

**Dodge
Ball**

VIOXX[®]
(rofecoxib)

OBSTACLE

“I am concerned with the potential edema that occurs with Vioxx.”

**Dodge
Ball**

VIOXX[®]
(rofecoxib)

OBSTACLE

“I am concerned with dose-related
increases in hypertension
with Vioxx.”

MRK-ABR 0008120

**Dodge
Ball**

VIOXX[®]
(rofecoxib)

OBSTACLE 3

“Can Vioxx be used in patients
using low dose aspirin?”

Dodge

Ball

VIOXX[®]

(rofecoxib)

OBSTACLE

“I am concerned about the
cardiovascular effects of Vioxx?”

Dodge

Ball

VIOXX[®]

(rofecoxib)

OBSTACLE

“The competition has been in my office telling me that the incidence of heart attacks is greater with Vioxx than Celebrex.”

MRK-ABR 0008123

**Dodge
Ball**

VIOXX[®]
(rofecoxib)

OBSTACLE

“There is no difference between
Vioxx and Celebrex, why
should I use Vioxx?”

**Dodge
Ball**

VIOXX[®]
(rofecoxib)

OBSTACLE 7

“Vioxx cannot be used for longer than five days when treating patients for acute pain?”

**Dodge
Ball**

VIOXX[®]
(rofecoxib)

OBSTACLE 3

“I use Celebrex. I’m concerned
about the safety profile with Vioxx?”

**Dodge
Ball**

VIOXX[®]
(rofecoxib)

OBSTACLE

“I understand the new COXIB,
Mobic, was just approved.”

MRK-ABR 0008127

**Dodge
Ball**

VIOXX[®]
(rofecoxib)

OBSTACLE

“Searle/Pfizer just presented me with data which showed Celebrex 800 mg daily did not exhibit dose dependent increases in side effects compared to the OA and RA doses, and that Vioxx exhibited dose dependent increases in side effects with the 50 mg dose.”

MRK-ABR 0008128

**Dodge
Ball**

VIOXX[®]
(rofecoxib)

OBSTACLE 1

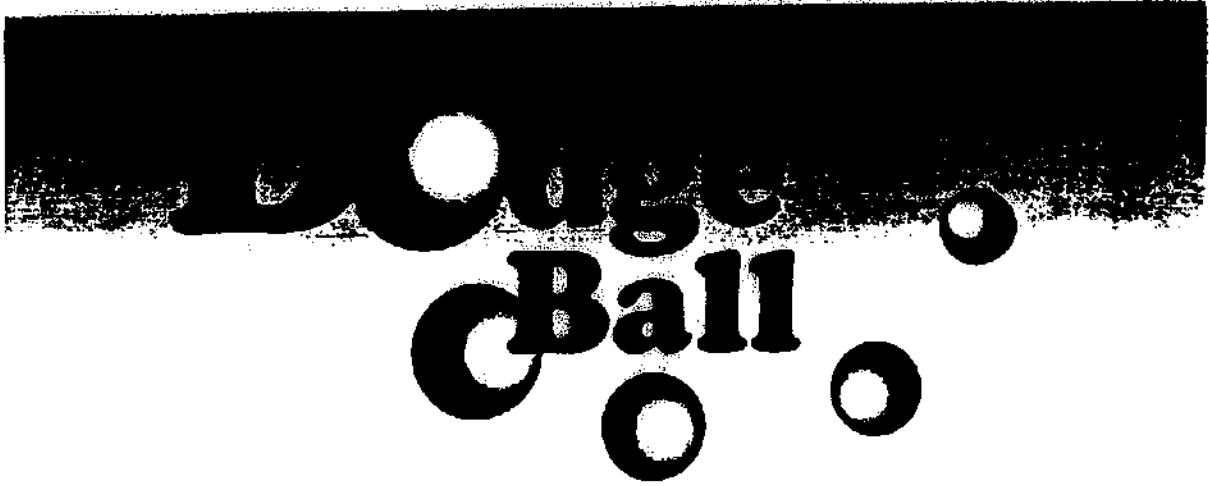
“The new narcotic data looks great,
now I’ll use Vioxx for all my acute
pain patients.”

**Dodge
Ball**

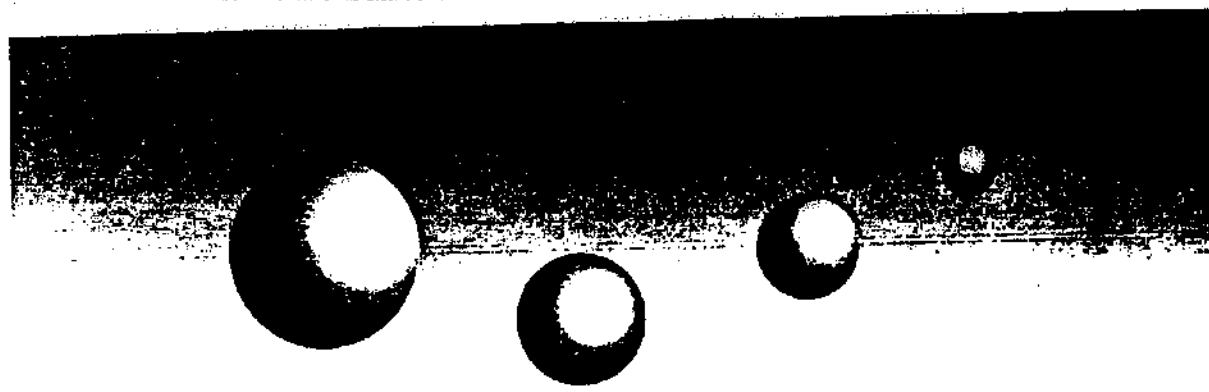
VIOXX[®]
(rofecoxib)

OBSTACLE 2

“I can't use Vioxx because the HMO's require the patients to be on generic NSAIDS first.”



VIOXX[®]
(rofecoxib)



DODGE!

Dodge

Ball

VIOXX[®]

(rofecoxib)

DODGE!

**Dodge
Ball**

VIOXX[®]
(rofecoxib)

DODGE!

MRK-ABR 0008133

Dodge

Ball

VIOXX[®]

(rofecoxib)

DODGE!

3T99 REFOCUS FOR VIOXX®

LEADER'S GUIDE FOR OBR REPRESENTATIVE MEETING

PRODUCT STRATEGY

Overtake Celebrex Through Clear Product Differentiation

CORE MESSAGES

Strength. Safety. QD Simplicity.

VERBATIM

Once daily power.

Copyright © 1999 by Merck & Co., Inc.

The intended users of this document are Business Managers and/or Lead Representatives as part of training and skill-development workshops.
This document contains proprietary information and trade secrets, and remains the property of Merck & Co.
Please shred before recycling.

LEH 0127226

3T99 REFOCUS WORKSHOP - VIOXX® OFFICE BASED REPRESENTATIVE LEADER'S GUIDE

GROUPS PARTICIPATING

- Office Based Sales Group

EQUIPMENT & RESOURCES NEEDED

- Overhead projector/proxima; flipchart
- 4 Physician profiles (Appendix)
- Message Grid (Appendix)
- 14 Questions To Ask Your Celebrex Representative (Appendix)
- Obstacle Response Guide for VIOXX®
- JeopardXX questions & answers (Appendix)

OVERVIEW

The primary purpose of this workshop is to give Office Based Representatives time to review and practice their understanding of VIOXX® and the top two competitors in their district, to identify the location of key messages in the package insert/detail aid for VIOXX® and the competitive package inserts, to practice obstacle handling, and to practice full product discussions. Representatives will be certified on how well they deliver product discussions using the detail piece, the package inserts for VIOXX® and competitors, and effective obstacle handling.

PLANNED OUTCOMES

At the completion of the workshop(s), participants will be able to do the following:

- Deliver differentiating and confident product discussions for VIOXX®, supported by the Top 5 Messages for VIOXX® and the detail aid for VIOXX®.
- Identify the segments within the detail aid for VIOXX®, package insert for VIOXX®, and competitive package inserts that support responses to obstacles and competitive challenges.
- Confidently handle obstacles for VIOXX® and transition back into a product discussion.

DISTRICT WORKSHOPS

Topic	Time	Method	Slide /Materials
Team Presentations - VIOXX® and Competitors	1 Hour	<ul style="list-style-type: none"> • Power Point presentations 	
Identification of Key Messages in Detail aid and Package Inserts	1 Hour 30 Minutes	<ul style="list-style-type: none"> • Group exercise 	
Discussion of Top Obstacles	30 Minutes	<ul style="list-style-type: none"> • Group exercise 	

3T99 REFOCUS WORKSHOP - VIOXX® OFFICE BASED REPRESENTATIVE LEADER'S GUIDE

	Obstacle JeopardXX	30 Minutes	<ul style="list-style-type: none"> • Team competition 	
	Progressive Discussion	1 Hour	<ul style="list-style-type: none"> • Role-play Activity 	
	Sales Discussion and Certification	30 Minutes	<ul style="list-style-type: none"> • Role-play Activity 	
	TOTAL TIME	5 Hours		

TE
TI
SENTATIONS - VIOXX® AND COMPETITORS

Material/Media	Instruction
Set-up	<ul style="list-style-type: none"> ■ Presentations by pre-selected teams on VIOXX® and top two competitors.
anned Outcomes	<ul style="list-style-type: none"> ■ This workshop will enable Representatives to understand the differences between VIOXX® and the top two competitors for the district. Representatives will give a ten minute overview of a pre-selected product that will focus on key areas of differentiation between that product and VIOXX®, leading representatives to conduct persuasive product discussions for VIOXX®. Teams will identify how to use the competitive package insert or the detail aid/package insert for VIOXX® to effectively sell VIOXX® against the competitor.
Workshop Kick-off by Trainer	<ul style="list-style-type: none"> ■ Begin the workshop by reviewing and reiterating the importance of two key elements: <ul style="list-style-type: none"> ✓ <i>Detail piece and Package Insert</i> ✓ <i>Top 5 Messages for VIOXX® (overhead)</i>
Instructions	<ul style="list-style-type: none"> ■ Instruct the representatives to move into their pre-assigned groups according to the product they were given (VIOXX® or a competitor).
Physician Profiles	<ul style="list-style-type: none"> ■ Ask for the groups with a competitive product to present first, leaving the group with VIOXX® to go last. <ul style="list-style-type: none"> ⇒ Explain to teams that their task is to present the attributes of the competitive product that are necessary to know to conduct effective product discussions of VIOXX®. ⇒ Note: the trainer and manager should monitor each presentation and add any missing points of differentiation. ⇒ Allow teams approximately 10 minutes to present their assigned product, then 10 minutes for a group discussion of their successful product discussions on territory.
	<ul style="list-style-type: none"> ■ Call time after 1 hour.
	<ul style="list-style-type: none"> ■ Comment on each presentation, pointing out key areas to leverage strengths and areas for improvement. Allow as much time for discussion and questions from other teams as practical.

LEH 0427228

3T99 REFOCUS WORKSHOP - VIOXX® OFFICE BASED REPRESENTATIVE LEADER'S GUIDE

At A Glance - Material/Media	Instruction
Transition	<ul style="list-style-type: none"> Transition to the next activity by saying that participants will have an opportunity to identify the key messages for VIOXX® within both the resources for VIOXX® and the competitive resources.
Learning Point	<p>Learning Point:</p> <p><i>Learning about your competitors will be invaluable in your success with VIOXX®.</i></p>

IDENTIFICATION OF KEY MESSAGES IN DETAIL AID AND PACKAGE INSERTS

Time: 1 hour, 30 Minutes

At A Glance - Material/Media	Instruction
Set-up	<ul style="list-style-type: none"> Ask all representatives to have their detail aid for VIOXX®, package insert for VIOXX®, and competitive package inserts ready. Look at the key messages of VIOXX®: <ul style="list-style-type: none"> Top 5 Messages for VIOXX® 3x3
Instructions	<ul style="list-style-type: none"> Explain that this workshop will deepen their understanding of what to reference in the detail aid for VIOXX®, package insert for VIOXX®, and the competitive package insert when conducting product discussions for VIOXX® in a competitive environment. Divide participants into 4 groups. Explain that each group represents a Key Messages team. Each team will have 30 minutes to identify the Top 5 Messages for VIOXX® and the 3x3 in whichever resource they are assigned. Divide the teams in the following way: <ul style="list-style-type: none"> detail aid for VIOXX® package insert for VIOXX® Celebrex package insert Other competitor package insert

3T99 REFOCUS WORKSHOP - VIOXX® OFFICE BASED REPRESENTATIVE LEADER'S GUIDE

At A Glance - Material/Media

Instruction

⇒ **Note:** The teams that are assigned the detail aid for VIOXX® and the package insert for VIOXX® should be able to complete the assignment as given. The team with that uses the competitive package inserts should identify areas within the package insert that are targeted by the Top 5 Messages for VIOXX® and the 3x3.

⇒ **Note:** Trainers should use the Message Grid (appendix) that is provided to check the responses for the detail aid for VIOXX®, package insert for VIOXX®, and the package insert for Celebrex. Trainers are responsible for completing this exercise for the other competitor.

- Call time after 30 minutes.
- Allow each group 15 minutes to present their findings and explain how they would use the resource within their product discussions for VIOXX®.
- Transition to the next activity by saying that participants will have an opportunity to discuss the current obstacles and the competition for VIOXX®.

Transition

Learning Point

Learning Point:
You can be very successful in a competitive selling environment if you understand all of the resources available to you.

DISCUSSION OF TOP OBSTACLES

Time: 30 Minutes

At A Glance - Material/Media

Set-up

Instructions

Instruction

- Ask the representatives to return to their original seats.
- Explain that now they will have the opportunity to discuss the obstacles for VIOXX® that they hear on territory.
- Ask the representatives to share the most common obstacles for VIOXX® they hear on territory.
- Flip their responses.

LEH 0127234

3T99 REFOCUS WORKSHOP – VIOXX® OFFICE BASED REPRESENTATIVE LEADER'S GUIDE



Transition

- Ask the representatives to rank the top five obstacles for VIOXX® from their original list.
 - Highlight or flip the top five most common obstacles for VIOXX®.
 - Review each obstacle for VIOXX® by asking the following questions:
 - How do you usually respond to this obstacle?
 - How do the physicians usually react to your response?
 - How are you successful when handling this obstacle?
 - Which resources do you use when handling this obstacle?
- ⇒ Note: verify that all obstacle responses match the responses found in the Obstacle Response Guide for VIOXX®.
- Take 5 minutes to discuss each obstacle (25 minutes total).
 - Transition to the next activity by saying that participants will have an opportunity to practice their obstacle handling responses in the following team activity.

Learning Point

Learning Point:

Effective obstacle handling will help representatives to confidently deliver product discussions for VIOXX®.

OBSTACLE JEOPARDXX

Time: 30 Minutes

At A Glance – Material/Media

Set-up

Planned Outcomes

Instruction

- Display JeopardXX game board slide on O/H. Trainer obtains JeopardXX hardcopy of Q&A in Appendix.
- Representatives will compete in 3 teams.
- This fun, interactive activity will help keep participants energized and maintain district momentum into the final workshop (*Sales Discussion & Certification*). Just as important, "Obstacle JeopardXX" reinforces Obstacle Handling knowledge that Representatives need to master

3T99 REFOCUS WORKSHOP - VIOXX® OFFICE BASED REPRESENTATIVE LEADER'S GUIDE

Instructions

Overhead Slide



regarding messages competitive products, and obstacle resolution.

- Divide participants into 3 groups.
- Explain that each group represents an Obstacle JeopardXX team. Each team's goal is to answer the most questions correctly and to score the most points.
 - ⇒ Note: It is suggested that each team rotate the individual answering for each new question. That way, everyone gets an opportunity to participate.
 - ⇒ Note: There should be a judge who specifically rules on which team raised their hand first to answer the question (it is difficult to read the question and monitor the hands at the same time).
- Display the Obstacle JeopardXX gameboard slide. Keep this slide visible for the duration of the activity, so the Representatives know which categories and point values are available.
 - ⇒ As each category/point value is selected, use a marker to X-out that box.
- Keep score on a flipchart page divided into 3 columns.
- Note: Use the "14 Questions To Ask Your Celebrex Representative" as an additional category during Obstacle Jeopardxx (found in the Appendix to this Leader's Guide). The first question can be phrased: "Recite one of the 14 Questions To Ask Your Celebrex Representative." Additional questions can be phrased: "Recite the Question To Ask Your Celebrex Representative that includes an FDA rejection." (Insert the topic of each question here).
- The game will end when all questions have been asked, or when you run out of time.

At A Glance - Material/Media

Transition

Learning Point

Instruction

- Note: Obstacle JeopardXX questions and answers can be found in the Appendix to this Leader's Guide.
- Transition to the next activity by saying that participants will have an opportunity to put all they have learned to use in an interactive skill practice session that follows.

Learning Point:

Consistent practice of obstacle handling and competitive issues will help

representatives to confidently deliver product discussions for VIOXX®

PROGRESSIVE DISCUSSION

Time: 1 hour

At A Glance - Material/Media

**Set-up
Instructions**

Instruction

- Divide into 2-3 groups.
- Explain that you and the business manager will play the role of physician, the physician will role-play with several different representatives to complete a sales discussion.
- Explain that you will throw a koosh ball to a representative, who must open the discussion, using appropriate materials and messages.
- Next, that representative throws the koosh ball to a different representative to deliver the next portion of the discussion.
- The koosh ball is thrown to a new representative for each discrete section of the discussion.

At A Glance - Material/Media

Instruction

- Explain that the koosh should be thrown back to the trainer (or physician) when appropriate within the product discussion (i.e., when questions are being asked, when representatives needs to check-in to make sure the physician is in agreement throughout the discussion, etc.).
- **Note to Facilitator:** This segment is meant to be fun and spontaneous. It should generate ideas that representatives can use when developing their sales discussions during the role-play/skill practice session.
- This is also an opportunity for the trainer or business manger to provide constructive feedback either after each participant response (toss of the koosh) or after the entire discussion is over. This feedback should direct them in their later role-play/skill practicing.
- Take each round of the koosh toss to the "close" or Call to Action.

LEH 0127234

3T99 REFOCUS WORKSHOP – VIOXX® OFFICE BASED REPRESENTATIVE LEADER'S GUIDE

<p>Transition</p>	<ul style="list-style-type: none">■ Note to Facilitator: There may be times when the trainer/business manager needs to stop the round and ask the group "where they are and what is needed next in the call".■ Optional: Trainer and business manager may choose to conduct a sample progressive discussion to provide participants with a model of "what good looks like".■ Several progressive discussions will be completed, each lasting approximately 10-15 minutes (including feedback to the group). This allows each representative several opportunities to practice their product discussion skills, and will allow you to observe each representative.■ Transition to the next activity by saying that participants will have an opportunity to put all they have learned to use in a role-play/skill practice session that follows.
<p>Learning Point</p>	<p>Learning Point:</p> <p><i>Constant practice of product discussions will help representatives to incorporate creative ideas and to prepare for their skill practice.</i></p>

SALES DISCUSSION AND CERTIFICATION

Time: 30 Minutes

At A Glance - Material/Media

Skill Practice Process

Two 15 minute Rounds:

- 3 minutes prep
- 5 minutes role-play
- 5 minutes feedback
- 2 minutes transition

Skill Practice Roles

Representative Role
Physician Profile to prep

Physician/Observer Role
Physician Profile to prep,
record observations

Instruction

- Explain that during this session, they will have an opportunity to practice formulating and delivering their product messages and using detail aids and/or package inserts.
- Ask participants to group into pairs.
- Explain that skill practice sessions will consist of two - 15 minute Rounds. Pre-Prepare flipchart showing break down of Rounds.
- Rounds consist of:
 - ⇒ 3 minutes prep
 - ⇒ 5 minutes role-play
 - ⇒ 5 minutes feedback
 - ⇒ 2 minutes transition
- Remind participants that they will be rotating in and out of two roles - representative and physician/observer. Pre-Prepare flipchart outlining each role.

3T99 REFOCUS WORKSHOP – VIOXX® OFFICE BASED REPRESENTATIVE LEADER'S GUIDE

At A Glance - Material/Media

Physician Profiles

<p>Feedback Process</p> <p>First – Representative Role</p> <p>Second – Physician/Observer Role</p>

Feedback Forms

Obstacle Handling Guide for VIOXX®



Instruction

- Explain that each role-play group will be given two **Physician Profiles**.
 - Explain that based on the direction and focus of the discussion, representatives should also incorporate an appropriate “close” or Call to Action in their discussion. Emphasize that feedback should be focused on all components of the Needs Based Selling process.
 - Explain that order for giving feedback is as follows: Representative first, physician/observer second. Pre-Prepare flipchart outlining feedback process.
-
- Ask pairs to begin *Round 1* of the skill practice.
 - Call time at each interval: prep, discussion, feedback, transition.
 - Call time at 15 minutes and ask pairs to transition to *Round 2* of skill practice.
 - **Note to Facilitator:** Trainer and manager should circulate and provide feedback to pairs. Reference the Obstacle Handling Guide for VIOXX® when giving feedback.
 - Ask how playing different roles helped them to see the sales discussion from a different perspective. Ask what lessons they learned through this experience.
 - **Note to facilitator:** Prepare a flipchart by placing a horizontal line at the top and a vertical line down the middle. On the left-hand column header write the word “Do’s”; on the right hand column header write “Don’ts”.
 - Ask representatives to share out the key learning points (do’s and don’ts) and insights that they gained by playing the roles of representative and physician/observer on a flipchart.
 - Thank representatives for their participation.

OBSTACLE JEOPARDXX

LEH 0127238

"I'm concerned about the potential edema that occurs with VIOXX"	"What hepatic effects can I expect with VIOXX?"	"I'm concerned about the CV effects of VIOXX"	"VIOXX cannot be used for longer than 5 days when treating patients for acute pain"	Overtake Celebrex	MYSTERY??
100	100	100	100	100	100
200	200	200	200	200	200
300	300	300	300	300	300
400	400	400	400	400	400
500	500	500	500	500	500

"I'm concerned about the potential edema that occurs with VIOXX."

Question:

- A) Provide a clarifying statement, and
- B) State two possible specific concerns a physician may have regarding edema.

Answer:

- A) Clarifying statement: What are your specific concerns regarding edema?
- B) Two possible specific concerns: 1) *overall* incidence of edema, 2) *dose related* increase of edema with once daily VIOXX® 50 mg.

- 100 -

"I'm concerned about the potential edema that occurs with VIOXX"

Question:

- A) What drug comparators are included in the AE Table
- B) State the overall incidence for VIOXX each comparator.

Answer:

- A) Ibuprofen, diclofenac, placebo
- B) VIOXX - 3.7%
 - Ibuprofen - 3.8%
 - Diclofenac - 3.4%
 - Placebo - 1.1%

- 200 -

"I'm concerned about the potential edema that occurs with VIOXX."

Question:

State the response if the physician is specifically concerned about the overall incidence of edema.

Response:

Doctor, edema is reported with all NSAIDs and is thought to result from cyclooxygenase inhibition in the kidney. Clinical trials with once daily VIOXX® 12.5 and 25 mg have shown renal effects such as edema similar to those observed with comparator NSAIDs. In these studies, the incidence rates for lower extremity edema were as follows: (in the AE table, point to row on edema under Body As A Whole)

- VIOXX® 12.5 mg or 25 mg once daily - 3.7%
- Ibuprofen 2400 mg - 3.8%
- Diclofenac 150 mg - 3.4%
- Placebo - 1.1%

- 300 -

"I'm concerned about the potential edema that occurs with VIOXX."

Question:

State the response if the physician is concerned about a dose related increase in edema with once daily VIOXX 50 mg.

Response:

Doctor, edema is reported with all NSAIDs and is thought to result from cyclooxygenase inhibition in the kidney.

Regarding the safety of once daily VIOXX® 50 mg, let me explain where the use of 50 mg is recommended. 50 mg is recommended for use in acute pain in adults and is not recommended for OA. In the analgesia studies, the renal effects of once daily VIOXX® - such as edema-were generally similar to comparator NSAIDs.

The 50 mg dose, while not recommended for OA, has been studied in clinical trials for up to 6 months. In these trials, the incidence of lower extremity edema was 6.3% for 50 mg. In the 6-week to 6-month studies with 12.5 or 25 mg, the incidence of lower extremity edema was 3.7%. Are you concerned about a 3.7% incidence rate of lower extremity edema in your OA patients?

- 400 -

Wild Card

Question:

What were the three endpoints once daily VIOXX demonstrated comparable efficacy to ibuprofen 2400 mg in a 6-week OA study?

Answer:

Primary - Pain on walking
Secondary - Physical function
Tertiary - Joint Tenderness

- 500 -

"What hepatic effects can I expect with VIOXX?"

Question:

- A) Provide a clarifying statement, and
- B) State two possible specific concerns a physician may have regarding hepatic effects.

Answer:

- A) Clarifying statement: What specific hepatic effects are you concerned about?
- B) Two possible specific concerns: 1) increase in liver function testing (LFTs), 2) metabolism of once daily VIOXX® 50 mg.

- 100 -

Wild Card

Question:

Enzyme *induction* can lead to an _____ (increased/decreased) rate of drug metabolism and corresponding _____ (increases/decreases) in the availability of the parent drug.

Answer:

increased, decreases

- 200 -

"What hepatic effects can I expect with VIOXX?"

Question:

In placebo-controlled trials, what percentage of patients taking once daily VIOXX 12.5 or 25 mg had notable elevations of ALT or AST?

Response:

Once daily VIOXX - approximately 0.5%
Placebo - 0.1%

- 300 -

"What hepatic effects can I expect with VIOXX?"

Question:

If the physician is concerned about the potential increase in liver function tests, how would you respond?

Response:

In controlled clinical trials of VIOXX, the incidence of borderline elevations of liver tests at doses of 12.5 and 25 mg daily was comparable to the incidence observed with ibuprofen and lower than that observed with diclofenac. In placebo-controlled trials, approximately 0.5% of patients taking once daily VIOXX 12.5 or 25 mg and 0.1% of patients taking placebo had notable elevations of ALT or AST. A patient who has an abnormal liver test while on once daily VIOXX should be monitored carefully for evidence of a more severe hepatic reaction.

Use of VIOXX is not recommended in patients with moderate or severe hepatic insufficiency.

- 400 -

"What hepatic effects can I expect with VIOXX?"

Question:

If the physician is concerned about the metabolism of once daily VIOXX, how would you respond?

Response:

Doctor, metabolism of once daily VIOXX is primarily mediated through reduction by cystolic enzymes in the liver. It is not primarily metabolized by the P450 system and is not known to inhibit the P450 system in the liver.

- 500 -

"I am concerned about the cardiovascular effects of VIOXX."

Question:

Provide a clarifying statement to uncover the physician's true obstacle.

Answer:

What is your specific concern?

- 100 -

"I am concerned about the cardiovascular effects of VIOXX."

Question:

State two possible specific concerns a physician may have regarding the potential CV effects of once daily VIOXX.

Answer:

- (1) "I am hesitant to use VIOXX in my patients because it may worsen CHF"
- (2) "VIOXX has the potential to increase the risk of MI"

- 200 -

Wild Card

Question:

The general safety profile of once daily VIOXX 50 mg q.d. in OA clinical trials of up to six months was similar to that with the recommended OA doses, except for a higher incidence of _____, _____, and _____.

Answer:

GI symptoms, lower extremity edema(6.3%), and hypertension (8.2)

- 300 -

"I am concerned about the cardiovascular effects of VIOXX."

Question:

If the physician is concerned that once daily VIOXX® may worsen CHF, how would you respond?

Response:

Doctor, as you know, there are precautions you should take when prescribing any NSAID for your patients with CHF. Because once daily VIOXX is an NSAID, you should consider taking these same precautions when considering the use of once daily VIOXX® for this specific patient population.

Clinical trials with once daily VIOXX® 12.5 mg and 25 mg have shown renal effects such as hypertension and lower extremity edema similar to those observed with comparator NSAIDs. VIOXX® should be used with caution and should be introduced at the lowest recommended dose in patients with fluid retention, hypertension, or edema.

- 400 -

"I am concerned about the cardiovascular effects of VIOXX."

Question:

If the physician is concerned about a potential increase in the risk of MI, how would you respond?

Response:

Doctor, once daily VIOXX has no effect on platelet aggregation. Once daily VIOXX® is therefore is not a substitute for aspirin for cardiovascular prophylaxis. However, once daily VIOXX 50 mg had no effect on the anti-platelet activity of low dose (81 mg daily) aspirin.

- 500 -

"VIOXX cannot be used for longer than five days when treating patients for acute pain"

Question:

According to the PI for VIOXX, what is the appropriate dosing for the management of acute pain?

Response:

The recommended initial dose of VIOXX is 50 mg once daily. Subsequent doses should be 50 mg once daily as needed. Use of VIOXX for more than 5 days in management of pain has not been studied.

- 100 -

Wild Card

Question:

In the postorthopedic surgical pain study, patients on once daily VIOXX consumed a significantly smaller amount of additional _____ medicine than patients treated with placebo during the entire five-day study.

Answer:

analgesic

- 200 -

**"VIOXX cannot be used for longer than five days
when treating patients for acute pain"**

Question:

Explain the rationale for the 5 day duration of the pain studies for VIOXX.

Response:

To obtain an indication for the management of acute pain in adults, all analgesic drugs are studied in short-term standard pain models as defined by the FDA. The maximum duration of these studies for once daily VIOXX® was 5 days.

- 300 -

Overtake Celebrex

Overtake Celebrex

Question:

Name two questions for the doctor to ask his/her
Celebrex Representative.

Answer:

Refer to list.

- 200 -

Overtake Celebrex

Overtake Celebrex

Question:

Name the Science Messages for VIOXX.

Answer:

- VIOXX has demonstrated no effect on platelet aggregation or bleeding time; no effect on bleeding time even at doses of up to 375 mg.
- VIOXX has an effective half-life of 17 hours
- VIOXX is not contraindicated in patients with sulfonamide allergies. Celebrex is contraindicated in patients with sulfonamide allergies.
- VIOXX is not primarily metabolized via the cytochrome P450 system and there are no special considerations for patients who are cytochrome P450 2C9

- 400 -

Overtake Celebrex

Mystery ?

Question:

When should physicians prescribe VIOXX® 12.5 mg, 25 mg, and 50 mg?

Response:

Whether you're treating OA or acute pain, once daily VIOXX® is always a simple once daily dose.

12.5 mg or 25 mg once daily for OA

Once daily VIOXX® 12.5mg is the starting dose for OA. If a patient requires greater pain relief, you have the flexibility to increase the dose to 25mg once daily at no additional cost to the patient.

50 mg once daily for Acute Pain and Primary Dysmenorrhea

In patients with moderate to severe acute pain, the dose is 50mg once daily. Once daily VIOXX® relieved moderate to severe pain following orthopedic surgery, dental surgery and primary dysmenorrhea.

(Appropriate balance: The use of Vioxx for more than 5 days for the management of pain has not been studied.)

Mystery ?

Mystery ?

Question: T/F

Like Celebrex, VIOXX is contraindicated for patients allergic to sulfonamides.

Answer: FALSE!

Once daily VIOXX is not contraindicated for patients with known sulfonamide allergies, commonly known as "sulfa allergies."

Unlike Vioxx, Celebrex contains a sulfonamide group (S-NH₂) which is associated with sulfonamide allergies. This contraindication is based on the specific chemical structure of Celebrex and is not a class effect.

- 300 -

Mystery ?

Question:

Mystery ?

Question:

Discuss the terms "selective" and "specific."

Answer:

The relationship between the desired and the undesired effects of a drug is termed its *selectivity*. Expressed in another way, *selectivity* is defined as the "ability of a drug to discriminate between specific targets." Thus a truly selective drug will interact with only one specific target irrespective of the dose of drug used. If this criterion is satisfied absolutely, that drug can be referred to as being *specific*.

- 500 -

Top 5 Messages for VIOXX

Messages to deliver in the context of balanced product discussions.

*Messages 1 and 2 should be delivered in reverse order for orthopedic surgeons.

1 VIOXX demonstrated ONCE-DAILY POWER in chronic osteoarthritis (OA) pain.

Supported by:

- Powerful pain relief all day and all night and into the next morning
- Power in one small tablet once daily comparable to ibuprofen dosed three times a day
- Powerful relief of chronic OA pain demonstrated over one year (52-week data)

This document must not be copied, distributed, or shown to anyone outside the company.

2 VIOXX demonstrated FAST ONSET of pain relief; VIOXX consistently demonstrated POWERFUL RELIEF across ALL moderate-to-severe acute-pain models studied.

This document must not be copied, distributed, or shown to anyone outside the company.

3 VIOXX demonstrated significantly fewer endoscopic ulcers than ibuprofen, and was consistent across all studies.

This document must not be copied, distributed, or shown to anyone outside the company.

4 Safety profile of VIOXX demonstrated in patients 80 years or older.

This document must not be copied, distributed, or shown to anyone outside the company.

5 VIOXX is **NOT** contraindicated in patients with sulfonamide allergies.

ONCE-DAILY POWER... One tablet, once a day, in all indications

These statements can be used by professional representatives in discussions with physicians.

This document must not be copied, distributed, or shown to anyone outside the company.

Be sure to provide appropriate balancing information as part of all product discussions.

ONCE DAILY
VIOXX
(rofecoxib)

REPRINT REVIEW

MESSAGES SUPPORTED

TYPE	TOPIC	AUTHOR/TITLE	OAH#	Strength	Safety	QD Simplicity	Science
Primary ¹	GI Safety	Laine. A Randomized Trial Comparing the Effect of Rofecoxib, a Cyclooxygenase 2-Specific Inhibitor, With That of Ibuprofen on the Gastroduodenal Mucosa of Patients With Osteoarthritis	2604(1)		X		
Obstacle Handling ²	Celebrex Renal Paper	Rosat. Renal Effects of Selective Cyclooxygenase-2 Inhibition in Normotensive Salt-Depleted Subjects	2605(1)				X
Supporting Clinical ³	Dental Pain	Morrison. Analgesic Efficacy of the Cyclooxygenase-2-Specific Inhibitor Rofecoxib in Post-Dental Surgery Pain: A Randomized, Controlled Trial	2602(1)	X		X	
	Primary Dysmenorrhea	Morrison. Rofecoxib, a Specific Cyclooxygenase-2 Inhibitor, in Primary Dysmenorrhea: A Randomized Controlled Trial	2603(1)	X		X	

1. Primary reprints should be used proactively during in-depth discussions with healthcare professionals.
2. Obstacle-handling reprints should only be used to address obstacles that arise during discussions.
3. Supporting clinical reprints should only be used when a healthcare professional requests additional clinical information.

ONCE DAILY
VIOXX
 (rofecoxib)

1T 2000 Top 5 Messages for VIOXX®

**Messages to deliver in the context of balanced product discussions.
(*Messages #1 and #2 should be delivered in reverse order for Orthopedic Surgeons)**

1. ***VIOXX demonstrated ONCE DAILY POWER in chronic osteoarthritis pain.
Supported by:**
 - **Powerful pain relief all day and all night and into the next morning**
 - **Power in one small tablet once daily comparable to ibuprofen dosed three times a day**
 - **Powerful relief of chronic OA pain demonstrated over one year (52 week data)**
2. ***VIOXX demonstrated FAST ONSET of pain relief; VIOXX consistently demonstrated POWERFUL RELIEF across ALL moderate- to- severe acute pain models studied.**
3. **VIOXX demonstrated significantly fewer endoscopic ulcers than ibuprofen, and was consistent across all studies.**
4. **Safety profile of VIOXX demonstrated in patients 80 years or older**
5. **VIOXX is NOT contraindicated in patients with sulfonamide allergies**

ONCE DAILY POWER... One tablet, once a day, in all indications

**These statements can be used by professional representatives in discussions with physicians.
This document must not be copied, distributed, or shown to anyone outside the company.
Be sure to provide appropriate balancing information as part of all product discussions.**