

DDMAC REVIEW

NDA#: 21-213
Drug: Mevacor CC Tablets (lovastatin)
Sponsor: Merck
Study: Four Step Label Comprehension Study, Reference 201
Study Report Date: October 5, 1999
Reviewer: Karen Lechter, J.D., Ph.D.
Reviewing Div: HFD-42
Review Completed: June 6, 2000

This review examines Label Comprehension Study 201 for the Mevacor CC Four Step Label, which is the culmination of an iterative label development process that also included studies 199 and 200. The Four Step Label is similar, but not identical, to the final labeling proposed by the sponsor. The sponsor conducted a series of studies to improve the label and made labeling changes to address deficiencies identified by study results. After testing the Four Step Label in this study, the sponsor made several changes and proposed the final label for the NDA submission. Both labels are attached.

Review Summary

This section is a short summary of this review. Study 201 examines whether consumers can understand the information on the package label and the material inside the package. The sponsor made a serious effort to capture a great deal of information about the participants and their understanding of the label, including low-literate consumers. However, label comprehension studies are sometimes difficult to design. The agency had no opportunity to provide feedback to the sponsor before the study began. As a result, although there is adequate information about some aspects of consumer comprehension of the tested label, there are gaps in the methodology and questioning that limit the conclusions we can draw from the results.

Based on these results, we can conclude that participants understand:

- the product is for lowering cholesterol
- the dosing is one capsule per day
- there are certain criteria for use relating to cholesterol levels, gender, age and menopausal status
- there are some situations in which the product should not be used
- the label contains a warning about drinking alcohol
- the label contains a warning about a muscle pain side effect that may be serious
- consumers should consult a physician before use with other cholesterol-lowering drugs

However, it is questionable whether significant numbers of consumers will understand who should not use the product. In addition, there is insufficient information to determine if consumers would understand there are several simultaneous requirements necessary to use the product.

There are a number of other issues for which there is inadequate information. For example, we do not know if consumers:

- understand they must get further cholesterol checks
- can apply the information on the label to a variety of use situations
- would appropriately self-select not to use the product or would understand they must see a physician before taking Mevacor CC if they have conditions mentioned on the label

Thus, there is inadequate information from this study to determine if consumers can understand the label well enough to self-select and use the product appropriately.

Communication Objectives

The stated objectives of the study are as follows. The primary elements, or key factors, according to the sponsor, are in bold.

1. Does the MEVACOR CC Four Step package label communicate the following:
 - **what condition this product is for**
 - the correct dosage
 - number of tablets at one time
 - **number of tablets on a daily basis**
 - number of tablets during a typical week
 - appropriate age/gender
 - for men: appropriate age for usage
 - **for women: appropriate menopausal status for usage**
 - things people need to know or have done before using this product:
 - **know their own total cholesterol level**
 - called the toll-free number if unsure about appropriateness
 - know names or types of other Rx products currently using
 - appropriate total and LDL cholesterol levels for using this product
 - when to talk to a doctor about using this product
 - total cholesterol over 240
 - **heart disease**
 - **stroke**
 - **diabetes**
 - high blood pressure
 - if someone has 3 or more alcohol-containing drinks most days of the week.

- warnings against using if
 - currently taking cyclosporine or erythromycin[‡]
 - currently taking other cholesterol-lowering drugs[‡]
 - currently taking 500 mg or more of niacin daily[‡]
 - **have or have had hepatitis or liver disease**
 - **pregnant, may become pregnant, or breast-feeding**
 - understanding that the label says
 - **Potentially serious muscle side effects may occur when MEVACOR™ CC is used with certain drugs.**
2. Do the internal Four Step package materials enhance comprehension of certain important elements?
 3. On elements on which they can be compared, does the Four Step label lead to fewer comprehension errors than the Red Arrow label in communicating the key messages?
 4. Do those respondents in the two key Four Step subgroups (described below) have an adequate level of comprehension of elements of communication (i.e., meet the criteria set for the total representative sample or not score significantly lower than respondents in the appropriate comparative group)?
 - safety risk consumers based on the label (contraindicated medication, allergy to lovastatin, or current hepatitis or liver disease); and
 - consumers with low literacy

The sponsor proposes that the goal for the primary elements be 80% comprehension and for the other elements 51%. If these goals are reached, the objective is met satisfactorily, according to the sponsor.

Comment: The agency does not use numerical goals to determine whether or not information is adequately understood. Instead, the agency examines the importance of the information, the way in which the question was asked, other aspects of the question, and the label text to determine whether the labeling requires modification. For some items, 80% correct may not be adequate; for others, less than 51% may be adequate.

Some of the communication objectives not designated as key by the sponsor should be key. These include all items in the section on when to talk to a doctor about using the product, which mentions total cholesterol over 240, high blood pressure, and drinking

[‡] Although the individual drugs that can cause interactions were considered important information by the sponsor, the sponsor stated that the critical warning regarding these drugs is the more general statement on the Four Step label that *potentially serious muscle side effects may occur when MEVACOR CC is used with certain drugs*. This statement is to alert consumers to the list of contraindicated drugs and the side effect of greatest concern that may signal the need for immediate medical care. Therefore, while the individual drugs are important, they were not considered “key factors” by the sponsor.

three or more alcoholic drinks daily on most days. The key items also should include all those under the list of warnings against using, including taking cyclosporine or erythromycin or other cholesterol-lowering drugs, or 500 or more mg. of niacin daily.

Methodology

Participants

Participants were representative of the total US population with regard to gender and age, based on census statistics. They were not necessarily concerned about their cholesterol. There were 502 participants, all age 18 and older. In addition to the general population, two subgroups were studied—"Safety Risk" and "Low Literate." These groups were augmented to reach approximately 100 in each group.

The demographic information for the participants showed that in general, the study population mirrored the census population with the following exceptions: fewer age 65 and older in the study population versus the census population (13% vs. 17%); fewer married in the study population (47% vs. 60%); more education in the study population (6% vs. 18% with less than high school; 27% vs. 17% with some college); more African Americans in the study population (14% vs. 11%), and slightly higher income in the study group.

The 96 Safety Risk participants had at least one of the following characteristics:

- taking a contraindicated medication
- allergic to lovastatin
- current hepatitis or liver disease

There were 84 Low Literate participants. These persons scored at the 8th grade level or below on the Rapid Estimate of Adult Literacy in Medicine (REALM) test.

Some participants were classified as "Other Ineligible" if they were not in the Safety Risk group. The Other Ineligible should not take the product for other reasons than those used for the Safety Risk group. Other Ineligible participants had at least one of the following characteristics:

- have heart disease
- have had a stroke
- have diabetes or high blood sugar
- taking 2+ blood pressure medicines
- currently on cholesterol-lowering drugs (excluding gemfibrozil and niacin, which are safety risks)
- too low or too high total cholesterol level
- do not know total cholesterol level
- had hepatitis or liver disease in the past
- women not 1 year past menopause
- men not over 40 years of age

Of these Other Ineligible characteristics, the following were in a section of the label stating that Mevacor CC should not be taken unless under the direction of a doctor: if you have had a stroke, diabetes, high blood pressure, heart disease, or total cholesterol above 240 mg/dL. Another section of the label stated that you must not take Mevacor CC with other cholesterol reducing drugs.

Comment: Responses of the "Other Ineligible" group were not analyzed separately in this study. It is not clear why these participants were classified into a separate category in this study if they were not analyzed as such.

Procedure

Participants were recruited in 28 geographically and demographically dispersed malls across the country. They were screened on the mall floor and, if eligible, invited into the research facility for the main study. The screening questionnaire for the augmented Safety Risk group contained questions about contraindicated medicines and medical conditions.

All participants took the REALM literacy test before the label comprehension portion of the study began. They were asked to read the Four Step package label as they would if they were considering buying the product. They then answered a series of comprehension questions relating to the communication objectives. The label was available to examine during questioning.

After being tested on the package label information, participants reviewed the materials inside the package and answered most of the comprehension questions again. They finished the study by answering questions about their medical history and current medical situation.

The materials inside the package consisted of a booklet about cholesterol and Mevacor CC entitled "Your Passport to Healthy Living;" a leaflet about Mevacor CC similar to a Patient Package Insert for prescription medications; coupons for purchases of Mevacor CC; a card with a list of the medications that preclude use of Mevacor CC, with spaces on the other side of the card to record three sets of lipid levels; and two stickers to remind users to take Mevacor CC with the evening meal.

Comment: The sponsor successfully dispersed the study sites to increase the probability that a variety of consumers would participate in the study. Using the REALM literacy test enabled the sponsor to categorize all participants as low-literate or not.

Questionnaires

Screening Questionnaires. The Screening Questionnaires are used to collect basic information from potential participants to determine if they are eligible to participate. They ask about the following issues:

- age

- participation in market research within the past 3 months
- employment of self, family, or friends in advertising or healthcare-related businesses
- concern about own blood pressure, cholesterol, and fiber and fat in the diet
- whether blood pressure and cholesterol are high, desirable, low, or don't know but is or is not a problem

The Augment Screening Questionnaire, designed to recruit persons taking the contraindicated drugs listed on the label, included questions about current medications and selected health conditions. Participants looked at cards that listed medications and conditions and indicated which applied to them. One card listed non-prescription drugs. Three other cards listed 26 prescription medications, all but two of which are contraindicated on the label. Participants who indicated they take any of the contraindicated drugs were included in the Safety Risk group.

The Screening Questionnaire for the low literate group was almost identical to the general Screening Questionnaire.

Comment: The questions about blood pressure and cholesterol in the Screening Questionnaires may alert participants to the orientation of the study, so that when they are asked later about what the drug is used for, they may be more likely to respond correctly. It is not clear why questions are asked about the participants' blood pressure and cholesterol, or participants' concern about cholesterol, blood pressure, fiber and fat. These questions are not used to screen participants out and the results are not analyzed according to these factors. However, responses to these questions were used to describe characteristics of the sample as a whole. Questions about medications taken may have sensitized participants to later mentioning of these drugs on the label.

Main Questionnaire. The main questionnaire begins with a series of questions relating to information on the package label. There is a mix of open-ended and closed-ended questions. Closed-ended questions provide a list of possible responses within the question, such as yes/no or a list of multiple choices. Open-ended questions do not provide the possible responses within the question. After participants answered questions about the package label, they examined the materials found inside the package, and they answered a second set of questions about the materials inside the package. The second set of questions was the same as the first, with the exception that the second set did not ask about what the product is used for or how many tablets to take. The questionnaire finished with questions about demographics and the personal health of the participant. Many of these questions could be used to categorize participants as being in the Safety Risk or Other Ineligible Group.

Comment: As the data for the Other Ineligible were not analyzed separately, and because there were no questions asking if the participant could use the product, there was no reason to have an Other Ineligible Group. Therefore, many of these questions were unnecessary.

Label comprehension questionnaires are difficult to design. There is almost no literature on the subject. Researchers coming from a market research orientation, as is often the case, may not apply the rigor that the agency believes is necessary for these studies. As a result, sponsors that do not receive feedback from the agency on the protocol and questionnaire design may produce research that does not answer some of the important questions adequately. That is the case with this study.

Ideally, questions should not be leading or biasing in any way, and they should tap more than the most superficial understanding of the information presented. This study questionnaire covers the communication objectives that were listed. However, a number of the questions in this study are not optimal. Some of the questions are leading, making it likely that more participants will answer correctly. Some of the multi-item multiple choice questions have most items that should be answered the same way. This may set up a response bias making correct responses more likely as participants proceed through the series of questions. More use of a variety of correct responses would have reduced this possibility.

Some questions ask if someone with particular characteristics could use Mevacor CC or whether that information is not on the label. Unfortunately, these questions do not ask what participants would conclude about using Mevacor CC if the information is not on the label. Finally, the questions do not test whether a consumer can apply the information on the label to hypothetical situations. Most of these shortcomings could have been avoided by other questioning methods. One such example is the use of scenario questions that present hypothetical situations in which information on the label must be applied. Therefore, although the questionnaire addresses the topics listed in the communication objectives, many questions do not call for more than the most basic lower-level reasoning, and some may be biased.

The agency is concerned that there are no questions to determine if participants understood that according to the label, the following three conditions must be met simultaneously by Mevacor CC users:

- 1. total cholesterol 200-240*
- 2. LDL \geq 130*
- 3. male age 40 or over, or female 1 year past last menstrual period*

Instead, participants are asked separately if each of the following persons can take the product or should not take it:

- 1. men younger than 40 years old*
- 2. men 40 years or older*
- 3. women who have not started menopause yet*
- 4. women past menopause*

Participants are also asked whether the following persons should talk to a doctor before use:

1. cholesterol 200-240
2. cholesterol >240
3. LDL \geq 130

A significant number of participants would not understand that all 3 requirements must be met before use. This study does not provide us with that critical information, because it does not ask.

Questions asking whether certain persons can use Mevacor CC or whether they must talk with a doctor first test only one element of the label at a time. For example, one question asks if a person who has a total cholesterol between 200 and 240 can use the product or whether that person must talk to a doctor. The question gives no information about whether other conditions of use are met, such as age or LDL level.

Some questions assume the participants understand certain label information. However, the participants may not understand that information until it is presented in the question. For example, one question asks how long after beginning to use the product someone should have his or her cholesterol tested. This question presupposes participants understand that users must test their cholesterol at some point after starting use. We do not know if they did understand this point before they read the question.

Other questions are leading. For example, one question asks if a typical person who decides to use Mevacor CC should talk to the doctor at some point. Responses to questions such as these may be affected by the nature of the question, which tends to suggest a "yes" response. It is difficult to design non-leading questions in some instances. However, if scenarios and open-ended questions are used, this difficulty can usually be overcome.

In summary, the questionnaire examines the communication objectives to some extent, without requiring participants to apply the information on the label to hypothetical situations that might represent typical use situations. Some questions are fairly easy to answer because they ask for information from the label to be used in a simple way. Some questions are leading, and some may be the subject of a response bias created by the pattern of correct responses to preceding questions. Some questions presuppose that participants know information that they may not know. There are no questions to determine if participants understand the three main requirements are needed together to take the medicine. In general, the study does not examine understanding at higher levels of cognitive functioning.

Results

After Reading Only the Package Label

The following is a discussion of the results after participants read only the package label.

Almost all participants understood that the purpose of the product is to treat cholesterol and that there is one tablet per dose and one tablet per day (96%-99%). Fewer (85%) understood they should get their cholesterol tested 8 weeks after beginning use. Table 1 presents these results.

Table 1. Questions about purpose, dosing and when to check cholesterol

Question Area	Correct %
Purpose to treat cholesterol	97
1 tablet/ dose	99
1 tablet/day	96
check cholesterol in 8 weeks	85

Comment: The question about when to get cholesterol tested after beginning use presumed participants knew they must test (“Based on the label, about how long after beginning to use this product should someone have their cholesterol level tested?”). This presumption may not have been true and should have been tested. We do not know if consumers who read the label understand they must have further cholesterol checks.

Participants varied in their understanding of who could use the product. They understood that women 1 year postmenopausal can take the product (92%) and that men age 40 or more could take it (94%). When asked if women who have not started menopause and men under age 40 could take the product, slightly more than half said each group should not take it (59% and 56%), and another third said the label doesn’t say, as shown in Table 2.

Table 2. Who can or cannot use the product by age, sex, and menopausal status

Question Area	Correct %	Label Did Not Say %
Women 1 year past menopause can take	92	3
Women pre-menopausal cannot take	59	28
Men 40+ can take	94	3
Men <40 cannot take	56	33

Comment—Due to the phrasing of questions and response choices about who can use the product, it is not clear how many understood who should not take the product. The questions about men above or below age 40 and women pre- or post-menopause give participants the option of saying they can take, should not take, or the materials don’t say. For the questions about the categories of people who should not take Mevacor CC, approximately 1/3 said the materials don’t say. We do not know if these participants could correctly conclude that therefore these categories of people should not take the medication. The questions should not have given the option of saying the information

was not on the label; if the questions did give that option, there should have been a further question about whether or not the product could be used in the situation described.

When asked about several different actions that might be taken before using Mevacor CC, participants generally scored 90% or more, as shown in Table 3.

Table 3. Possible actions before use

Question Area	Correct %
Before use know total cholesterol	91
Before use know names of other Rx drugs are taking	94
Call toll-free number if unsure about using	93
Don't need a hearing test	94*

*Percent who said "label doesn't say"

Comment: These questions did not have much probative value. It would have been better for the question to be open-ended so participants would have to generate their own list of things to do before using the product. We do not know from these questions if they understand they must also know other things, such as their LDL level and their medical conditions.

When given a list of persons with various medical conditions and asked if the person listed can use the product or should talk to a doctor before use, 90%-92% of participants understood that persons should consult a physician if they have heart disease, stroke, diabetes, or high blood pressure. Table 4 presents results for these conditions.

Table 4. Talk to a doctor with certain medical conditions

Question Area	Correct %
Talk to a doctor before use if:	
Heart disease	92
Stroke	93
Diabetes	92
High blood pressure	90

However, participants had more trouble understanding which range of total cholesterol and LDL requires a doctor's advice. Table 5 presents the results of questions asking about use with various levels of total cholesterol and LDL.

Table 5. Use with various total cholesterol and LDL's—OK to use or talk to doctor

Question Area	Correct %	Incorrect % (actual response)
Total cholesterol 200-240 can use	81	16 (talk to doctor)
Total cholesterol >240 talk to doctor before use	70	18 (can use)
LDL \geq 130 can use	61	22 (talk to doctor)

Comment: These figures demonstrate difficulty in knowing when it is safe to use the product without consulting a doctor. There may be a tendency to consult a doctor when it is not necessary (e.g., total cholesterol 200-240), but there may also be a tendency to use the product without medical consultation when consultation is necessary (e.g., total cholesterol >240). The results suggest that substantial proportions of potential users may use the product inappropriately based on their cholesterol levels. Furthermore, if questions had addressed the need to meet total cholesterol, LDL cholesterol, and male age or menopause requirements simultaneously, it is likely that even fewer consumers would have demonstrated the ability to choose the product appropriately.

Participants were given a list of nine types of persons and were asked if the label specifically states these persons should not take Mevacor CC or whether the label does not say. Six of the questions should have been answered that the label says not to take the product; for three, the label was silent. The list mentioned two drugs that appeared on the label (erythromycin and cyclosporine). The questions about these two drugs resulted in correct responses rates of about 80%. The scores for the six questions covered by the label are in Table 6.

Table 6. Situations in which the label says not to use the product

Type of Person	Correct %
Pregnant or breast feeding	93
Hepatitis or liver disease	83
Use other cholesterol drugs	88
Use \geq 500 mg niacin daily	90
Use erythromycin	80
Use cyclosporine	81

Three other questions were about information that was not mentioned on the label. Correct responses are that the person can use the product. From 3%-25% incorrectly stated that the label states these persons should not use the product. Table 7 shows these results. The percentages reflect **incorrect** responses; these are the percentages who answered that the label states these people should not use the product.

Table 7. Incorrect responses (should not use Mevacor CC) about use in situations not mentioned on the label

Type of Person	Incorrect %
Taking an MAOI drug	25
Experiences motion sickness	12
Recently had a flu shot	7

Comment: The fact that 25% of participants said someone who is taking an MAOI drug should not use the product may suggest a tendency to say not to use or to consult a physician whenever another drug is taken. It is not a safety risk for persons with these conditions to avoid using Mevacor CC or to consult a physician before use.

Two questions asked about use of Mevacor CC with other cholesterol-lowering drugs. One multiple-choice question asked what someone taking another cholesterol-lowering drug and who is thinking about using Mevacor CC should do. Several drugs were mentioned by name. Eighty-six percent (86%) of the total group of participants correctly stated persons taking the specified cholesterol-lowering drugs should not take Mevacor CC.

Comment: This question about use with other cholesterol-lowering drugs is a good example of a scenario-type question in which participants are asked to apply the information on the label to a specific situation.

The other question about use with other cholesterol-lowering drugs was a yes/no format. It asked whether or not someone on another cholesterol-lowering drug should consult a physician before using Mevacor. Ninety-seven percent (97%) answered correctly.

Comment: This question is leading and likely to evoke the correct response. A scenario-type question or an open-ended direct question may have worked better here. The prior question about use with specific drugs is a better gauge of participants' understanding of this concept.

In another question, participants were asked whether or not the label contains certain warnings. Of the three warnings presented, two were on the label. Participants answered these correctly at the 91% level for both that were on the label, and slightly lower for the warning not on the label, as shown in Table 8.

Comment: If scenario questions had been used here, we would have had a much better sense of whether participants could understand and apply this warning information.

Table 8. Whether certain warnings were on the label

Type of Warning	Correct %
On label--Talk to doctor before use if 3+ alcoholic drinks per day	91
On label--Potentially serious side effects if used with other drugs, including muscle pain, tenderness or weakness that may require immediate medical attention	91
Not on Label--Use caution when operating motor vehicle or machinery	88

One question based on the package label alone was a leading question asking whether potential users should talk with the doctor about using the product at some point. Ninety-six percent (96%) answered this correctly.

Comment: As this was a leading question, it is not surprising that a high percent of participants answered correctly. This question does not adequately demonstrate that users would understand, without prompting, that they must see a doctor. However, it is difficult to ask that type of question directly. A scenario question would have been better.

Low literacy results. The low literacy participants (N=84) scored lower than the non-low literacy participants (N=317) on some of the questions. Differences in scores were determined by t-tests at the $p \leq .05$ level, with no adjustment for multiple comparisons. Areas in which the low literacy group scored lower are listed in Table 9. For some items listed here, low-literate participants had fewer correct responses than the non-low-literates for items that should have been answered affirmatively. They had more incorrect responses than the non-low-literates for items that should have been answered negatively.

Table 9. Questions for which the low literacy group scored differently than the non-low literacy group.

Question Area	Low Literacy Score—Affirmative Responses (%)	Non-Low Literacy Score—Affirmative Responses (%)
Questions that should have been answered affirmatively:		
Women 1 year postmenopausal can take	83	93
Women not started menopause should not take	44	62
Men over 40 can take	87	95
Total cholest. 200-240 can take	68	84
Total cholest. >240 talk to doctor	57	71
LDL \geq 30 can take	42	64
Heart disease talk to doctor	85	93
Must not take if taking erythromycin	66	82
Stroke talk to doctor	85	94
High blood pressure talk to doctor	81	92
Typical person should talk to doctor at some point	99	95
Questions that should have been answered negatively:		
Arthritis talk to doctor	29	15
Hemorrhoids talk to doctor	16	7
Must not take if taking MAOI drug	36	24
Must not take if get motion sickness	25	9
Must not take if recent flu shot	17	6

Safety Risk results. The Safety Risk group performed similarly to the non-Safety Risk group with a few minor exceptions, which are listed in Table 10. Differences in scores were determined by t-tests at the $p \leq .05$ level, with no adjustment for multiple comparisons. As there were some safety Risk participants in the general sample, the sponsor conducted a further analysis, in which all Safety Risk members of the total sample were moved to the safety risk category. The table below is based on completely separated groups.

Table 10. Questions for which the safety risk group scored lower than the non safety risk group.

Question Area	Non-Safety Risk Correct Responses (%)	Safety Risk Correct Responses (%)
Heart disease talk to doctor before use	92	83
Diabetes talk to doctor before use	92	84
Arthritis OK to use	10	16

After Reading Package Label and Materials Inside the Package

The following is a discussion of the results after participants read both the package and all the materials inside the package.

After answering questions about the package label, participants read the materials inside the package. Participants were then asked most of the same questions again. Participants achieved higher scores for some of the questions. Table 11 presents the questions in which there was a difference in scores between the two sets of questions, based on t-tests. The first column in each set of columns represents the percent who answered correctly. The second number represents the percent who answered “materials don’t say” or “don’t know.”

Table 11. Percentages giving correct responses after reading the package label and after reading all of the materials

Question Area	After Package Label (%)		After All Materials (%)	
	Correct (%)	Materials Don't Say/Don't Know (%)	Correct (%)	Materials Don't Say/Don't Know (%)
Women pre-menopausal should not take	59	30	77	16
Male responses only: Women pre-menopausal should not take	53	35	73	20
Men <40 should not take	56	34	74	20
Person with hemorrhoids OK to use	7	85	3	92
Person with arthritis OK to use	10	73	6	82

In the low literacy subgroup, only one score improved significantly ($p \leq .05$) after all the materials were read. This involved the question about men under age 40 not taking the product (48% correct after package label; 74% after all materials).

The sponsor compared the responses of males and females on the questions about which women and which men can take the product. After reading just the package label, women scored higher (64%) than men (53%) on the question about whether premenopausal women can use the product. After reading all the materials, females scored higher (76%) than males (71%) on the question about men under age 40 taking the product.

Comment: The best way to test if the package label, along with the materials inside the package, improve comprehension beyond the package label alone, is to assign participants randomly to read only the package label or all of the materials and compare the results of the two groups. The methodology used here is common in label comprehension studies. However, we do not know the cause of improved scores after reading the materials inside the package. Improved scores could have been due to the content of the additional materials, additional exposure to the information, knowledge from the first questionnaire about which issues were important prior to reading the information again, exposure to the first test, or to other methodological factors. Therefore, we cannot conclude with confidence that the increased scores were due to the use of the additional materials.

Other Issues

The sponsor presented the results of this Four Step Study along with results of an earlier study using a different label (Red Arrow) in a effort to demonstrate better understanding for the more recent label. However, because the two labels were not tested head-to-head, we cannot make such comparisons.

The agency believes that labeling for this product must advise consumers to see their health care providers before deciding whether or not to use this product. This label does not include such advice, and therefore the critical advice to see a physician before use was not tested in the study.

Label Changes as a Result of the Study

After testing the Four Step label, the sponsor identified as a key area of improvement better communication of the women and men who should not use the product. The sponsor revised the final proposed draft label to address this shortcoming. The new label puts the information about which women can use the product before the information about men. In the label tested in this study, information about men came first. Further, after stating that men 40 years or older can use the product, the new label states “men less than 40 years old, talk to your doctor before use.” This information was not on the tested label.

Conclusion

The study covers the communication objectives with questions that, in most cases, do not require participants to do more than repeat or identify the presence of information on the label. Therefore, we do not know how well consumers can use the information and interpret it correctly. Of particular interest is the fact that there were no questions to determine if participants understood that they must meet all 3 of the following criteria to use the product:

1. cholesterol 200-240
2. LDL \geq 130
3. males \geq 40 years; females at least 1 year past menopause

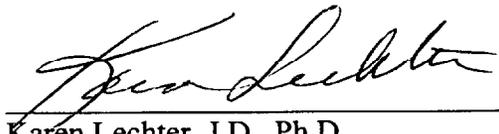
Most questions produced fairly high scores. However, these scores are a function, in part, of the difficulty of the questions, whether the questions are leading, and other aspects of the questioning. The scores are not unbiased measures of comprehension. It is likely that questions requiring participants to apply the information on the label to hypothetical situations would have produced lower scores, but would have given us a better assessment of how well the label is understood.

The results indicate that there may not be good understanding of who cannot take the product, including men under 40 and pre-menopausal women. The phrasing of the question on this issue permitted responses that the information was not on the label. We do not know if participants understood well who could not use the product if the information was not on the label. These results about who should not use the product, coupled with the incomplete information on participants' understanding about who can take the product, raise concerns about appropriate self-selection. Although a few scores improved substantially after participants read the materials inside the package, correct responses remained in the 74-77% range for questions about pre-menopausal women and men under 40, and improved scores after reading all the materials may have been due to the study methodology rather than the effect of the additional materials.

Although the questionnaire collected information about the personal health status of participants, participants were never asked if they could use the product themselves. This information would have been useful in determining how well consumers could self-select and might have overcome some of the shortcomings of the other questions about who could and could not use the product.

As is often the case, the low literate participants had problems understanding some of the important messages. They had particular problems understanding if Mevacor CC can be used by persons with various total cholesterol and LDL levels and by women before menopause.

This study does not provide us with sufficient information to conclude confidently that consumers can self-select to use the product appropriately; or whether they understand key information such as the fact they must check cholesterol after beginning use.



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Label Tested in Label Comprehension Study 201

4 EASY STEPS

To see if MEVACOR[®] CC is right for you.

1 What is your age and cholesterol level?

2 Who should NOT use.

3 What medicines are you taking?

4 Talk to your doctor.

If MEVACOR CC is right for you...

You are now ready to make MEVACOR CC part of your healthy lifestyle that includes exercise, eating right and seeing your doctor regularly. Taken once-a-day, MEVACOR CC will help you lower your cholesterol, which may reduce your risk of heart disease.

If you are not sure if MEVACOR CC is right for you, call us at 1-800-MEVACOR. Product Specialists are available to help you understand any of the information on this package.

Drug Facts

Active ingredient (in each tablet)	Purpose
Lovastatin 10 mg.....	Cholesterol Controller

Use: MEVACOR[®] CC should be used to help lower total cholesterol which may lead to a healthier heart.

Who should use MEVACOR CC:

- Your total cholesterol is between 200–240 mg/dL AND your LDL ("bad") cholesterol is over 130 mg/dL, AND
 - You are a woman past menopause (at least 1 year since last menstrual period)
 - You are a man 40 years or older (men less than 40 years old, talk to your doctor before use)

Warnings

Allergy alert: Do NOT use if you are allergic to any of the ingredients in this drug.

Liver disease: Do NOT use if you have hepatitis or other liver disease.

Women: Do NOT use if you are pregnant, may become pregnant or are breast-feeding.

Do NOT use unless you are past menopause.

Do not use MEVACOR CC with the following medicines†:

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| • erythromycin, or clarithromycin-Biaxin (for infections) | • other cholesterol-reducing drugs such as: |
| • ketoconazole-Nizoral, or itraconazole-Sporanox (for fungal infections) | • niacin at daily doses of 500 mg or more, or gemfibrozil |
| • nefazodone-Serzone (for depression) | • prescription statin drugs including: |
| • cyclosporine (for immune suppression) | simvastatin-Zocor [®] , pravastatin-Pravachol, |
| • protease inhibitors (for HIV/AIDS) | fluvastatin-Lescol, atorvastatin-Lipitor, |
| | cerivastatin-Baycol, or lovastatin-Mevacor [®] |

Potentially serious side effects may occur when MEVACOR CC is used with these drugs. Seek immediate medical attention if you get unexplained muscle pain, tenderness, or weakness. If you are not sure if your medicine contains one of these drugs, call your doctor, pharmacist or 1-800-MEVACOR.

Do not use MEVACOR CC unless directed by your doctor if you have a continuing medical condition including the following. You may need prescription strength cholesterol medicine or further medical care.

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| • total cholesterol above 240 mg/dL (you may be at a greater risk for heart attack) | • high blood pressure |
| • heart disease, such as having had a heart attack or angina | • diabetes |
| | • had a stroke |

Ask a doctor before use if you have 3 or more alcoholic drinks most days or had liver disease in the past.

Keep out of reach of children. This product should not be given to children.

In case of overdose, get medical help or contact a Poison Control Center right away.

Directions

- Take only one tablet with food every evening
- After about 8 weeks, you should have a cholesterol test
 - if your cholesterol goes down, continue using MEVACOR CC along with eating a low-fat diet and exercising, or your cholesterol may go back up
 - if your cholesterol does not go down, talk to your doctor
- You should tell your doctor that you are taking MEVACOR CC as part of a heart healthy program

Inactive ingredients: cellulose, lactose, magnesium stearate, red ferric oxide, starch. Butylated hydroxyanisole (BHA) is added as a preservative.

Questions? See inside package for additional information or call toll free 1-800-MEVACOR. If after buying this product you decide it is not right for you, return it for a full refund.