccurate or outdated **claims about benefits** of the product

❒ 4. No inaccurate or outdated **claims about risks** of product

❒ 5. No other inaccurate or **outdated information** was found by this rater

H. Information is readily comprehensible and legible

❒ 2. **Short paragraphs** with a single topic (not more than 5 sentences if info not bulleted)

❒ 3. Limited use of **medical / technical terms** (for important terms, examples are provided in plain language)

❒ 5. **Black box warning** on pregnancy is printed in **bold-face or box** (all caps not sufficient)

❒ 7. **Ads** or coupons for other products or non-pharmacy services are absent.

Comments:

Appendix E: Consumer Medication Information (CMI) Evaluation Form – Metformin

NOTE: Highlighting indicates items not included in summated scores

A. Drug names and indications for use

- ❒ 1. **Generic** name (metformin)
- ❒ 2. **Phonetic spelling** of generic name (met-FOR-min)
- ❒ 3. **Brand** names (e.g., Fortamet™, Glucophage®, Glucophage® XR, Glumetza™, Riomet™)
- ❒ 4. **Indication**: Diabetes, type 2
- ❒ 5. Physical **description** of the drug or FDA **imprint** code is mentioned
- ❒ 6. **Off-label use** mentioned (e.g., "this drug can be prescribed for other uses" or reference to specific off-label indications)

  If specific off-label indications are mentioned, please specify:

……

B. Specific directions about how to use, monitor, and get most benefit

- ❒ 1. Administration**: by mouth**
- ❒ 2. Administration**:** with **meals**
- ❒ 3. **Usual Dosing** (e.g., "the regular tablet is usually taken 1-3 times a day")
- ❒ 4. Recommendation to **follow individual dosing** instructions
  - ❑ **Personal dosing** instructions are inserted in leaflet
- ❒ 5. **Missed dose** – action to take: reasonable recommendation (e.g., "Take a missed dose as soon as you remember it. If it is almost time for the next dose, skip the missed dose. Do not take a double dose to make up for a missed one.")
- ❒ 6. **Overdose** – action to take: contact poison control center or emergency services
  - ❑ **Phone** number for **poison control** center provided
- ❒ 7. **Safety monitoring** (general statement that monitoring is needed)
  - ❑ **Rena**l function
  - ❑ Vitamin **B12**
  - ❑ **Frequency of tests** (e.g., "renal function checked at initiation and annually during use")
  - ❑ Action to take: **ask about lab tests**

    ……..
- ❒ 8. **Effectiveness monitoring** (general statement that monitoring is needed)
  - ❑ **Glycosylated hemoglobin** (HbA1c or A1c)
  - ❑ **Self-monitoring** of glucose recommended
  - ❑ **Monitoring schedule** (e.g., "your HbA1c should be monitored at least every six months")
  - ❑ Action to take: **ask about lab tests**

    ……

C. Contraindications "do not use"

- ❒ 1. **80** years or older and **no test for kidney function** ❒
- ❒ 2. **Renal** or kidney disease ❒
- ❒ 3. **Liver** problems ❒
- ❒ 4. Serious **dehydration** or "have lost a lot of water from your body" ❒
- ❒ 5. **X-ray** / contrast agent (NOT general reference to "procedure" or "test") ❒
- ❒ 6. Planned **surgery** ❒
- ❒ 7. **Serious condition**, such as heart attack, severe infection, or a stroke ❒
- ❒ 8. **Metabolic acidosis:** acute or chronic (e.g., "have acid in the blood" ❒
- ❒ 9. **Hypoxemia** (e.g., "low oxygen in tissue") ❒
- ❒ 10. **Hypersensitivity** to metformin ❒

D. Specific precautions and how to avoid harm while using it

❒ 1. **Lactic acidosis**

- ❑ **Frequency** of lactic acidosis ("rare" or numeric estimate)
- ❑ Case **fatality rate** or statement that it can be fatal
- ❑ **Symptoms** described (e.g., "tired, muscle/stomach pain, cold, dizzy, tachycardia")

Actions to take: ❒ Contact provider immediately ❒ don't take medication

❒ 2. **Alcohol** use

❒ 3. **Pregnancy**

- ❑ Action to take: **Tell your doctor** if you are pregnant or breast feeding

4. **Drug-drug interactions**

- ❒ G**eneral statement that** some drugs interact with metformin
- ❒ List of **specific** drugs that interact with metformin
  - ❒ Statement that list is **not complete**
- ❑ **Action** to take: Inform healthcare provider about all medications you take

…….

5. **Children under 10**

- ❑ Has not been tested in children under 10
- ❑ Should not be used / is not recommended in children under 10

E. Symptoms* of s*erious or frequent adverse reactions and what to do

1. **Serious side effects**

- ❑ **Hypoglycemia** or **symptoms** (e.g., "shakiness, cold sweats, tachycardia, fainting, tingling, hunger")

Action to take: ❒ Contact provider immediately ❒ don't take medication

2. **Common side effects**

- ❑ **Diarrhea, Indigestion, Abdominal** Discomfort
- ❑ **Nausea/Vomiting**
- ❑ **Flatulence**
- ❑ **Asthenia /** tiredness or weakness or similar references to asthenia
- ❑ **Headache**
- ❑ **Metallic taste** in mouth
- ❑ **Action** to take: Tell your doctor or pharmacist if any of these do not go away or bother you

…….

❒ 3. Statement that **list** of side effects is **not complete** (specific statement in side effect section required)

F. General information and encouragement to ask questions

❒ 1. **Sharing medication:** do not give this medicine to others

❒ 2. **Out of reach of children**

❒ 3. **Storage directions** (e.g., "at room temperature and away from light, excess heat, and moisture")

❒ 4. **Leaflet does not include all** information (uses, precautions, interactions, adverse reactions, or side effects)

❒ 5. Name of **publisher**

❒ 6. **Date of publication** / most recent revision / expiration date

❒ 7. **Ask doctor or pharmacist** if you have any questions or concerns

❒ 8. More **detailed written information** is available from pharmacist or physician (PI)

G. Information is scientifically accurate, unbiased, up-to-date

❒ 1. Information is **neutral** in content and tone

❒ 2. **No promotional** messages about a specific brand, manufacturer, or distributor (may compare chemical entities)

❒ 3. No inaccurate or outdated **claims about benefits** of the product

❒ 4. No inaccurate or outdated **claims about risks** of product

❒ 5. No other inaccurate or **outdated information** was found by this rater

H. Information is readily comprehensible and legible

❒ 2. **Short paragraphs** with a single topic (not more than 5 sentences if info not bulleted)

❒ 3. Limited use of **medical / technical terms** (for important terms, examples are provided in plain language)

❒ 5. **Black box warning** on lactic acidosis is printed in **bold-face or box**

❒ 7. **Ads** or coupons for other products or non-pharmacy services are absent.

Comments:

Appendix F: CMI Evaluation Form – Staff Assessment of Legibility/Comprehensibility

The following will be assessed by research staff:

- ❑ Has adequate space between lines (≥ 2.2 mm)
- ❑ Has adequate white space around text (≥=.5 inch)
- ❑ Font size: < 8 pt ___ 8 pt ___ 10 pt ___ 12 pt ___ >12 point ___
- ❑ Has good-ink paper contrast (if print is too light to easily read, do not check)
- ❑ Uses fonts with serifs
- ❑ Line length is ≤6" long
- ❑ Minimal use of italics or ornate typefaces that are hard to read
- ❑ Upper and lower case lettering used
- ❑ Emphasis provided by **bolded text** NOT by all caps
- ❑ Headings placed on separate lines (not on same line as text)
- ❑ Bullets used to enhance readability

The remaining items will be determined from scanned text

Total Word Count _____

Word Count of Longest Paragraph _____

Reading Level (Flesch-Kincaid) _____

COMMENTS:

Consumer ID: _____
Leaflet #_____

Appendix G: Consumer Evaluation Form

Thank you for reading and answering some questions about the attached patient information sheet. Only a few people are being asked to help evaluate this material so your opinions are important. All answers will be kept confidential.

1. Below is a list of words describing the attached information sheet. For each item, please **circle one number** that best describes how **you** would feel if you were taking this medicine for the first time and received this information sheet from the pharmacy.

Poor print size	1	2	3	4	5	Good print size
Poor print quality	1	2	3	4	5	Good print quality
Poor spacing between lines	1	2	3	4	5	Good spacing between lines
Poorly organized	1	2	3	4	5	Well organized
Poor length	1	2	3	4	5	Good length
Unclear	1	2	3	4	5	Clear
Unhelpful	1	2	3	4	5	Helpful
Incomplete	1	2	3	4	5	Complete
Hard to find important information	1	2	3	4	5	Easy to find important information

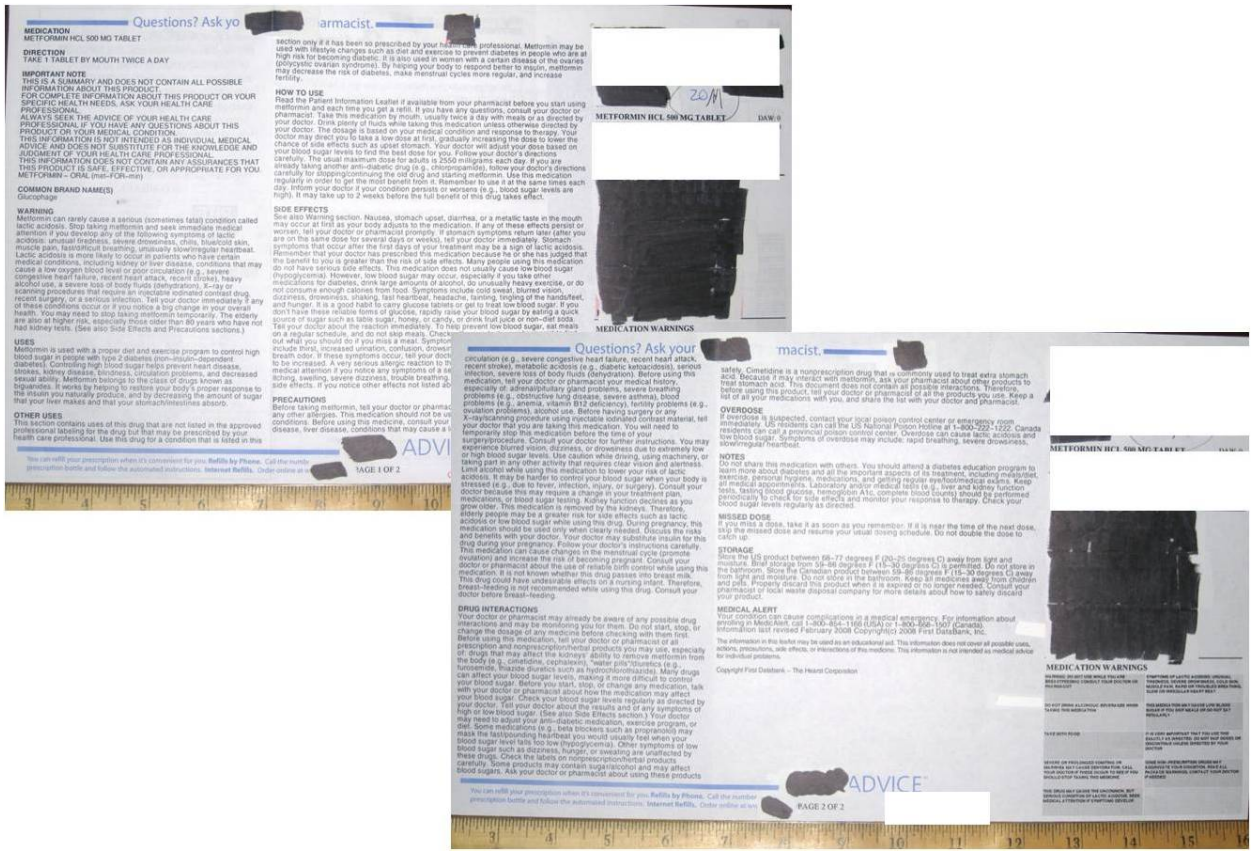
2. **Overall,** what is your opinion about this information sheet. Please **circle** one number that best describes how **you** would feel if you received this information sheet.

Hard to read	1	2	3	4	5	Easy to read
Hard to understand	1	2	3	4	5	Easy to understand
Not useful	1	2	3	4	5	Useful

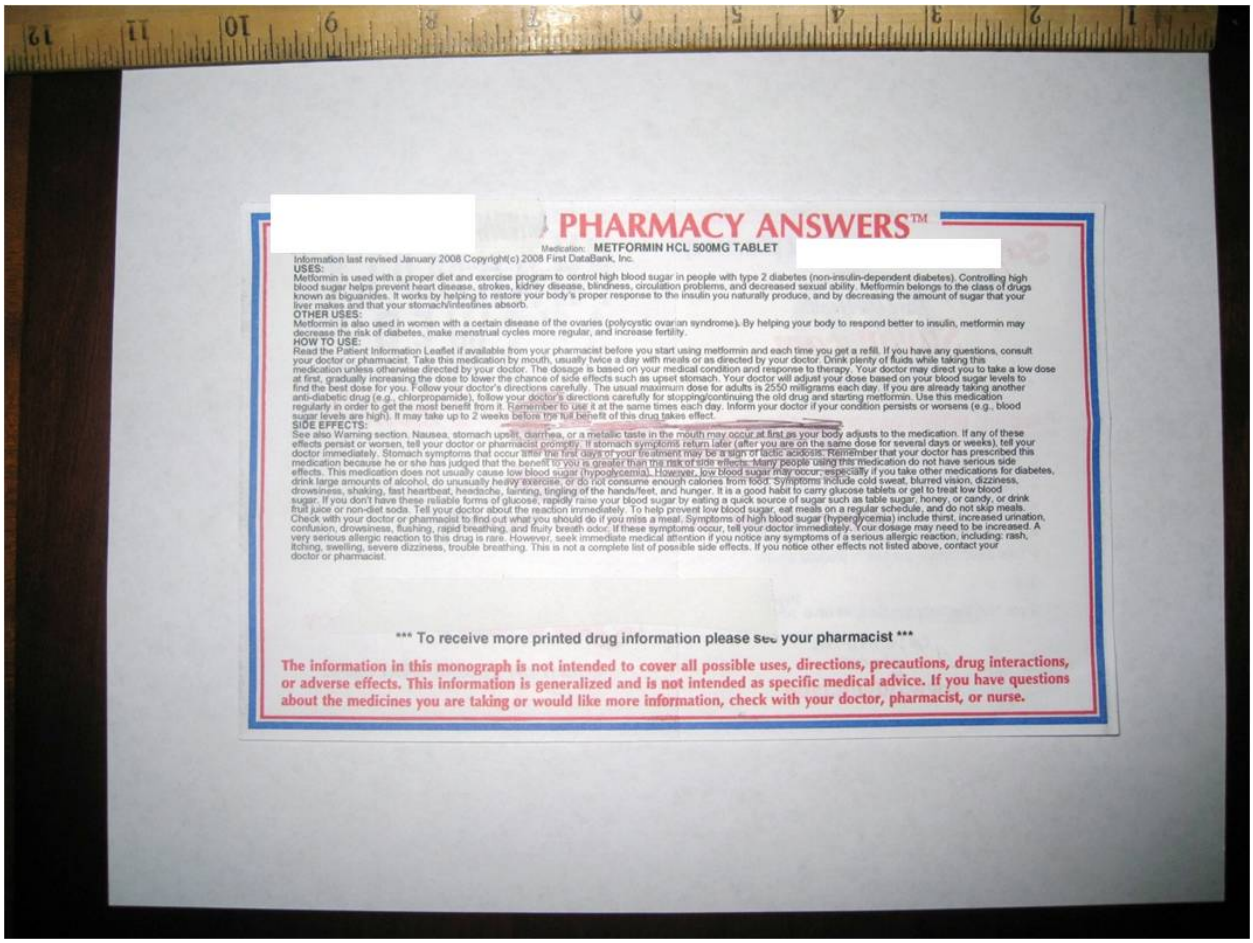
3. Do you have any other comments about this information sheet? (Write on back of page if you wish)

Developed by Svarstad Bl and Mount JK 2001 available at http://www.fda.gov/cder/reports/prescriptioninfo/default.htm.

Appendix H: Examples of leaflets from First Databank and Wolters Kluwer publishers with differing length and content.



Information last revised February 2008 Copyright © 2008 First Databank, Inc.



PHARMACY ANSWERS™

Medication: METFORMIN HCL 500MG TABLET

Information last revised January 2008 Copyright(c) 2008 First DataBank, Inc.

USES:
Metformin is used with a proper diet and exercise program to control high blood sugar in people with type 2 diabetes (non-insulin-dependent diabetes). Controlling high blood sugar helps prevent heart disease, strokes, kidney disease, blindness, circulation problems, and decreased sexual ability. Metformin belongs to the class of drugs known as biguanides. It works by helping to restore your body's proper response to the insulin you naturally produce, and by decreasing the amount of sugar that your liver makes and that your stomach/intestines absorb.

OTHER USES:
Metformin is also used in women with a certain disease of the ovaries (polycystic ovarian syndrome). By helping your body to respond better to insulin, metformin may decrease the risk of diabetes, make menstrual cycles more regular, and increase fertility.

HOW TO USE:
Read the Patient Information Leaflet if available from your pharmacist before you start using metformin and each time you get a refill. If you have any questions, consult your doctor or pharmacist. Take this medication by mouth, usually twice a day with meals or as directed by your doctor. Drink plenty of fluids while taking this medication unless otherwise directed by your doctor. The dosage is based on your medical condition and response to therapy. Your doctor may direct you to take a low dose at first, gradually increasing the dose to lower the chance of side effects such as upset stomach. Your doctor will adjust your dose based on your blood sugar levels to find the best dose for you. Follow your doctor's directions carefully. The usual maximum dose for adults is 2550 milligrams each day. If you are already taking another anti-diabetic drug (e.g., chlorpropamide), follow your doctor's directions carefully for stopping/continuing the old drug and starting metformin. Use this medication regularly in order to get the most benefit from it. Remember to use it at the same times each day. Inform your doctor if your condition persists or worsens (e.g., blood sugar levels are high). It may take up to 2 weeks before the full benefit of this drug takes effect.

SIDE EFFECTS:
See also Warning section. Nausea, stomach upset, diarrhea, or a metallic taste in the mouth may occur at first as your body adjusts to the medication. If any of these effects persist or worsen, tell your doctor or pharmacist promptly. If stomach symptoms return later (after you are on the same dose for several days or weeks), tell your doctor immediately. Stomach symptoms that occur after the first days of your treatment may be a sign of lactic acidosis. Remember that your doctor has prescribed this medication because he or she has judged that the benefit to you is greater than the risk of side effects. Many people using this medication do not have serious side effects. This medication does not usually cause low blood sugar (hypoglycemia). However, low blood sugar may occur, especially if you take other medications for diabetes, drink large amounts of alcohol, do unusually heavy exercise, or do not consume enough calories from food. Symptoms include cold sweat, blurred vision, dizziness, drowsiness, shaking, fast heartbeat, headache, fainting, tingling of the hands/feet, and hunger. It is a good habit to carry glucose tablets or gel to treat low blood sugar. If you don't have these reliable forms of glucose, rapidly raise your blood sugar by eating a quick source of sugar such as table sugar, honey, or candy, or drink fruit juice or non-diet soda. Tell your doctor about the reaction immediately. To help prevent low blood sugar, eat meals on a regular schedule, and do not skip meals. Check with your doctor or pharmacist to find out what you should do if you miss a meal. Symptoms of high blood sugar (hyperglycemia) include thirst, increased urination, confusion, drowsiness, flushing, rapid breathing, and fruity breath odor. If these symptoms occur, tell your doctor immediately. Your dosage may need to be increased. A very serious allergic reaction to this drug is rare. However, seek immediate medical attention if you notice any symptoms of a serious allergic reaction, including: rash, itching, swelling, severe dizziness, trouble breathing. This is not a complete list of possible side effects. If you notice other effects not listed above, contact your doctor or pharmacist.

*** To receive more printed drug information please see your pharmacist ***

The information in this monograph is not intended to cover all possible uses, directions, precautions, drug interactions, or adverse effects. This information is generalized and is not intended as specific medical advice. If you have questions about the medicines you are taking or would like more information, check with your doctor, pharmacist, or nurse.

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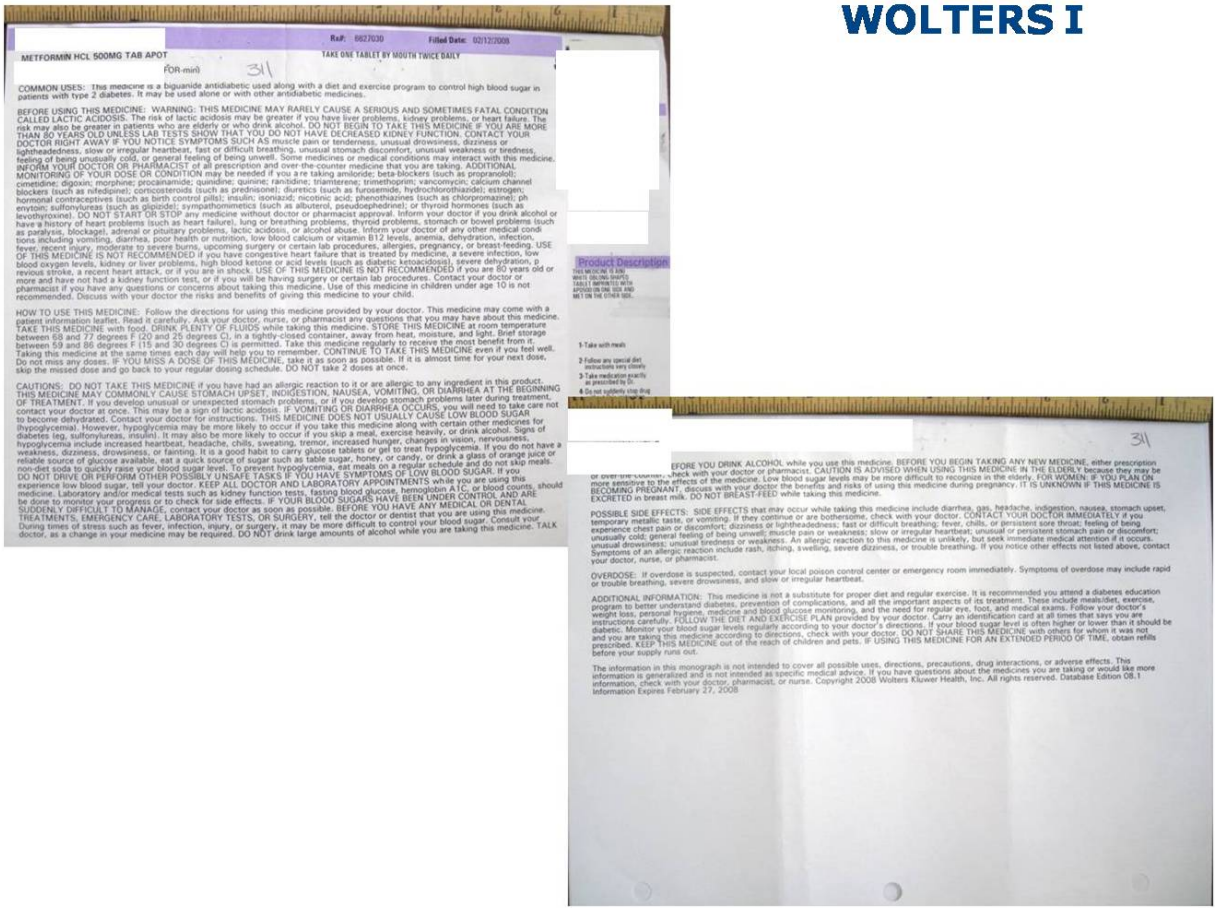
WOLTERS I



METFORMIN HCL 500MG TAB APOT

TAKE ONE TABLET BY MOUTH TWICE DAILY

FOR-min 31

COMMON USES: This medicine is a biguanide antidiabetic used along with a diet and exercise program to control high blood sugar in patients with type 2 diabetes. It may be used alone or with other antidiabetic medicines.

BEFORE USING THIS MEDICINE: WARNING: THIS MEDICINE MAY RARELY CAUSE A SERIOUS AND SOMETIMES FATAL CONDITION CALLED LACTIC ACIDOSIS. The risk of lactic acidosis may be greater if you have liver problems, kidney problems, or heart failure. The risk may also be greater in patients who are elderly or who drink alcohol. DO NOT BEGIN TO TAKE THIS MEDICINE IF YOU ARE MORE THAN 80 YEARS OLD UNLESS LAB TESTS SHOW THAT YOU DO NOT HAVE DECREASED KIDNEY FUNCTION. CONTACT YOUR DOCTOR RIGHT AWAY IF YOU NOTICE SYMPTOMS SUCH AS muscle pain or tenderness, unusual drowsiness, dizziness or lightheadedness, slow or irregular heartbeat, fast or difficult breathing, unusual stomach discomfort, unusual weakness or tiredness, feeling of being unusually cold, or general feeling of being unwell. Some medicines or medical conditions may interact with this medicine. INFORM YOUR DOCTOR OR PHARMACIST of all prescription and over-the-counter medicine that you are taking. ADDITIONAL MONITORING OF YOUR DOSE OR CONDITION may be needed if you a re taking amiloride; beta-blockers (such as propranolol); cimetidine; digoxin; morphine; procainamide; quinidine; quinine; ranitidine; triamterene; trimethoprim; vancomycin; calcium channel blockers (such as nifedipine); corticosteroids (such as prednisone); diuretics (such as furosemide, hydrochlorothiazide); estrogen; hormonal contraceptives (such as birth control pills); insulin; isoniazid; nicotinic acid; phenothiazines (such as chlorpromazine); ph enytoin; sulfonylureas (such as glipizide); sympathomimetics (such as albuterol, pseudoephedrine); or thyroid hormones (such as levothyroxine). DO NOT START OR STOP any medicine without doctor or pharmacist approval. Inform your doctor if you drink alcohol or have a history of heart problems (such as heart failure), lung or breathing problems, thyroid problems, stomach or bowel problems (such as paralysis, blockage), adrenal or pituitary problems, lactic acidosis, or alcohol abuse. Inform your doctor of any other medical conditions including vomiting, diarrhea, poor health or nutrition, low blood calcium or vitamin B12 levels, anemia, dehydration, infection, fever, recent injury, moderate to severe burns, upcoming surgery or certain lab procedures, allergies, pregnancy, or breast-feeding. USE OF THIS MEDICINE IS NOT RECOMMENDED if you have congestive heart failure that is treated by medicine, a severe infection, low blood oxygen levels, kidney or liver problems, high blood ketone or acid levels (such as diabetic ketoacidosis), severe dehydration, p revious stroke, a recent heart attack, or if you are in shock. USE OF THIS MEDICINE IS NOT RECOMMENDED if you are 80 years old or more and have not had a kidney function test, or if you will be having surgery or certain lab procedures. Contact your doctor or pharmacist if you have any questions or concerns about taking this medicine. Use of this medicine in children under age 10 is not recommended. Discuss with your doctor the risks and benefits of giving this medicine to your child.

HOW TO USE THIS MEDICINE: Follow the directions for using this medicine provided by your doctor. This medicine may come with a patient information leaflet. Read it carefully. Ask your doctor, nurse, or pharmacist any questions that you may have about this medicine. TAKE THIS MEDICINE with food. DRINK PLENTY OF FLUIDS while taking this medicine. STORE THIS MEDICINE at room temperature between 68 and 77 degrees F (20 and 25 degrees C), in a tightly-closed container, away from heat, moisture, and light. Brief storage between 59 and 86 degrees F (15 and 30 degrees C) is permitted. Take this medicine regularly to receive the most benefit from it. Taking this medicine at the same times each day will help you to remember. CONTINUE TO TAKE THIS MEDICINE even if you feel well. Do not miss any doses. IF YOU MISS A DOSE OF THIS MEDICINE, take it as soon as possible. If it is almost time for your next dose, skip the missed dose and go back to your regular dosing schedule. DO NOT take 2 doses at once.

CAUTIONS: DO NOT TAKE THIS MEDICINE if you have had an allergic reaction to it or are allergic to any ingredient in this product. THIS MEDICINE MAY COMMONLY CAUSE STOMACH UPSET, INDIGESTION, NAUSEA, VOMITING, OR DIARRHEA AT THE BEGINNING OF TREATMENT. If you develop unusual or unexpected stomach problems, or if you develop stomach problems later during treatment, contact your doctor at once. This may be a sign of lactic acidosis. IF VOMITING OR DIARRHEA OCCURS, you will need to take care not to become dehydrated. Contact your doctor for instructions. THIS MEDICINE DOES NOT USUALLY CAUSE LOW BLOOD SUGAR (hypoglycemia). However, hypoglycemia may be more likely to occur if you take this medicine along with certain other medicines for diabetes (eg, sulfonylureas, insulin). It may also be more likely to occur if you skip a meal, exercise heavily, or drink alcohol. Signs of hypoglycemia include increased heartbeat, headache, chills, sweating, tremor, increased hunger, changes in vision, nervousness, weakness, dizziness, drowsiness, or fainting. It is a good habit to carry glucose tablets or gel to treat hypoglycemia. If you do not have a reliable source of glucose available, eat a quick source of sugar such as table sugar, honey, or candy, or drink a glass of orange juice or non-diet soda to quickly raise your blood sugar level. To prevent hypoglycemia, eat meals on a regular schedule and do not skip meals. DO NOT DRIVE OR PERFORM OTHER POSSIBLY UNSAFE TASKS IF YOU HAVE SYMPTOMS OF LOW BLOOD SUGAR. If you experience low blood sugar, tell your doctor. KEEP ALL DOCTOR AND LABORATORY APPOINTMENTS while you are using this medicine. Laboratory and/or medical tests such as kidney function tests, fasting blood glucose, hemoglobin A1C, or blood counts, should be done to monitor your progress or to check for side effects. IF YOUR BLOOD SUGARS HAVE BEEN UNDER CONTROL AND ARE SUDDENLY DIFFICULT TO MANAGE, contact your doctor as soon as possible. BEFORE YOU HAVE ANY MEDICAL OR DENTAL TREATMENTS, EMERGENCY CARE, LABORATORY TESTS, OR SURGERY, tell the doctor or dentist that you are using this medicine. During times of stress such as fever, infection, injury, or surgery, it may be more difficult to control your blood sugar. Consult your doctor, as a change in your medicine may be required. DO NOT drink large amounts of alcohol while you are taking this medicine. TALK

Product Description

1-Take with meals

2-Follow any special diet instructions very closely

3-Take medication exactly as prescribed by Dr.

4-Do not suddenly stop drug

31

BEFORE YOU DRINK ALCOHOL while you use this medicine. BEFORE YOU BEGIN TAKING ANY NEW MEDICINE, either prescription or over-the-counter, check with your doctor or pharmacist. CAUTION IS ADVISED WHEN USING THIS MEDICINE IN THE ELDERLY because they may be more sensitive to the effects of the medicine. Low blood sugar levels may be more difficult to recognize in the elderly. FOR WOMEN: IF YOU PLAN ON BECOMING PREGNANT, discuss with your doctor the benefits and risks of using this medicine during pregnancy. IT IS UNKNOWN IF THIS MEDICINE IS EXCRETED in breast milk. DO NOT BREAST-FEED while taking this medicine.

POSSIBLE SIDE EFFECTS: SIDE EFFECTS that may occur while taking this medicine include diarrhea, gas, headache, indigestion, nausea, stomach upset, temporary metallic taste, or vomiting. If they continue or are bothersome, check with your doctor. CONTACT YOUR DOCTOR IMMEDIATELY if you experience chest pain or discomfort; dizziness or lightheadedness; fast or difficult breathing; fever, chills, or persistent sore throat; feeling of being unusually cold; general feeling of being unwell; muscle pain or weakness; slow or irregular heartbeat; unusual or persistent stomach pain or discomfort; unusual drowsiness; unusual tiredness or weakness. An allergic reaction to this medicine is unlikely, but seek immediate medical attention if it occurs. Symptoms of an allergic reaction include rash, itching, swelling, severe dizziness, or trouble breathing. If you notice other effects not listed above, contact your doctor, nurse, or pharmacist.

OVERDOSE: If overdose is suspected, contact your local poison control center or emergency room immediately. Symptoms of overdose may include rapid or trouble breathing, severe drowsiness, and slow or irregular heartbeat.

ADDITIONAL INFORMATION: This medicine is not a substitute for proper diet and regular exercise. It is recommended you attend a diabetes education program to better understand diabetes, prevention of complications, and all the important aspects of its treatment. These include meals/diet, exercise, weight loss, personal hygiene, medicine and blood glucose monitoring, and the need for regular eye, foot, and medical exams. Follow your doctor's instructions carefully. FOLLOW THE DIET AND EXERCISE PLAN provided by your doctor. Carry an identification card at all times that says you are diabetic. Monitor your blood sugar levels regularly according to your doctor's directions. If your blood sugar level is often higher or lower than it should be and you are taking this medicine according to directions, check with your doctor. DO NOT SHARE THIS MEDICINE with others for whom it was not prescribed. KEEP THIS MEDICINE out of the reach of children and pets. IF USING THIS MEDICINE FOR AN EXTENDED PERIOD OF TIME, obtain refills before your supply runs out.

The information in this monograph is not intended to cover all possible uses, directions, precautions, drug interactions, or adverse effects. This information is generalized and is not intended as specific medical advice. If you have questions about the medicines you are taking or would like more information, check with your doctor, pharmacist, or nurse. Copyright 2008 Wolters Kluwer Health, Inc. All rights reserved. Database Edition 08.1 Information Expires February 27, 2008

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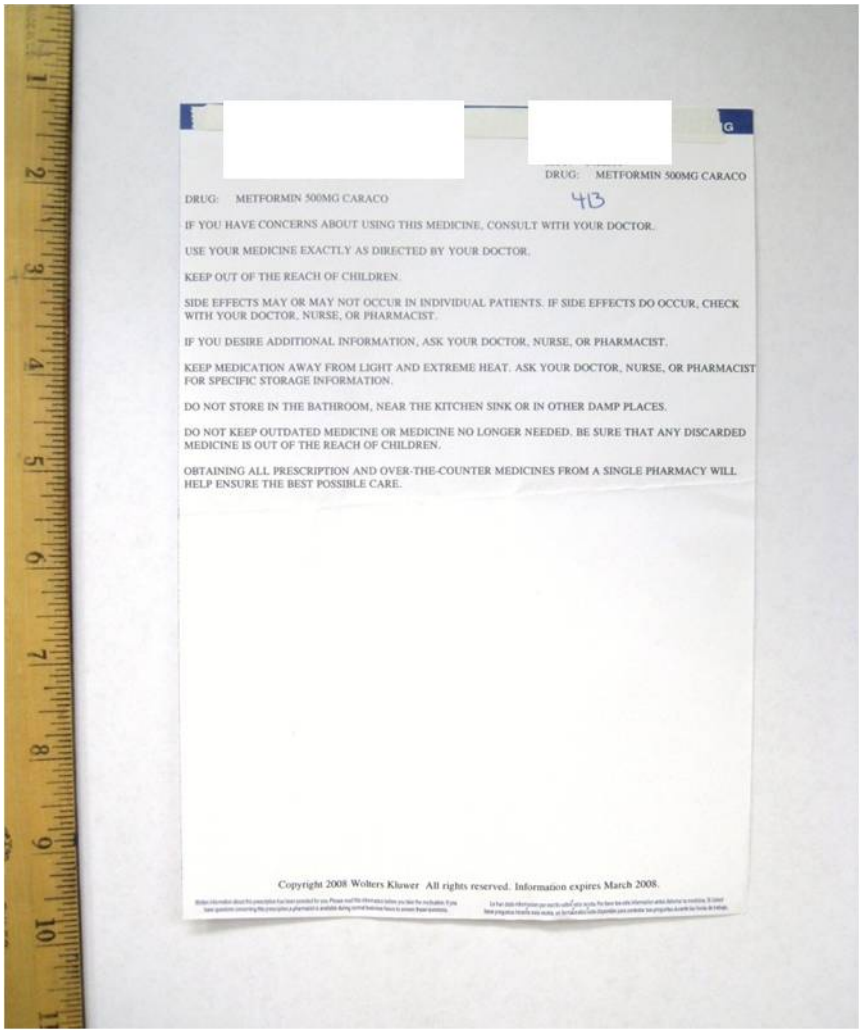

DRUG: METFORMIN 500MG CARACO

DRUG: METFORMIN 500MG CARACO

43

IF YOU HAVE CONCERNS ABOUT USING THIS MEDICINE, CONSULT WITH YOUR DOCTOR.

USE YOUR MEDICINE EXACTLY AS DIRECTED BY YOUR DOCTOR.

KEEP OUT OF THE REACH OF CHILDREN.

SIDE EFFECTS MAY OR MAY NOT OCCUR IN INDIVIDUAL PATIENTS. IF SIDE EFFECTS DO OCCUR, CHECK WITH YOUR DOCTOR, NURSE, OR PHARMACIST.

IF YOU DESIRE ADDITIONAL INFORMATION, ASK YOUR DOCTOR, NURSE, OR PHARMACIST.

KEEP MEDICATION AWAY FROM LIGHT AND EXTREME HEAT. ASK YOUR DOCTOR, NURSE, OR PHARMACIST FOR SPECIFIC STORAGE INFORMATION.

DO NOT STORE IN THE BATHROOM, NEAR THE KITCHEN SINK OR IN OTHER DAMP PLACES.

DO NOT KEEP OUTDATED MEDICINE OR MEDICINE NO LONGER NEEDED. BE SURE THAT ANY DISCARDED MEDICINE IS OUT OF THE REACH OF CHILDREN.

OBTAINING ALL PRESCRIPTION AND OVER-THE-COUNTER MEDICINES FROM A SINGLE PHARMACY WILL HELP ENSURE THE BEST POSSIBLE CARE.

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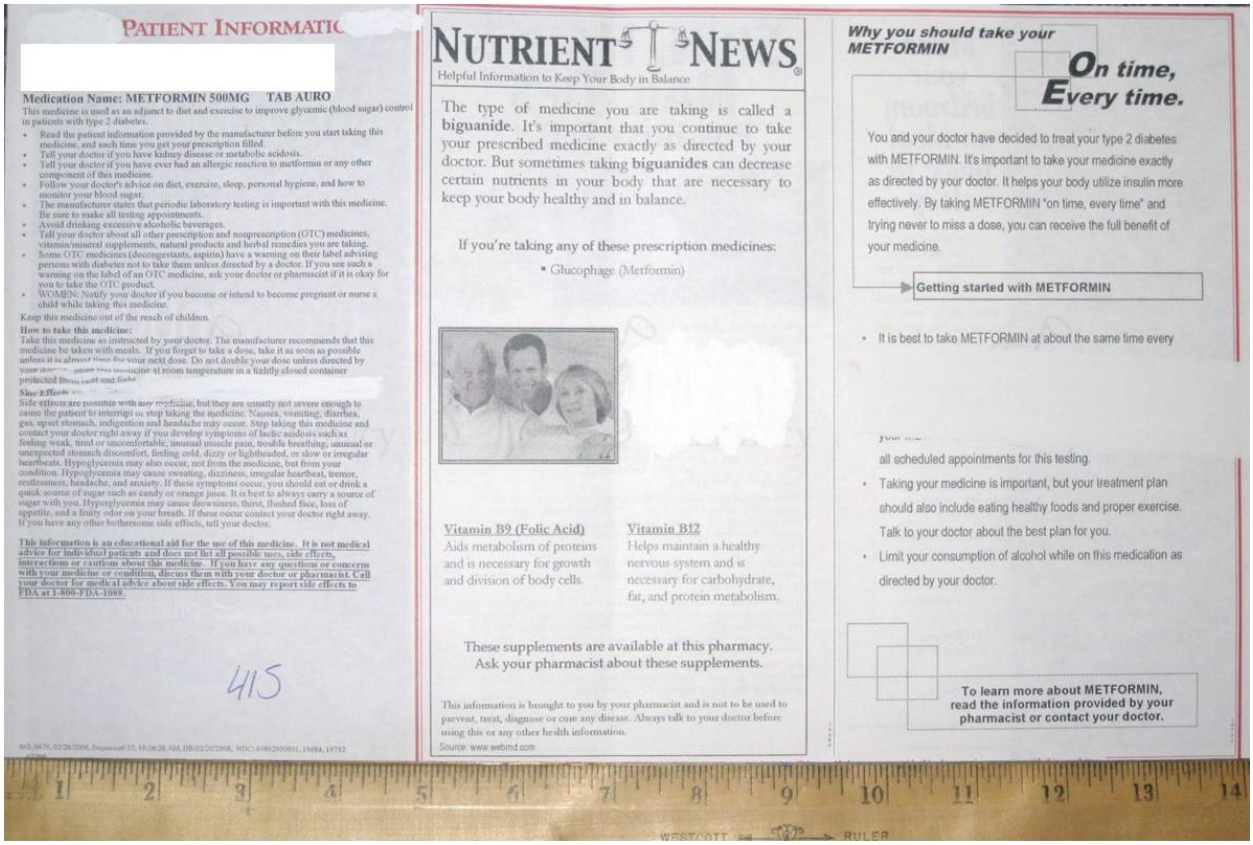
Appendix I: Example (front and back) of a leaflet with information that could distract from medication information.



PATIENT INFORMATIC

Medication Name: METFORMIN 500MG TAB AURO

This medicine is used as an adjunct to diet and exercise to improve glycemic (blood sugar) control in patients with type 2 diabetes.

- Read the patient information provided by the manufacturer before you start taking this medicine, and each time you get your prescription filled.
- Tell your doctor if you have kidney disease or metabolic acidosis.
- Tell your doctor if you have ever had an allergic reaction to metformin or any other component of this medicine.
- Follow your doctor's advice on diet, exercise, sleep, personal hygiene, and how to monitor your blood sugar.
- The manufacturer states that periodic laboratory testing is important with this medicine. Be sure to make all testing appointments.
- Avoid drinking excessive alcoholic beverages.
- Tell your doctor about all other prescription and nonprescription (OTC) medicines, vitamin/mineral supplements, natural products and herbal remedies you are taking.
- Some OTC medicines (decongestants, aspirin) have a warning on their label advising persons with diabetes not to take them unless directed by a doctor. If you see such a warning on the label of an OTC medicine, ask your doctor or pharmacist if it is okay for you to take the OTC product.
- WOMEN: Notify your doctor if you become or intend to become pregnant or nurse a child while taking this medicine.

Keep this medicine out of the reach of children.

How to take this medicine:

Take this medicine as instructed by your doctor. The manufacturer recommends that this medicine be taken with meals. If you forget to take a dose, take it as soon as possible unless it is almost time for your next dose. Do not double your dose unless directed by your doctor. Store this medicine at room temperature in a tightly closed container protected from [illegible] and light.

Side Effects:

Side effects are possible with any medicine, but they are usually not severe enough to cause the patient to interrupt or stop taking the medicine. Nausea, vomiting, diarrhea, gas, upset stomach, indigestion and headache may occur. Stop taking this medicine and contact your doctor right away if you develop symptoms of lactic acidosis such as feeling weak, tired or uncomfortable, unusual muscle pain, trouble breathing, unusual or unexpected stomach discomfort, feeling cold, dizzy or lightheaded, or slow or irregular heartbeats. Hypoglycemia may also occur, not from the medicine, but from your condition. Hypoglycemia may cause sweating, dizziness, irregular heartbeat, tremor, restlessness, headache, and anxiety. If these symptoms occur, you should eat or drink a quick source of sugar such as candy or orange juice. It is best to always carry a source of sugar with you. Hyperglycemia may cause drowsiness, thirst, flushed face, loss of appetite, and a fruity odor on your breath. If these occur contact your doctor right away. If you have any other bothersome side effects, tell your doctor.

This information is an educational aid for the use of this medicine. It is not medical advice for individual patients and does not list all possible uses, side effects, interactions or cautions about this medicine. If you have any questions or concerns with your medicine or condition, discuss them with your doctor or pharmacist. Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

415

NUTRIENT NEWS®

Helpful Information to Keep Your Body in Balance

The type of medicine you are taking is called a **biguanide**. It's important that you continue to take your prescribed medicine exactly as directed by your doctor. But sometimes taking **biguanides** can decrease certain nutrients in your body that are necessary to keep your body healthy and in balance.

If you're taking any of these prescription medicines:

- Glucophage (Metformin)

Vitamin B9 (Folic Acid)
Aids metabolism of proteins and is necessary for growth and division of body cells.

Vitamin B12
Helps maintain a healthy nervous system and is necessary for carbohydrate, fat, and protein metabolism.

These supplements are available at this pharmacy.
Ask your pharmacist about these supplements.

This information is brought to you by your pharmacist and is not to be used to prevent, treat, diagnose or cure any disease. Always talk to your doctor before using this or any other health information.

Source: www.webmd.com

Why you should take your METFORMIN

On time, Every time.

You and your doctor have decided to treat your type 2 diabetes with METFORMIN. It's important to take your medicine exactly as directed by your doctor. It helps your body utilize insulin more effectively. By taking METFORMIN "on time, every time" and trying never to miss a dose, you can receive the full benefit of your medicine.

Getting started with METFORMIN

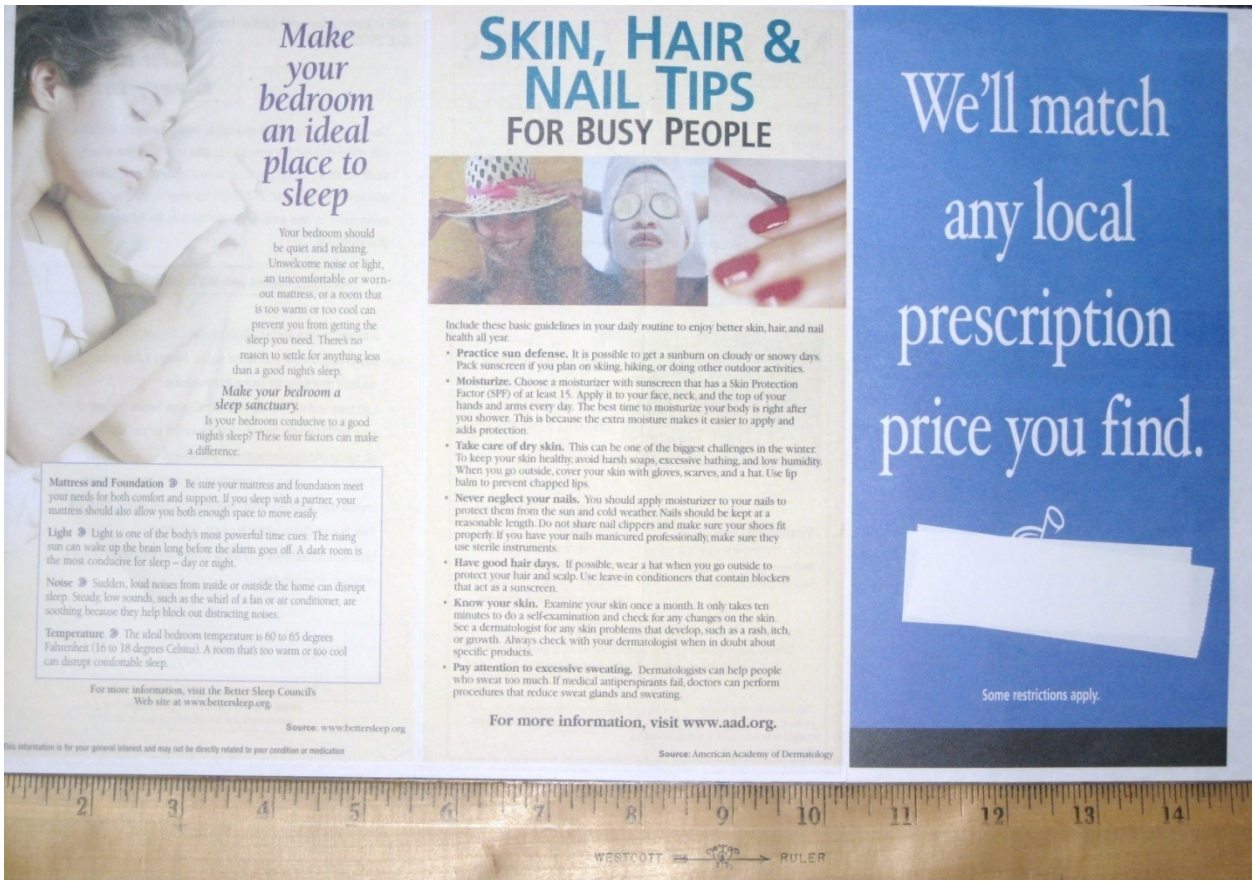
- It is best to take METFORMIN at about the same time every [illegible]

all scheduled appointments for this testing.

- Taking your medicine is important, but your treatment plan should also include eating healthy foods and proper exercise. Talk to your doctor about the best plan for you.
- Limit your consumption of alcohol while on this medication as directed by your doctor.

To learn more about METFORMIN, read the information provided by your pharmacist or contact your doctor.

WESTCOTT RULER



Make your bedroom an ideal place to sleep

Your bedroom should be quiet and relaxing. Unwelcome noise or light, an uncomfortable or worn-out mattress, or a room that is too warm or too cool can prevent you from getting the sleep you need. There's no reason to settle for anything less than a good night's sleep.

Make your bedroom a sleep sanctuary.

Is your bedroom conducive to a good night's sleep? These four factors can make a difference:

Mattress and Foundation Be sure your mattress and foundation meet your needs for both comfort and support. If you sleep with a partner, your mattress should also allow you both enough space to move easily.

Light Light is one of the body's most powerful time cues. The rising sun can wake up the brain long before the alarm goes off. A dark room is the most conducive for sleep – day or night.

Noise Sudden, loud noises from inside or outside the home can disrupt sleep. Steady, low sounds, such as the whirl of a fan or air conditioner, are soothing because they help block out distracting noises.

Temperature The ideal bedroom temperature is 60 to 65 degrees Fahrenheit (16 to 18 degrees Celsius). A room that's too warm or too cool can disrupt comfortable sleep.

For more information, visit the Better Sleep Council's Web site at www.bettersleep.org.

Source: www.bettersleep.org

This information is for your general interest and may not be directly related to your condition or medication

SKIN, HAIR & NAIL TIPS
FOR BUSY PEOPLE

Include these basic guidelines in your daily routine to enjoy better skin, hair, and nail health all year.

- **Practice sun defense.** It is possible to get a sunburn on cloudy or snowy days. Pack sunscreen if you plan on skiing, hiking, or doing other outdoor activities.
- **Moisturize.** Choose a moisturizer with sunscreen that has a Skin Protection Factor (SPF) of at least 15. Apply it to your face, neck, and the top of your hands and arms every day. The best time to moisturize your body is right after you shower. This is because the extra moisture makes it easier to apply and adds protection.
- **Take care of dry skin.** This can be one of the biggest challenges in the winter. To keep your skin healthy, avoid harsh soaps, excessive bathing, and low humidity. When you go outside, cover your skin with gloves, scarves, and a hat. Use lip balm to prevent chapped lips.
- **Never neglect your nails.** You should apply moisturizer to your nails to protect them from the sun and cold weather. Nails should be kept at a reasonable length. Do not share nail clippers and make sure your shoes fit properly. If you have your nails manicured professionally, make sure they use sterile instruments.
- **Have good hair days.** If possible, wear a hat when you go outside to protect your hair and scalp. Use leave-in conditioners that contain blockers that act as a sunscreen.
- **Know your skin.** Examine your skin once a month. It only takes ten minutes to do a self-examination and check for any changes on the skin. See a dermatologist for any skin problems that develop, such as a rash, itch, or growth. Always check with your dermatologist when in doubt about specific products.
- **Pay attention to excessive sweating.** Dermatologists can help people who sweat too much. If medical antiperspirants fail, doctors can perform procedures that reduce sweat glands and sweating.

For more information, visit www.aad.org.

Source: American Academy of Dermatology

We'll match any local prescription price you find.

Some restrictions apply.