Unknown

From: Cummins, Bruce [JAN]
Sent: Monday, September 13, 1999 4:57 AM
To: Grant, Martine [HCS]
Cc: Butler, Dave [JAN]; Jones, Colleen [JAN]
Subject: Omnicare Rebates

Martine,

I am sending you all of the copies of information that I received from Omnicare last week in association with the ongoing rebate dilemma. There have been a couple of new twists added.

*The amount of $702,761.30 that was brought to our attention Omnicare for purchases made outside of the JJHCS contract was incorrect. This amount was actually the amount of the 1% overlay for 1998-1999. The $300,000 educational funding amount was generated for the 1% overlay from 1997-1998, which Omnicare figured to be $339,852.00. These amounts were generated based on an oral agreement between Denny Sherrill and Dan Maloney, in essence because, Omnicare's contract was missing the page that described performance tiers needed to qualify for rebates.

*The amount requested by Omnicare for rebates lost from ordering outside the contract were as follows and will be included in my mailings to you. (Please refer this information to Bonnie Stocker and Sue Griffin).

Rebates Lost

3rd Quarter 1997	$ 75,106.11
4th Quarter 1997	$ 23,111.57
1st Quarter 1998	$ 23,343.77
2nd Quarter 1998	$103,114.93
3rd Quarter 1998	$ 86,613.10
4th Quarter 1998	$ 49,329.01
Total	$360,618.49

Unknown

From: Cummins, Bruce [JAN]
Sent: Tuesday, September 28, 1999 3:44 PM
To: Butler, Dave [JAN]
Cc: Jones, Colleen [JAN]; Grant, Martine [HCS]
Subject: $300,000 Contractual Agreement

Dave,

September 28.doc
(23 KB)

Here is a copy of the letter I have sent to Mark Lehman requesting his signature for the completion of the Omnicare Initiative. Once I have recieved it, I will authorized HCS to send out a payment of $300,000.

Bruce

September 28, 1999

Mark Lehman
Director of Clinical Services-
Omnicare, Inc.
100 East Rivercenter Blvd.
Suite 1500
Covington, Ky. 41011

Dear Mark,

Enclosed are two contractual agreements for the $300,000 program in helping Omnicare's consultant pharmacists overcome objections from physicians. This program will be especially effective in overcoming obstacles pertaining to resistance in prescribing Risperdal. Once the agreement has been signed, please return it to me. I will then instruct JJHCS to cut a check for $300,000 to Omnicare, Inc.

Regards,

Bruce Cummins

cc: Dave Butler
Colleen Jones
Martine Grant

LONG-TERM CARE GROUP

JANSSEN PHARMACEUTICA · RESEARCH FOUNDATION · ◆ ORTHO BIOTECH ORTHO-McNEIL

RETURN TO TB'S DESK 11/15/99

October 25, 1999

Tim Bien, R.Ph. FASCP
Senior Vice President –
Professional Services & Purchasing
Omnicare, Inc.
100 East RiverCenter Blvd.
Suite 1500
Covington. Ky. 41011

Dear Tim,

Enclosed is the Initiative Partnership Agreement between Omnicare and Johnson & Johnson Health Care Systems Inc. This agreement calls for educational assistance in overcoming objections and obstacles pertaining to the Risperdal Initiative. A funding check of $300,000 will be forthcoming.

We are also very close in completing the analysis on Omnicare purchases made outside of the Johnson & Johnson Health Care Systems contract. I feel strongly that this issue will be completed by the end of October so that all of my attention can be placed on concluding the issues surrounding the 1% overlay during 1998-1999.

The Procrit Meeting at Ortho-Biotech was extremely successful. I am in the process of coordinating the following follow-up steps:

- Coordination of clinical information (studies, etc.) as well as reimbursement protocols for each state to be sent to Nora Flint.
- Meeting with Gary Erwin and Nora Flint, as well as OBI clinical department – Mitch Slavin and Loretta Itri focusing on a similar presentation that you gave on October 7th to insure "buy-in" from OBI clinical department. (The original date of October 25th has had to be revised, possibly to November 5th because of scheduling conflicts).
- Coordination of funding the "Pilot Program" of $200,000 through Lorraine Sulick-Morecraft at OBI to W. Gary Erwin at Omnicare.
- Introduction of either Tom Hiriack or Craig Phillips at OBI (bringing them up to date) to facilitate issues from an OBI perspective.

I also talked with Dan Maloney and Mark Lehman pertaining to both Levaquin and Risperdal market shares throughout the third quarter. I would like to stress the importance of sharing this regional site information with our Long Term Care group. By doing this we can emulate those manager's resources that are being placed in high share areas as well as looking to provide additional resources for those areas that are not meeting share goals. Mark wanted to talk with you about this issue before sending me any information. I believe our relationship has gone toward a "mutually beneficial" arrangement and I guarantee that any information we would receive in this area would be held in highest confidence.

Regards,

Bruce Cummins

Bruce Cummins

cc: D. Butler
T. Lerman
C. Jones

OMNI-MA 033998

INITIATIVE PARTNERSHIP

Agreement Between

Omnicare, Inc.

100 East River Center Blvd.,

Covington, KY 41011

Attn: Mark Lehman

Director of Clinical Services

REDACTED

Referred to as: "Omnicare"

AND

Johnson & Johnson Health Care Systems Inc.

425 Hoes Lane

P.O. Box 6800

Piscataway, New Jersey 08855-6800

Attn: Contract Administration

REDACTED

Referred to as "J&JHCS"

Agreement period 10/1/99 - 9/31/00

JOHNSON & JOHNSON HEALTHCARE SYSTEMS INC.

Bruce Cummins

Name: Bruce Cummins

Title: LTC Account Director

Date: 10/13/99

Name: Martine T. Grant

Title: Manager, Business Analysis

Date: 10-15-99

OMNICARE, INC.

Mark Lehman

Name: Mark Lehman

Title: Director, Clinical Services

Date: October 13, 1999

OMNI-MA 033999

INTRODUCTION

Agreement. Under this Agreement, J&JHCS will provide financial assistance to partially defray the cost to Omnicare in developing and marketing mutually acceptable broad-based formulary intervention initiatives, and to assist Omnicare consultant pharmacists overcome obstacles and objections they encounter in implementing intervention programs.

Parties.

J&JHCS. is a New Jersey corporation and a wholly owned subsidiary of Johnson & Johnson, a New Jersey corporation. It is Supplier's mission to provide Manager with one interface to high quality Johnson & Johnson products and health management programs as well as other products and programs from selected partners. Supplier coordinates the consumer, diagnostic, medical & surgical, and pharmaceutical expertise of Johnson & Johnson's affiliates to emphasize wellness, provide early diagnosis, deliver cost-effective treatment and encourage health maintenance. Supplier is responsible to Manager for compliance with all the provisions of this Agreement and will cause its affiliates to cooperate with Manager in that endeavor.

Omnicare. is a Delaware corporation and an independent provider of professional pharmacy and related services for long term care institutions such as nursing homes, retirement centers, home healthcare and other institutional healthcare facilities.

AGREEMENT PROVISIONS

J&JHCS shall pay Omnicare a "Program Fee" to partially defray the cost of developing, implementing and operating "Initiatives" as described herein.

1. Payment Terms:

a) J&JHCS shall pay the Program Fee of $300,000 on October 1, 1999 by check or electronic wire transfer.

b) If this Agreement is terminated or expires prior to completion of the Initiatives, Omnicare shall refund the full amount to J&JHCS minus the fair market value for Initiatives actually completed by Omnicare as documented pursuant to Section 3.

c) Omnicare acknowledges that the Program Fee is not be tied to or conditioned on favorable formulary positioning or purchasing commitments is not tied to volume or value of utilization of J&JHCS' products or services.

2. Initiatives: The Program Fee may be used to fund or partially fund any or all of the mutually acceptable initiatives below. The amount of the Program Fee apportioned to any Initiative may not exceed the fair market value of the service provided to J&JHCS for that Initiative.

a) **Training Services** –Providing training to health care professionals concerning the appropriate, FDA-approved use of J&JHCS' products.

- Training sessions may be held at J&JHCS' facilities or independent teaching centers.

b) **Development of educational materials or disease management programs** – Developing educational materials of disease management programs for J&JHCS' in clinical areas of interest to J&JHCS.

- J&JHCS will obtain licenses or other rights to use materials or programs developed.

c) **Product Intervention and Communication Programs** - Omnicare will provide information about J&JHCS' product to physicians or to patients having certain conditions . Such arrangements must meet the following conditions:

- J&JHCS may not obtain confidential patient-identifiable medication information from Omnicare
- Information may only be provided with respect to J&JHCS' products that are clinically appropriate competing products or alternative therapies.
- Payment for communications by Omnicare must be made on an aggregate flat fee or "per letter basis" that is consistent with fair market value
- The specific content of communications must be reviewed and approved by J&JHCS to ensure compliance with FDA advertising standards.
- No payment may be made for services that a pharmacist or other health care professional is already required to provide to patients as part of professional dispensing practices.

- Communications to patients must disclose J&JHCS' sponsorship of the program but J&JHCS will not receive any confidential patient information
- Communications must offer the patient the alternative not to receive similar communications in the future and how to do so.

d) **Development and Dissemination of Patient / Provider Educational Materials** – Omnicare will develop or disseminate educational materials to physicians or patients (e.g., information on disease states or clinical treatment protocols) upon approval of such programs by J&JHCS.

- J&JHCS may not provide grants where Omnicare is already required to, or ordinarily undertakes to, provide such educational materials as part of its business
- J&JHCS may not provide funding for activities that are more in the nature of advertising

3. **Progress Review:** Omnicare shall prepare and submit a report to J&JHCS outlining Omnicare's activities pursuant to this Agreement after six months and again at the expiration of this Agreement. The parties shall meet to review Omnicare's report including activities performed to determine progress made towards attaining the Initiatives. At the six month review, either party may suggest modifications to this Agreement.

GENERAL TERMS AND CONDITIONS

1. ***Subordination.*** In case of an inconsistency between any provision of these General Terms and Conditions and any other provision of this Agreement, such other provision shall govern.

2. ***Notices.*** Any notice given in connection with this Agreement shall be sufficient if in writing and delivered by messenger or sent by postage prepaid mail or by facsimile to the address of the recipient as set forth on the cover page to this Agreement or as changed by the recipient by notice given hereunder. Notices or communications shall be effective when received by or otherwise known to the recipient or its legal representative. This provision is not intended to be exclusive, and any notice actually received shall be sufficient.

3. ***Entire Agreement.*** This Agreement constitutes the entire agreement between the parties concerning the Products and subject matter hereof and supersedes all prior negotiations, agreements and understandings between the parties, whether oral or in writing, concerning the Products and subject matter hereof. This Agreement may be modified only in writing signed by the party against whom such modification is asserted provided that the terms of any purchase order, invoice or similar document used to implement this Agreement shall not modify and shall be subject to this Agreement.

4. ***Assignment.*** Neither party may assign this Agreement or any of its rights or obligations hereunder without the prior written consent of the other party. For purposes of this paragraph assignment shall include any assignment by operation of law and any change in control of a party.

5. ***Independent Contractors.*** The parties hereto are independent contractors engaged in the operation of their own respective businesses. Nothing herein shall be deemed or construed to create any other relationship between the parties.

6. ***Publicity.*** Neither party shall permit or generate any publicity, advertising or promotion concerning this Agreement without the prior written consent of the other party.

7. ***Confidentiality.*** Neither party shall use information contained in this Agreement for any purpose not contemplated by this Agreement, and each party shall restrict access to this Agreement to personnel within its organization who need such access in order to perform duties related to the implementation of this Agreement or as required by law.

8. ***Term.*** The term of this Agreement is set forth on the cover page hereof. Either party may terminate this Agreement earlier by giving 30 days' notice to the other party pursuant to the provisions of Paragraph 1.b. of the Agreement Terms. The provisions of these General Terms and Conditions shall survive termination of this Agreement.

9. ***Audit.*** J&JHCS shall have the right to audit all records of Omnicare relating to Omnicare's performance of services pursuant to this Agreement.

10. ***Legal Changes.*** If any governmental entity shall enact or amend a law or adopt or amend a regulation, or if any governmental entity or court of competent jurisdiction shall adopt or amend an interpretation of a law or regulation, or if a judgment/award is rendered in litigation/arbitration, that has the effect of (a)

prohibiting any right or obligation of a party under this Agreement, (b) making any such right materially less valuable or any such obligation materially more burdensome to a party, or (c) changing materially the economic conditions underlying any portion of this agreement, then such party may upon notice to the other party terminate immediately such right or obligation or portion of the agreement insofar as such law, regulation or interpretation judgment or award applies.

11. ***Force Majeure.*** Noncompliance with any obligation under this Agreement for reasons of force majeure (such as: acts, regulations or laws of any government; war or civil commotion; destruction of production facilities or materials; fire, earthquake or storm; labor disturbances; failure of public utilities or common carriers; and any other causes beyond the reasonable control of the party affected) shall not constitute a breach of this Agreement.

12. ***Dispute Resolution.*** Any controversy or claim arising out of or relating to this Agreement, or the breach thereof, shall be settled by arbitration in accordance with the Commercial Arbitration Rules of the American Arbitration Association, and judgment upon the award rendered by the arbitrator may be entered in any court having jurisdiction thereof. The arbitration shall be held in New Jersey and the arbitrator shall apply the substantive law of New Jersey, except that the interpretation and enforcement of this arbitration provision shall be governed by the Federal Arbitration Act. The arbitrator shall not award any party punitive or consequential damages, and each party hereby irrevocably waives any right to seek such damages in arbitration or in judicial proceedings.

13. ***Execution***. This Agreement will not be considered valid until all required signatures as indicated on the Cover Page have been affixed.

OMNI-MA 034004

MEMORANDUM

re-sent to JFG 4/25/01

To: Joel

From: Tim

Date: April 3, 2001

Re: Re•View Grant Money

As you are aware, in 2000 I raised almost $1,000,000 from the drug industry for the purpose of getting results with our "one extra script per patient (Re•View) program".

If there was a bonafide expense associated with Re•View, I asked Tom Marsh to expense from the Re•View grant money and not my department budget. I was very frugal in using this pool of money as we still have a balance of over $925,000! Every payment I authorized was for something we were going to do anyway, or had your explicit approval.

This year I am requesting even more money for the same purpose, and I believe we will get about $1.1 million in additional funds. This will give us a "war chest" of over $2,000,000 to advance our Re•View program.

Tom Marsh recently informed me that I am not authorized to expense ANY money from the Re•View Grant money.

Joel, please give me advice on how to get the results you want. Some pharmacies need training, some may need other forms of help to accomplish our goal.

Is it possible for me to have some pre-approved amount, that you authorize, so I can stimulate some positive results on Re•View?

6/23/00 12:07 PM

DRAFT 6/23/00
OMNICARE MEMORANDUM
Professional Services

DATE: **June 26, 2000**

TO: **Regional Vice Presidents**
Omnicare Operations Managers (copy and distribute to all Omnicare pharmacists)
Regional Clinical Directors

FROM: **Mark E. Lehman, Pharm.D. FASCP**
Director, Clinical Services

RE: **Definition of Clinical Priorities/Initiatives**

CC: **Patrick E. Keefe, R.Ph.**
Timothy E. Bien, R.Ph., FASCP
Lisa R. Welford, R.Ph., FASCP

As we approach the end of the second quarter of 2000, I feel it is appropriate to provide a treetops view of our clinical priorities from an Omnicare corporate perspective as you direct the activities of your professional staff.

1. **Formulary Management Programs (goal%):** a continued emphasis on formulary management and the PSTI process, including histamine-2 antagonists (95%), Risperdal® (65%), Zestril® (70%), Prevacid® (95%), Levaquin® (70%), KCl (75%) and the addition of Celebrex® (75%) as the "selected" COX-2 inhibitor.
   As operations managers, you must make sure that the physician authorization letter (PAL) process is strictly enforced in all pharmacies, and that a zero-tolerance mentality be implemented for letting eligible prescriptions slip through due to staffing concerns or other confounding variables. Our lack of rapid progress with the Lipitor® program and a slippage in our Levaquin® market share may be the beginning signs of problems with the prospective intervention processes we worked so hard to develop and implement. This cannot be allowed to happen.

2. **Re*View Health Management:** Omnicare's program to address under recognition, under diagnosis and under treatment of conditions common in the elderly, including:

- Heart Failure - ACE inhibitors and spironolactone
- Osteoporosis - PIXI® testing and adding appropriate therapies such as Vitamin D/calcium, Fosamax®, Actonel®, Miacalcin®, Evista® or estrogen therapy
- Depression - under recognition of depression and changing potentially inappropriate treatment, moving from older TCA's (amitriptyline, imipramine, trazodone and doxepin) to the SSRI's
- Immunization - for influenza and pneumococcus
- Pain Management - including moving from "unacceptable" analgesics such as propoxyphene to more appropriate, effective alternatives, while assessing the overall analgesic therapy
- Behavior Management in Dementia - encompassing the appropriate use of antipsychotics and going from the typical to the newer and better tolerated atypical antipsychotics; also focuses on the treatment of aggression and the use of Depakote®
- Urinary Health Management - focusing on recognition and treatment of urinary incontinence
- Dementia/Early Alzheimer's disease - a program in development, highlighting the prevalence of undiagnosed or unrecognized cognitive impairment, and highlighting early treatment.

3. Moving "unacceptable" and Beers' criteria medications to more appropriate alternatives, and moving from high-risk medications to safer, equally effective alternatives. Examples include:
   - Propoxyphene to acetaminophen, Ultram® or a COX-2 inhibitor
   - Traditional NSAID's to COX-2 inhibitors in residents at risk for NSAID gastropathy or with a GI history (ibuprofen, naproxen, diclofenac, etc. to Celebrex®)
   - Typical antipsychotics to atypicals (thioridazine, chlorpromazine, haloperidol to Risperdal®)
   - Sucralfate tablets and liquid to Prevacid® as the preferred medication for both PUD and GERD
   - Clonidine, terazosin, doxazosin and methyldopa (central and peripheral alpha-blockers) to better tolerated antihypertensive therapy in the elderly such as Zestril®
   - Inappropriate sleep medication to better, safer alternatives, such as flurazepam and estazolam to Ambien® or temazepam

6/23/00 10:08 AM

This is far from a comprehensive list, just a few examples to help you focus on the most important tasks at hand, namely to be responsible for managing the drug therapy of the residents we serve. If we are unable to comprehensively and consistently impact the prescribing habits of the physicians we work with, we have failed in our attempts to be both resident advocates and a clinical company.

This effort requires close cooperation and communication between the operations managers and staff, and the clinical coordinators and their staff. I urge you to continue to strive to be the best clinical force in the long-term care industry. We cannot afford to rest on our laurels.

As always, I greatly appreciate your dedication, efforts and support and welcome any and all questions or comments. Thank you.

Timothy E. Bien

Omnicare

Re•View

Another look. A new focus.

January 6, 2000

Johnson & Johnson Long Term Care Group
Mr. Bruce Cummins
Account Director

REDACTED

Dear Bruce:

Omnicare is requesting your support as we develop and launch a new health management (formerly disease management) program, called "Re*View: Another look. A new focus", that will positively impact the geriatric population we serve. Omnicare's philosophy and culture center on enhancing the quality of life for our residents by assuring they receive appropriate drug therapy. The medical literature is full of citations indicating the under-diagnosis and under-treatment of disease in the geriatric population. "Re*View" involves identifying these under-treated or inappropriately treated conditions common in the elderly, and instituting the appropriate therapy through direct interventions with prescribers.

A couple of programs either being implemented or planned deal directly with behavior management/agression and early identification of Alzheimer's disease.

Omnicare is requesting an educational grant in the amount of $50,000 to support the development and implementation of these initiatives, and others as we look at undertreatment and inappropriate treatment. Our tax identification number is REDACTEDThe check should be made out to Omnicare and can be forwarded to my attention. Thank you, in advance, for your consideration and ongoing support of Omnicare's mission as a geriatric pharmaceutical care company. If you have additional questions, please feel free to contact me at

REDACTED

Sincerely,

Timothy E. Bien, R.Ph. FASCP
Senior Vice-President, Professional Services
Omnicare Inc.

OMNI-MA 741040

An Omnicare initiative that will take another look at undertreatment and inappropriate treatment to improve the quality of life for the residents we serve.

Omnicare, Inc.
Re-View Grants
A/C # 011-2225-000

Prepared by: SDK
Reviewed by: RSR
12-Jan-01

	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)	(10)	(11)	(12)	(13)	(14)	(15)	(16)	(17)	(18)	(19)
(1)	Donor or	Pfizer	Roche Labs	J & J	Barr Labs	Wyeth-Ayerst	SmithKline	Tap Hldgs.	Novo	Alza	Astra	Pharmacia	Merck & Co.	Eli Lilly	Searle	Abbott Labs	Novartis	Bayer	Ending Balance
(2)	Intended Activity						Beecham		Nordisk		Zeneca	UpJohn						Phmctls.	
(3)																			
(4)	Balance @01/01/00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00		$0.00
(5)																			
(6)	3/9/2000 Deposit				($10,000.00)														($10,000.00)
(7)																			
(8)	Balance @03/31/00				($10,000.00)														($10,000.00)
(9)																			
(10)	No Activity																		
(11)																			
(12)	Balance @04/30/00				($10,000.00)														($10,000.00)
(13)																			
(14)	4/27/00 Deposit			($1,000.00)		($40,000.00)	($50,000.00)	($50,000.00)											($141,000.00)
(15)	(Rcls entry May-64)																		
(16)																			
(17)	Balance @05/31/00			($1,000.00)	($10,000.00)	($40,000.00)	($50,000.00)	($50,000.00)											($151,000.00)
(18)																			
(19)	06/09/00 Deposit								($35,000.00)	($50,000.00)									($85,000.00)
(20)	06/28/00 Deposit			($100,000.00)							($75,000.00)								($175,000.00)
(21)	06/30/00 Deposit			($100,000.00)								($50,000.00)							($150,000.00)
(22)																			
(23)	Balance @06/30/00			($201,000.00)	($10,000.00)	($40,000.00)	($50,000.00)	($50,000.00)	($35,000.00)	($50,000.00)	($75,000.00)	($50,000.00)							($561,000.00)
(24)																			
(25)	7/26/00 Deposit												($25,000.00)						($25,000.00)
(26)																			
(27)	06/00 Deposits		($20,000.00)											($50,000.00)	($25,000.00)	($50,000.00)			($145,000.00)
(28)																			
(29)																			
(30)	Balance @7/31/00		($20,000.00)	($201,000.00)	($10,000.00)	($40,000.00)	($50,000.00)	($50,000.00)	($35,000.00)	($50,000.00)	($75,000.00)	($50,000.00)	($25,000.00)	($50,000.00)	($25,000.00)	($50,000.00)			($731,000.00)
(31)																			
(32)	08/04/00 Deposit		($25,000.00)																($25,000.00)
(33)	08/22/00 Deposit			($50,000.00)											($2,951.15)				($52,951.15)
(34)	08/28/00 Deposit	($50,000.00)																	
(35)																			$0.00
(36)																			
(37)	Balance @8/31/00	($50,000.00)	($45,000.00)	($251,000.00)	($10,000.00)	($40,000.00)	($50,000.00)	($50,000.00)	($35,000.00)	($50,000.00)	($75,000.00)	($50,000.00)	($25,000.00)	($50,000.00)	($27,951.15)	($50,000.00)			($858,951.15)
(38)																			
(39)	09/01/00 Deposit																($50,000.00)		($50,000.00)
(40)																			
(41)	Balance @9/30/00	($50,000.00)	($45,000.00)	($251,000.00)	($10,000.00)	($40,000.00)	($50,000.00)	($50,000.00)	($35,000.00)	($50,000.00)	($75,000.00)	($50,000.00)	($25,000.00)	($50,000.00)	($27,951.15)	($50,000.00)	($50,000.00)		($908,951.15)
(42)																			
(43)	No Activity																		
(44)																			
(45)	Balance @10/31/00	($50,000.00)	($45,000.00)	($251,000.00)	($10,000.00)	($40,000.00)	($50,000.00)	($50,000.00)	($35,000.00)	($50,000.00)	($75,000.00)	($50,000.00)	($25,000.00)	($50,000.00)	($27,951.15)	($50,000.00)	($50,000.00)		($908,951.15)
(46)																			
(47)	11/24/00 Deposit					($10,000.00)													($10,000.00)
(48)																			
(49)	Balance @11/30/00	($50,000.00)	($45,000.00)	($251,000.00)	($10,000.00)	($50,000.00)	($50,000.00)	($50,000.00)	($35,000.00)	($50,000.00)	($75,000.00)	($50,000.00)	($25,000.00)	($50,000.00)	($27,951.15)	($50,000.00)	($50,000.00)		($918,951.15)
(50)																			
(51)	No Activity																		
(52)																			
(53)	Balance @12/31/00	($50,000.00)	($45,000.00)	($251,000.00)	($10,000.00)	($50,000.00)	($50,000.00)	($50,000.00)	($35,000.00)	($50,000.00)	($75,000.00)	($50,000.00)	($25,000.00)	($50,000.00)	($27,951.15)	($50,000.00)	($50,000.00)	$0.00	($918,951.15)
(54)																			
(55)	1/11/01 Deposit																	(10,000.00)	(10,000.00)
(56)																			
(57)	Preliminary 01/31/01 Balance	($50,000.00)	($45,000.00)	($251,000.00)	($10,000.00)	($50,000.00)	($50,000.00)	($50,000.00)	($35,000.00)	($50,000.00)	($75,000.00)	($50,000.00)	($25,000.00)	($50,000.00)	($27,951.15)	($50,000.00)	($50,000.00)	($10,000.00)	($928,951.15)

OMNI-MA 018135

JANSSEN PHARMACEUTICA RESEARCH FOUNDATION · ORTHO BIOTECH · ORTHO-McNEIL PHARMACEUTICAL

Omnicare

1600 RiverCenter II

100 East RiverCenter Boulevard

Covington, Ky. 41011

Coordinating RESOURCES

JANSSEN PHARMACEUTICA RESEARCH FOUNDATION · ORTHO BIOTECH · ORTHO-McNEIL PHARMACEUTICAL

Executive Summary

- Omnicare is the largest independent Provider of professional pharmacy and related services for long term care initiatives such as nursing homes, retirement centers, and other institutional facilities.
- Omnicare services 635,000 nursing homes beds or 32% of the total nursing home beds in America.
- Omnicare operates in 43 states and services 8,800 skilled nursing facilities.
- Omnicare represents the fifth largest Contract Research Organization in the world.
- Omnicare's CRO's provides comprehensive clinical research services for the pharmaceutical, biotechnology and medical device industries in 23 countries worldwide.

Coordinating RESOURCES

JANSSEN PHARMACEUTICA RESEARCH FOUNDATION | ORTHO BIOTECH | ORTHO-McNEIL PHARMACEUTICAL

Charter Statement

- Johnson & Johnson provides pharmaceuticals to Omnicare that enhance patient quality of life within the long-term care marketplace.

Coordinating RESOURCES

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Situation Appraisal

Customer Business Situation

- Omnicare is the largest pharmacy provider in country servicing over 635,000 nursing home residents in 43 states.
- Omnicare drives pharmaceutical initiatives at six individual regional areas, by Regional Clinical Directors.
- Omnicare is currently facing dramatic state Medicaid reimbursements cuts throughout the country.
- Assisted living facilities accounted for roughly 20% of Omnicare's total population.
- Omnicare currently purchases 130 million dollars of Johnson & Johnson pharmaceuticals.

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Situation Appraisal

Customer Business Situation

- Prospective Payment System has produced pricing pressures, overall census weakness, decline in Medicare census, and market decline in acuity/utilization.
- Annualized revenues of over 2 Billion dollars. Strong balance sheet. Positive earnings and cash flow generator.
- Omnicare philosophy "Increase pharmaceutical use, decrease medical costs"
- Omnicare operates specific health-management programs under the "Review" program. (Alzheimer's, Behavior Management, and Pain Management). Generated over 11,000 new prescriptions for antipsychotics.

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Situation Appraisal

Customer Business Situation

- Omnicare Senior Health Outcome offers corporations value added services for retirement population (GTE)
- Mergers and head reductions have trimmed operating units to 138 and employment to 1819.
- Value drivers for 2001:
  - Expand core distribution business
  - Leverage core business through development of clinical and information services

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Customer's View of Our Industry

- Omnicare's goal is to optimize drug therapy for the elderly, making it appropriate, affordable and available regardless of setting. Further development and expansion of its clinical services is a significant element of Omnicare's value creation strategy.
- The contract research business allows omnicare to play a major role in creating value for both pharmaceutical companies and the geriatric population
- Omnicare believes that providing services today, is different than what is was five years ago, and that they will emerge as a stronger company than before.

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Customer's View of Our Industry

- Key Players
  - Joel Gemunder, President, Omnicare, Inc.
  - Tim Bien, Senior Vice President of Purchasing and Professional Services, Omnicare, Inc.
  - Gary Erwin, President, Senior Health Outcomes, Omnicare, Inc.
  - Dan Maloney, Vice President of Purchasing, Omnicare, Inc.
  - Mark Lehman, Director of Clinical Services, Omnicare, Inc.
  - Lise Welford, Associate Direcor of Clinical Services, Omnicare, Inc.

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Customer's View of Our Industry

- Purchase Trends 2000

Risperdal	75 M	54%
Duragesic	18.2M	53%
Levaquin	14.3M	63%
Procrit	13 M	90%
Ultram	4.7 M	47%

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SALES

	1999	2000
• 1st Quarter	11.8M	33.0M
• 2nd Quarter	12.6M	30.3M
• 3rd Quarter	15.2M	34.3M
• 4th Quarter	18.7M	34.3M
Total	58.3M	127.7M

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Customer's View of Our Competition

How Customer Sees (Scale from 1:Worst to 10:Best)	Competition	J & J Pharmaceutical Companies
Level of business relationship	6	8
Understanding of customer's business situation	7	8
Product fit to customer's needs	6	8
Positioning in customer's organization	8	10
Product/Service reputation	7	8
Prices	5	5
Helpfulness to customer	6	7
Total	45	52

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Customer's View of Our Industry

- Omnicare has had tremendous financial pressures based on operating under the Prospective Payment System and state Medicaid reimbursement cuts.
- Omnicare has been able to demonstrate an ability to drive market share on performance based initiatives.
- J&J is the largest supplier of pharmaceuticals to Omnicare, purchasing close to 120 million dollars in products.

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Customer's View of Our Industry

Team Evaluation of the Account (Scale from 1:Worst to 10:Best)	***Score***
Its sales trend (2 – 3 years out) (In their own market)	10
Its growth vs. our strengths	9
How coachable its people are	6
How much we enjoy working with the account	7
Showcase/referral source for us	10
Recent trends of others	8
How much it helps us (Give & take or all take, no give)	8
Total	58

Compare this team evaluation to that of the customer's view of us and our competition

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Situation Appraisal Summary

- Strengths
  - Omnicare is the largest pharmacy provider in the United States.
  - Omnicare purchases more pharmaceuticals from J&J than any other pharmaceutical company.
  - Omnicare can move market share through P.S.T. I. programs.
  - Omnicare has one the the industry's premier formularies with the "Geriatric Guidelines" produced annually.

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Situation Appraisal Summary

- Opportunities
  - Risperdal "Re-Ignition" Program
  - Propoxphene Initiative (Ultram)
  - Alzheimeirs Initiative (Reminyl)
  - PPI Initiative (Aciphex)
  - ESRD Program (Procrit)
  - Pain Management Program.

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Situation Appraisal Summary

- Trends
  - Prospective Payment System has state Medicaid reimbursement Cuts depleted stock value and made making a profit in the pharmacy provider arena difficult.
  - Demographics of an aging population with higher drug utilization position Omnicare well for the future.
  - Outsourcing of clinical research produces another revenue stream and positions Omnicare well for geriatric specific studies.
  - Reductions in headcount and merging of sites continue to save dollars. (18 month program saves 46 million dollars)

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Putting It All Together

- Charter Statement
  - Johnson & Johnson supplies high quality products and services and jointly created clinical business programs that aid Omnicare in meeting corporate goals and objectives.

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Putting It All Together

- Drive Risperdal market share to 62% by re-energizing Risperdal Initiative. Programs to include MRDD/Schizophrenia pilot program and re-ignition of Behavior Management program.
- Initiate and successfully launch Reminyl in AD market.
- Establish relationships with Omnicare's CRO and repository for prospective and retrospective studies.
- Synergize efforts in working toward state Medicaid reimbursement issues.

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Putting It All Together

- Three Best Goals
  1. Synergize efforts on disease-state management programs, particularly Risperdal, Reminyl, and Levaquin.
  2. Educational programs at "grass-roots" level.
  3. Improve relationships with Corporate and Regional sites.

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Putting It All Together

- Single Best Opportunity
  - Risperdal "Re-Ignition" program..

Coordinating RESOURCES

Timothy E. Bien
Senior Vice President
Professional Services and Purchasing

Omnicare

Omnicare, Inc.
1600 RiverCenter II
100 East RiverCenter Boulevard
Covington, Kentucky 41011
REDACTED

June 15, 1999

Johnson & Johnson
Mr. Bruce Cummins
LTC Account Director
REDACTED

Dear Bruce,

On August 19th-23rd, Omnicare will once again be hosting its annual Manager's Meeting at Amelia Island, Florida. Omnicare, Inc. is requesting an amount of $45,000 from the Long Term Care Group to be used for the unrestricted use of continuing education at this program. We will use these funds, to further advance our expertise in management activities including management of our clinical programs such as our Risperdal initiative. These approaches should involve proper and appropriate dosages and patient selection criteria.

I look forward to hearing from you.

Sincerely,

Timothy E. Bien
Sr. Vice President of
Professional Services and Purchasing

** TX CONFIRMATION REPORT ** AS OF AUG 17 '99 12:52 PAGE. 1

OMNICARE

COMMAND #176

	DATE	TIME	TO/FROM	MODE	MIN/SEC	PGS	STATUS
001	8/17	12:51	REDACTED	EC---S	00'42"	002	OK

Omnicare, Inc.
100 E. RiverCenter Blvd.
Suite 1500
Covington, KY 41011
REDACTED

FAX COVERSHEET

From: Tim Bien	Date: 8-17-99
Donna Fairbanks	Number of Pages: 2
To: Bruce Cummins	Fax: Phone: REDACTED

Please call Donna Fairbanks at REDACTED **if you do not receive all pages**

hard Copy to Follow in Mail

OMNICARE INC.
Professional Services

DATE: June 12, 1997

TO: Regional Clinical Directors

FROM: Mark E. Lehman

RE: Risperdal PSTI Draft 2

Attached for your review and comments is the second draft of the Risperdal PSTI. As you will see, I have added much more emphasis on geriatric behavior use and decreased the emphasis on schizophrenia. I also added a quick "cheat" sheet on differences between the atypicals and the conventional antipsychotic drugs. I need your feedback as soon as possible. I anticipate the GPCG supplement going to print in the next week to ten days, and I (we) need to coordinate the launch of this formulary initiative. Thanks and call if you have questions!

OMNICARE INC.

Patient Specific Therapeutic Interchange Protocol (PSTI - 15)

Diagnoses: Behavioral Disturbances Associated with Dementia

Therapeutic Class: Anti-Psychotic Agents

Selected Agent: Risperidone (Risperdal®)

Approved: June, 1997
Timothy E. Bien, R.Ph., FASCP
Senior Vice President, Professional Services
Omnicare Inc.

OMNICARE INC.
Risperidone (Risperdal®) Medical Review

When evaluating the selection of one drug from a drug class as the "selected" agent, several critical elements must be evaluated: 1) efficacy, 2) safety, 3) ease of use and related nursing considerations in the long-term care facility, 4) application to a geriatric population, and 5) costs to the payer of the medication bill. The anti-psychotic agents as a class remain an often used modality in long-term care for treating behavioral disturbances associated with dementia. Risperidone (Risperdal®) has several characteristics which make it a "select" agent in the population we serve.

CLINICAL PHARMACOLOGY

1. The mechanism of action of Risperdal, as with other anti-psychotic drugs, is unknown. However, it has been proposed that this drug's anti-psychotic activity is mediated through a combination of dopamine type 2 (D2) and serotonin type 2 (5-HT2) antagonism. Antagonism at receptors other than D2 and 5HT2 may explain some of the other effects of Risperdal. In general, improvement of negative symptoms and lessened risk of EPS are thought to result from blockade of serotonin $5HT_2$ receptors. Improvement of positive symptoms is thought to result from blockade of dopamine D_2 receptors in the limbic system.
2. Risperdal is a selective monoaminergic antagonist with high affinity for the serotonin type 2 (5HT2), dopamine type 2 (D2), alpha 1 and alpha 2 adrenergic, and H1 histaminergic receptors. Risperdal antagonizes other receptors, but with lower potency. Risperdal has low to moderate affinity for the serotonin 5HT1C, 5HT1D, and 5HT1A receptors, weak affinity for the dopamine D1 and haloperidol-sensitive sigma site, and no affinity for cholinergic muscarinic or beta 1 and beta 2 adrenergic receptors.

PHARMACOKINETICS

1. Risperdal is well absorbed. It is extensively metabolized in the liver by cytochrome P450 IID6 to a major active metabolite, 9-hydroxyrisperidone, which is the predominant circulating specie, and appears approximately equi-effective with Risperdal with respect to receptor binding activity and some effects in animals). Consequently, the clinical effect of the drug likely results from the combined concentrations of Risperdal plus 9-hydroxyrisperidone.
2. Food does not affect either the rate or extent of absorption of Risperdal thus, the drug can be given with or without meals.
3. Following oral administration of Risperdal solution or tablet, mean peak plasma concentrations occurred at about 1 hour. Peak 9-hydroxyrisperidone occurred at about 3 hours in extensive metabolizers, and 17 hours in poor metabolizers. The apparent half-life of Risperdal was three hours (CV=30%) in extensive metabolizers and 20 hours (CV=40%) in poor metabolizers. The apparent half-life of 9-hydroxyrisperidone was about 21 hours (CV=20%) in extensive metabolizers and 30 hours (CV=25%) in poor metabolizers.

4. Steady-state concentrations of Risperdal are reached in 1 day in extensive metabolizers and would be expected to reach steady state in about 5 days in poor metabolizers. Steady state concentrations of 9-hydroxyrisperidone are reached in 5-6 days (measured in extensive metabolizers).
5. Risperdal and 9-hydroxyrisperidone are approximately equi-effective, thus, the sum of their concentrations is pertinent. The pharmacokinetics of the sum of Risperdal and 9-hydroxyrisperidone, after single and multiple doses, were similar in extensive and poor metabolizers, with an overall mean elimination half-life of about 20 hours.
6. The plasma protein binding of Risperdal was about 90% over the in vitro concentration range of 0.5 to 200 ng/mL and increased with increasing concentrations of alpha1-acid glycoprotein. The plasma binding of 9-hydroxyrisperidone was 77%. Neither the parent nor the metabolite displaced each other from the plasma binding sites.

EFFICACY IN SPECIFIC DISEASES/INDICATIONS

A. Schizophrenia:

North American Trial:

The clinical efficacy of Risperdal was documented in over 500 patients in the North American trial. The data from the North American trial formed the basis for the approval of Risperdal by the Food and Drug Administration (FDA). The North American trial was split into United States (Marder, 1994) and Canadian investigators (Chouinard, 1993) for publication purposes.

1. Marder (1994)

Marder (1994) conducted an 8-week multi-center double-blind study to compare the safety and efficacy of Risperdal 2, 6, 10 or 16 mg/day, haloperidol 20 mg/day and placebo in 388 schizophrenic patients. The main efficacy measures included the Positive and Negative Syndrome Scale (PANSS) and the Clinical Global Impression (CGI) scale.

2. Chouinard (1993)

Chouinard (1993) conducted an 8-week multi-center parallel-group double-blind study of 135 chronic schizophrenic patients who were randomized to Risperdal 2, 6, 10, 16 mg/day, haloperidol 20 mg/day or placebo. Efficacy measures included the Positive and Negative Syndrome Scale (PANSS) and the Clinical Global Impression (CGI) of Severity of Illness and Improvement.

3. Results

The combined results of the North American Trial are reported below:

Clinical Improvement: On both the total PANSS and total (PANSS and CGI) scales, Risperdal at a dose of 6 mg was superior to placebo and haloperidol 20 mg in the percentage of patients with clinical improvement.

Positive symptoms: On the PANSS positive subscale, Risperdal at a dose of 6 mg was superior to placebo and haloperidol 20 mg.

Negative symptoms: On the PANSS negative subscale, Risperdal at a dose of 6 mg was superior to placebo and haloperidol 20 mg.

B. Geriatric patients

The results of numerous open trials and case reports in which Risperdal was evaluated in geriatric patients have recently been reported. In general, lower doses of Risperdal were reported in these studies.

A review of published reports is provided below. In addition, a summary of these reports is presented in Table 1.

1. Aronson et al. reported the results of a retrospective study of 32 patients with diagnoses of behavioral disturbances in dementia (BDD), schizophrenia, bipolar, major depressive disorder with psychotic features and delusions disorder. The patients, with a mean age of 74.3 years, received Risperdal at a mean dose of 2.72 mg/day for a mean duration of 6.6 months. Improvement was reported in 31 of the 32 patients. Based on the Clinical Global Impression (CGI) score which was used to assess efficacy, 24 patients were reported to improve to a clinically significant degree. No patients had to discontinue treatment and none reported adverse effects.

2. In an open-label study conducted by Berman et al. in 10 schizophrenic patients with a mean age of 71 years who received Risperdal, statistically significant improvement in psychiatric scores was reported on the PANSS total (positive and negative symptom scale; $p = 0.002$), negative ($p=0.03$) and general symptoms ($p=0.02$). Statistically significant improvement was also reported on cognitive scores (Mini-Mental State Exam, Digit symbol; $p < 0.05$). No changes in vital signs or ECG were reported. Preexisting agitation, constipation, sleep problems and restlessness persisted in some patients. No patient reported significant EPS. One case of syndrome of inappropriate secretion of antidiuretic hormone, which resolved after discontinuation of risperidone, was reported in one patient.

3. Frenchman et al. conducted a chart review of 186 geriatric patients ($\geq$ 65 years) with Alzheimer's dementia, senile dementia NOS, or organic brain syndrome. Sixty patients had been treated with Risperdal (mean 1 mg/day), 83 with haloperidol (mean 2 mg/day) and 43 with thioridazine (mean 33 mg/day). Ninety-five percent of patients who received Risperdal had improvement in their target symptoms which included violence, shouting, delusions, paranoia, pacing, and mixed behaviors. Sixty-six percent and 65% of patients who received haloperidol and thioridazine respectively had improvement in their target symptoms. EPS was reported in fewer patients who received Risperdal(7%) than haloperidol (22%) and thioridazine (18%).

4. Gierz et al. presented in a poster, the pooled results of three open-label studies conducted in 35 older patients with schizophrenia, organic delusional disorder, bipolar and dementias of different etiologies. The ranges of the mean age and Risperdal dose for the three studies were respectively 55.6-71 years and 1.75-5.64 mg/day. Sixty percent (21/35) of the patients were considered to improve considerably with only 6% showing signs of worsening of symptoms. Side effects which occurred in some patients were considered tolerable.

5. In a poster, Goldberg reported the use of Risperdal in dementia-related disturbed behavior in nursing home residents. Sixty-four patients with dementia-related behavioral disturbances were treated with low doses of Risperdal (0.25-0.5 mg twice daily) for 6 months. Their ages ranged from 43-98 years with a mean of 80.4 years. The patients' behavior was recorded on questionnaires by the nursing staff for up to 6 months. Symptoms that showed the greatest improvements included agitation, verbal outbursts, physical aggression, depressed mood, anxiety, and abnormal movements. In general, Risperdal was well-tolerated and reported to be very helpful in 26 (41%) patients, moderately helpful in 17 (27%), slightly helpful in 10 (16%), and not helpful in 11 (17%) patients.

6. In a letter to the editor, Jeanblanc and Davis reported the use of Risperdal in five elderly patients (4 with dementia of the Alzheimer's type and 1 with vascular dementia). The age range was 70-91 years. A marked reduction or elimination of the patients' dementia-related agitation or violent behavior was observed within 7-10 days at Risperdal doses of 1.5-2.5 mg/day. Mild extrapyramidal symptoms were reported in two patients.

7. Kopala and Honer reported the use of Risperdal(1.5 mg) for persistent vocalizations in two elderly patients (92 and 78 years) with combined Alzheimer-vascular dementia. Vocalizations were reported to decrease to less than 20% of baseline ratings with Risperdal. Moreover, a decrease in Extrapyramidal System Rating Scale (ESRS) score was noted in one patient with dyskinesia.

8. Lacro et al. reported the results of 4 pooled open-label independent studies involving 47 patients (mean age 67.9) with schizophrenia, dementia, delusional disorder and mood disorder with psychotic features who received Risperdal at a mean dose of 3.2 mg/day for a mean duration of 10.8 weeks. Target symptoms which included psychotic symptoms and severe behavioral disturbances were reported to improve in 85% of the patients after Risperdal was initiated. Statistically significant ($p < 0.01$) improvement in cognitive function (mean scores on the Mini-mental State Exam) was also reported in a subsample of 19 patients. Adverse effects reported included hypotension (5), sedation (5), salivation (3) and EPS (1).

9. Lavretsky et al. conducted a 10-week open-label study of Risperdal for the treatment of agitation in 15 elderly patients (mean 78 years) with dementia. The range of Risperdal dose was 0.5 - 3.0 mg. All patients who received Risperdal were improved or very much improved at 10 weeks based on the Clinical Global Impression scale (CGI). After 2 weeks of treatment, 50% of patients were reported to improve on the Overt Aggression Scale (OAS) while 50% improvement was reported on the Cohen-Mansfield Agitation Inventory (CMAI) after 8 weeks treatment with Risperdal. Four patients reported EPS. Mean Mini-Mental State Exam (MMSE) scores decreased and Unified Parkinson's Disease Rating Scale (UPDRS) scores increased over 10 weeks.

10. In a letter to the editor published in the Lancet, Allen et al. described three patients with Lewy body dementia (LBD) who were treated with low dose Risperdal (0.5 to 1 mg per day). All three patients showed improvement in their behavioral and psychotic symptoms as measured by the Alzheimer's disease rating scale. Cognitive function either improved or stayed the same during Risperdal therapy.

11. Lee et al. reported the use of Risperdal in a 74-year-old female patient with senile dementia of Lewy body type (SDLBT). The patient received Risperdal 5 mg/day which was titrated over 10 days. Due to drowsiness and increased confusion, Risperdal was reduced to 1 mg bd. The patient's mental and cognitive state showed a gradual improvement after the dose reduction. In a letter to the editor, Mc Keith et al. cautioned about the possibility of sensitivity reactions to Risperdal in Lewy body dementia.

12. In a case series, Madhusoodanan et al. reported the efficacy of Risperdal in 11 geriatric patients (mean age 69.4 years) with schizophrenia, schizoaffective, bipolar and senile dementia. The mean dose of Risperdal was 4.9 mg/day. Overall, 8 patients responded to Risperdal and 7 had marked decreases in their positive and negative symptoms. Decreases in EPS and tardive dyskinetic symptoms were also reported in 4 patients. Adverse events reported such as hypotension, orthostatic hypotension, somnolence, headache, abdominal cramps and dizziness were considered negligible.

13. Madhusoodanan et al. reported the results of a 12-week open multicenter study to evaluate the efficacy and safety of Risperdal used at a mean dose of 2.4 mg/day in 103 elderly (mean age 71 years) with schizophrenia or schizoaffective disorder. Statistically significant reductions in severity of symptoms were reported on the Positive and Negative Symptoms Scales (PANSS) total and subscales. When efficacy was assessed by the Clinical Global Impression Scale (CGI), 62% of the patients were reported to at least minimally improved at endpoint (11% very much improved, 24% much improved, 27% minimally improved). Patients who received Risperdal $\leq$ 3 mg/day (64% improved) were more likely to improve than > 3 mg/day (58% improved). The most frequently reported side effects were dizziness, insomnia, agitation, somnolence and injury. EPS was reported to decrease from baseline to endpoint.

14. In a letter to the editor, Meco et al. suggested that Risperdal(range 0.25-1.25) may be effective for hallucinations in six levodopa-treated elderly (mean age 71.17 years) patients with Parkinson's disease. No worsening of EPS was reported.

15. Raheja et al. reported the successful use of Risperdal in two geriatric (76 and 82 years) patients to control behavioral disorders. The Risperdal dose in the two patients was 3 mg/day.

16. Reyntjens et al. conducted a 5-week pilot study to evaluate the effect of Risperdal in forty geriatric patients with behavioral disturbances. Risperdal was started at 0.5 mg bid and the dose was adjusted based on therapeutic response and side effects. The results suggested that Risperdal is an effective and well tolerated drug for the management of behavioral symptoms in geriatric patients.

17. Zarate et al. conducted a retrospective study to evaluate the use of Risperdal in 122 elderly patients with diagnoses of dementia, mood and psychotic disorders. The mean dose of Risperdal was 1.6 mg. Risperidone was effective in 85% of the 108 patients who continued treatment based on the Clinical Global Impression improvement scale (CGI-I).

The common adverse events reported included hypotension (29%), EPS (11%) and symptomatic orthostasis (10%).

18. Borison et al. reported on the use of Risperdal in 22 elderly patients with schizophrenia or dementia (Alzheimer's disease).

19. Czobor P, et al. reported on the positive effect of Risperdal on hostility in elderly with schizophrenia.

INDICATIONS, USES, DOSE RECOMMENDATIONS

1. Risperdal is indicated for the management of the manifestations of psychotic disorders.
2. ***Elderly:*** In general, a lower starting dose is recommended for an elderly patient, reflecting a decreased pharmacokinetic clearance in the elderly, as well as a greater frequency of decreased hepatic, renal, or cardiac function, and a greater tendency to postural hypotension. In healthy elderly subjects renal clearance of both Risperdal and 9-hydroxyrisperidone was decreased, and elimination half-lives were prolonged compared to young healthy subjects. Dosing should be modified accordingly in the elderly patients.
3. The recommended **initial dose** is 0.5 mg BID in patients who are elderly or debilitated, patients with severe renal or hepatic impairment, and patients either predisposed to hypotension or for whom hypotension would pose a risk. **Dosage increases in these patients should be in increments of no more than 0.5 mg bid.** Increases to dosages above 1.5 mg BID should generally occur at intervals of at least 1 week. In some patients slower titration may be medically appropriate. Elderly or debilitated patients, and patients with renal impairment, may have less ability to eliminate Risperdal than normal adults. Patients with impaired hepatic function may have increases in the free fraction of the Risperdal, possibly resulting in an enhanced effect. Patients with a predisposition to hypotensive reactions or for whom such reactions would pose a particular risk likewise need to be titrated cautiously and carefully monitored.

SAFETY ISSUES

1. The favorable safety profile of Risperdal demonstrated in 6-8 week short-term studies has been confirmed in seven 1-year safety studies involving over 1100 patients. The most common side effects reported with Risperdal in short-term studies are insomnia, agitation, EPS, headache, anxiety, rhinitis .

2. The long-term safety of Risperdal has been reported in 1,156 patients enrolled in seven 1-year clinical trials (Brecher, 1996). Adverse events reported in these 1-year trials were consistent with the findings from short-term double-blind studies. The range of the mean dose of Risperdal in the long term trials was 7.6-9.4 mg/day. Although the mean dose of Risperdal was higher than the doses used in practice (avg. dose for schizophrenia: 4.7 mg/day; all conditions: 3.2 mg/day) and found to be optimal in clinical trials (4-6 mg), the adverse events' profile of Risperdal from the long-term studies was similar to that reported in short-term pivotal trials.

Extrapyramidal symptoms/Tardive dyskinesia

3. Risperdal's potent effects at $5HT_{2A}$ receptors may be responsible for the low incidence of neurological adverse effects, such as EPS, associated with its use. Importantly, Risperdal at a dose of ≤10 mg/day has demonstrated an incidence of extrapyramidal symptoms (EPS) comparable to placebo (Risperdal product labeling). Marder (1994) reported that there was no significant differences in Extrapyramidal Symptom Rating Scale (ESRS) score between patients receiving placebo and Risperdal ≤ 6 mg.

4. In a study of 36 schizophrenic patients, Borison (1992) concluded that Risperdal decreased the signs of tardive dyskinesia. Chouinard (1995) determined that Risperdal had a significant beneficial effect on tardive dyskinesia in the Canadian Multi-center Risperdal study of 135 schizophrenic patients. In a post hoc analysis, Chouinard (1995) further examined the effects of Risperdal in patients with tardive dyskinesia from the Canadian Multi-center Risperdal study. The author reported that Risperdal at 6mg/day had the most beneficial effect on tardive dyskinesia.

5. Brecher (1996) evaluated the long-term safety of Risperdal (mean dose 7.6-9.4 mg/day) in 1156 patients enrolled in seven 1-year clinical trials. Only four cases (0.3 %) of tardive dyskinesia were reported in the long term studies.

Anticholinergic side effects

6. Risperdal's low affinity for muscarinic receptors is consistent with the relatively low incidence of anticholinergic adverse events reported in clinical trials conducted to evaluate its safety and efficacy. In these trials, the incidence of constipation was 3% in the placebo group and 7% in patients who received Risperdal in a dose of less than 10 mg/day, and 13% of patients who received 16 mg/day (Risperdal Product labeling). In a study conducted by Marder and Meibach (1994), the incidence of constipation was reported as 1.6% for both 2 and 6 mg daily doses of Risperdal.

Orthostatic hypotension

7. Risperdal may induce orthostatic hypotension especially during the initial dose-titration period, which is reflective of its alpha-adrenergic antagonistic properties. Orthostatic hypotension may be minimized, however, by following the recommended dose titration schedule. Syncope was reported in 0.2% (6/2670) of Risperdal-treated patients (Risperdal Product labeling).

Weight gain

8. Brecher (1996) reported a small weight gain with a mean increase in body weight per patient of 2.6 kg over the 1 year time period.

Sedation/Somnolence

9. The incidence of somnolence was reported as 3.2% and 3.1% respectively for 2 and 6 mg daily doses of Risperdal by Marder (1994) and is consistent with Risperdal's relatively low affinity for histamine H_1 receptors.

Laboratory monitoring

10. Laboratory monitoring, such as liver enzymes or white blood cell count is not required during Risperdal therapy since increased liver enzymes or white blood cells disorders have not consistently been reported in the pre-marketing studies or the post-marketing experience.

Other adverse effects

11. The most common adverse events reported in patients treated with Risperdal in pre-marketing clinical trials were insomnia, agitation, EPS, headache, anxiety, and rhinitis.

RISPERDAL SHORT AND LONG TERM SAFETY

	Risperdal Safety Information	
Adverse effects	Short term safety	Long term safety

Anticholinergic side effects	• No affinity for muscarinic cholinergic receptors
	• Minimal risk of anticholinergic side effects
	e.g, constipation:
	  • 3% placebo
	  • 7% RIS ≤ 10 mg/day
	  • 13% RIS 16 mg/day
		• The rate of anticholinergic side effects is comparable to short term studies

Extrapyramidal symptoms	• The incidence of EPS with Risperdal at doses ≤ 10 mg is comparable to placebo.
	• Incidence of EPS:
	  • Placebo 16%
	  • RIS ≤ 10 mg/day: 17%
	  • RIS 16 mg: 34%
		• Long term data indicates that the risk of EPS does not increase with extended use

Tardive dyskinesia	• Risperdal may have a beneficial effect on tardive dyskinesia in some patients	• Only four cases of (0.3%) of tardive dyskinesia reported in long term studies
Somnolence	• Risperdal causes minimal somnolence at ≤ 10 mg/day • RIS ≤ 10 mg/day: 3% • RIS 16 mg/day: 8% • Placebo: 1%	• The rate of somnolence is comparable to short term studies
Weight gain	• The incidence of weight gain (≥7% of body weight) with Risperdal has been reported as 18% compared to 9% with placebo	• Weight gain data from long term studies revealed a mean increase in body weight of 2.6 kg (range 1.8 - 3.3 kg) or 5.72 lb. (range 3.96 - 7.26 lb.). The mean duration of exposure was 213 days

	Risperdal safety information	
Adverse effects	Short term safety	Long term safety
Prolactin	• Greater plasma prolactin elevations than haloperidol • No correlation between prolactin-related adverse effects (e.g., gynecomastia, galactorrhea, oligomenorrhea, erectile and ejaculatory dysfunction) and prolactin levels in men and women	• Limited available data are similar to short term data • Long term study in progress
Electrocardiographic changes	• Mean QTc changes: Range -5.5 to + 2.7 msec Clinically insignificant	• Mean QTc changes: Range -0.9 to + 4.4 msec Clinically insignificant
Liver enzymes monitoring	• No monitoring required	• No monitoring required
White blood cell monitoring	• No monitoring required	• No monitoring required

DRUG INTERACTIONS

1. There have been no systematic evaluations of interactions between Risperdal and other drugs, to date. Given the primary central nervous system effects of Risperdal, caution should be used when Risperdal is taken in combination with other centrally acting drugs or alcohol.

2. Risperdal may antagonize the effects of levodopa and dopamine agonists.

3. Chronic administration of carbamazepine with Risperdal may increase the clearance of Risperdal.

4. Chronic administration of clozapine with Risperdal may decrease the clearance of Risperdal.

DRUG ADMINISTRATION FACTORS

1. Risperdal 1 mg/ml oral solution has been approved by the Food and Drug Administration (FDA) and is commercially available.

2. Data submitted to the FDA demonstrated that the Risperdal 1 mg/ml oral solution is bioequivalent to the 1 mg tablets. Gutierrez presented, in a poster, the results of an open-label, randomized, two-way crossover study comparing the bioavailability of Risperdal as a 1-mg tablet and 1-mg/ml oral solution in 23 healthy male subjects. The tablet and the oral solution were given as a single 1-mg dose and were separated by a 10-day washout period. The 90% confidence intervals on the relative bioavailability for Risperdal, 9-hydroxyrisperidone, and total Risperdal for Cmax and AUC were within the equivalence range of 80-120%. Both formulations are bioequivalent and were well tolerated.
3. The oral solution is supplied in 100 ml bottles with a calibrated (in milligrams and milliliters) pipette. The minimum calibrated volume is 0.25 mL., while the maximum calibrated volume is 3 mL.
4. **Tests indicate that Risperdal oral solution is compatible in the following beverages: water, coffee, orange juice, and low-fat milk; it is NOT compatible with either cola or tea.**

COST

1. Utilizing Risperdal as the branded anti-psychotic of choice in behavioral disturbances associated with dementia will provide cost savings to the payer of the pharmacy bill. When compared to the other branded anti-psychotic currently available on the market (Zyprexa®).

SUMMARY

Risperdal possess several characteristics that make it a "select" agent for use in the geriatric population. Risperdal has been proven effective for the positive and negative symptoms of psychosis while exhibiting an excellent safety profile, unlike the older, first generation anti-psychotic agents. Risperdal can be administered by tablet or liquid, can be given in a twice daily regimen, and, when compared to the other branded anti-psychotic, provides a cost savings to the payer of the pharmacy bill. For these reasons we are initiating an intervention program to:

1. **Initiate anti-psychotic therapy with Risperdal when a new, atypical agent is selected for use.**

2. **Suggest Risperdal as the anti-psychotic of choice when a resident has experienced adverse effects or therapeutic failure with a trial of a conventional anti-psychotic.**

REFERENCES

Available for review.

CONVENTIONAL VS. ATYPICAL ANTIPSYCHOTICS

The new atypical antipsychotic agents include clozapine (Clozaril ®), risperidone (Risperdal ®) and olanzapine (Zyprexa)®. Although there is no universally accepted definition for atypicality, in general an atypical antipsychotic has a higher 5HT2 (serotonin 2) to D2 (dopamine 2) ratio resulting in less extrapyramidal symptoms and improved efficacy against the negative symptoms associated with schizophrenia. In addition the atypical antipsychotic drugs carry a lower risk of tardive dyskinesia than the conventional antipsychotic agents.

Mechanism of action...

1. The conventional antipsychotics primarily block the *dopamine* D_2 receptors
2. The atypical antipsychotics block the *dopamine* D_2 and *serotonin* $5HT_2$ receptors to various degrees
3. The atypical antipsychotics have higher $5HT_2$ to D_2 ratios than the conventional antipsychotics

Safety...

1. The conventional antipsychotics, especially the high-potency agents, frequently cause extrapyramidal side effects such as pseudoparkinsonism, acute dystonia, and akathisia
2. The atypical antipsychotics cause less extrapyramidal side effects due to a higher $5HT_2$ to D_2 ratio
3. The atypical antipsychotic agents have a lower risk of tardive dyskinesia

RISPERDAL...

* **Extra Pyramidal Symptoms**

Short term studies have shown that the incidence of EPS with Risperdal at doses ≤ 10 mg is comparable to placebo

- **Placebo: 16%;**
- **RIS ≤ 10 mg/day: 17%**
- **RIS 16 mg: 34%**

Long term data indicates that the risk of EPS does not increase with extended use

* **Tardive dyskinesia**

- **Low incidence (0.3%) in long term studies**
- **Risperdal may have a beneficial effect on tardive dyskinesia**

References

1. Kane JM. Schizophrenia. N Eng. J Med 1996; 334(1): 34-41.
2. Love RC. Novel versus conventional antipsychotic drugs. Pharmacotherapy 1996; 16(1 Pt 2): 16S-10S.
3. Risby BR, Donnigan D, et al. Formulary considerations for treating psychiatric disorders: Schizophrenia. Formulary 1997; 32:142-55.

Table 1: Summary of published reports on the use of Risperidone in the geriatric population

Study	Patients	Risperidone dosing	Efficacy results	Safety results
Aronson et al. Retrospective	**n=32; mean age 74.3 yrs Behavioral disturbances in dementia, schizophrenia, bipolar, major depressive disorder with psychotic features, delusional disorders**	**mean=2.72 mg/day Duration 6.6 months**	**Improved CGI (31) Clinically significant improvement CGI scores (24)**	**None reported**
Berman et al. Open-label	**n=10, mean age 71 years Schizophrenia**	**Maximum 6 mg/day**	**Statistically significant improvement in psychiatric scores: PANSS total (p=0.002), negative (p=0.03), general score (p=0.02) Statistically significant improvement on cognitive scores (MMSE, Digit Symbol; p<0.05)**	**Preexisting agitation, constipation, sleep problems and restlessness persisted No patient reported significant EPS Syndrome of inappropriate secretion of antidiuretic hormone (1)**
Frenchman et al. Retrospective	**n=186; ≥ 65 years Alzheimer's disease, senile dementia, organic brain syndrome.**	**RIS: 1 mg/day Haloperidol: 2 mg/day Thioridazine: 33 mg/day**	**Target symptoms improvement: RIS: 95% Haloperidol: 66% Thioridazine: 65%**	**EPS: RIS 7% Haloperidol 22% Thioridazine 18%**
Gierz et al. Open-label	**n=35; Age: 55.6-71 years Schizophrenia, organic delusional disorder, bipolar, dementias**	**Range: 1.75-5.64**	**60% improved considerably (21/35)**	**6% showed signs of worsening of symptoms Side effects tolerable**
Jeanblanc & Davis Case reports	**n=5; Age: 70-91 years Alzheimer's and vascular dementia**	**1.5-2.5 mg/day**	**Marked reduction in dementia-related agitation/violence in all patients**	**No sedation Mild EPS (2)**

Kopala and Honer Case reports	**n=2, Age=92-78 Combined Alzheimer-vascular dementia**	**1.5 mg**	**Vocalizations decreased by 20% of baseline ratings Decrease in ESRS score in one patient with dyskinesia**	**None**
Lacro et al. Pooled open studies	**n=47; mean age 67.9 Schizophrenia, dementia, delusional disorder, mood disorder with psychotic features**	**Mean 3.2 mg/day 10.8 weeks**	**Target symptom improvement in 85% of patients MMSE improved in subsample of 19 patients, p<0.01**	**Hypotension (5) Sedation (5) Salivation (3) EPS (1)**
Lavretsky et al. Open-label	**n=64; Mean age 78 Agitation in dementia**	**Range 0.5-3.0 mg**	**All patients improved or very much improved via CGI at 10 wk CMAI: 50% improvement after 8 wks OAS: 50% improvement after 2 wks**	**EPS (4) Mean MMSE decreased over 10 wks Mean UPDRS increased over 10 wks**
Allen et al Case reports	**n=3; Age 66-78 Lewy body dementia**	**range 0.5-1 mg/day**	**All three patients improved in their behavioral and psychotic symptoms via Alzheimer's rating scale Cognitive function improved or stayed the same**	**Worsening in EPS (1)**
Lee et al. Case reports	**n=1; 74 years Lewy body type dementia**	**1 mg bd**	**Gradual improvement in mental and cognitive state**	**Drowsiness and confusion**

Madhusoodanan et al. Case reports	n=11; mean age 69.4 Schizophrenia, schizoaffective, bipolar, senile dementia	4.9 mg/day	8 patients responded 7 had marked decrease in positive and negative symptoms Decrease in preexisting EPS and tardive dyskinesia (4)	No changes in ECG/vital signs Hypotension Orthostatic hypotension Somnolence, headache, abdominal cramps, dizziness
Madhusoodanan et al. Open label, multicenter	n=103; Mean age 71 Schizophrenia and schizoaffective	2.4 mg/day	Statistically significant reductions in PANSS total and subscales 62% minimally improved via CGI Patients who received RIS ≤ 3 mg/day (64% improved) more likely to improve than > 3 mg/day (58% improved).	Most frequently adverse effects: dizziness, insomnia, agitation, somnolence, injury EPS decreased from baseline to endpoint
Meco et al. Letter to the Editor	n=6; Mean 71.17 years Hallucinations / parkinson's disease	range 0.25-1.25 mg/day	Effective for hallucinations in L-dopa-treated patients	No worsening of EPS
Raheja et al. Case reports	n=2, 76, 82 years Behavioral disorders	3 mg/day	Symptoms improvement in both patients	No adverse events reported
Reyntjens et al. Open-label	n=40; Behavioral disturbances	Starting dose 0.5 mg bid. Titrated based on response and side effects	Effective for the management of behavioral disturbances	None reported
Zarate et al. Retrospective	n=122; ≥ 65 years old Dementia, mood and psychotic disorders	mean 1.6 mg/day	Effective in 85% of patients via CGI-I	Hypotension (29%) EPS (11%) Orthostasis (10%)

OMNICARE MEMORANDUM
Professional Services

PRO 98-10

DATE: August 25, 1998

TO: Omnicare Consultant Coordinators
Omnicare Formulary Champions

FROM: Mark E. Lehman
Director, Clinical Services

RE: Re-Issue of Risperdal PSTI Protocol

CC: Timothy E. Bien
Regional Vice Presidents
Regional Clinical Directors

As you are aware, Omnicare has made the Risperdal Patient Specific Therapeutic Interchange program a very high priority for the third and fourth quarters of 1998 and beyond. In support of this initiative, please find attached an updated, revised edition of the Risperdal PSTI protocol. In addition to the comprehensive medical review previously circulated, this PSTI protocol also contains important strategies and intervention scenarios for both operations and consultant clinicians, and sample drug regimen review comments for use in your facilities. Please feel free to adapt and change these comments for your use.

Please copy and distribute this important information to all Omnicare pharmacists and nurse consultants dealing with formulary intervention programs. It is imperative that all formulary management intervention programs be implemented as quickly and comprehensively as possible, using both operations and consultant resources.

This intervention, and all Omnicare formulary initiatives will be discussed, in great detail, during the upcoming Professional Services Committee/Formulary Champions Meeting in Covington, KY on September 9-10, 1998. I look forward to seeing many of you at this important meeting. In the meantime, if you have questions or comments please contact your Regional Clinical Director or myself. As always, thank you for your continued efforts and support

OMNI 125120

OMNI-PA0438698

Confidential

OMNICARE INC.

Patient Specific Therapeutic Interchange Protocol (PSTI – 15)

Diagnoses: Behavioral Disturbances Associated with Dementia

Therapeutic Class: Anti-Psychotic Agents

Selected Agents: Risperidone (Risperdal®)

Approved: June, 1997
Timothy E. Bien, R.Ph., FASCP
Senior Vice President, Professional Services
Omnicare Inc.
Revised: August, 1998

When evaluating the selection of one drug from a drug class as the "selected" agent, several critical elements must be evaluated: 1) efficacy, 2) safety, 3) ease of use and related nursing considerations in the long-term care facility, 4) application to a geriatric population, and 5) costs to the payer of the medication bill. The anti-psychotic agents as a class remain an often used modality in long-term care for treating behavioral disturbances associated with dementia. Risperidone (Risperdal®) has several characteristics which make it a "select" agent in the population we serve.

CLINCAL PHARMACOLOGY

1. The mechanism of action of Risperdal, as with other anti-psychotic drugs, is unknown. However, it has been proposed that this drug's anti-psychotic activity is mediated through a combination of dopamine type 2 (D2) and serotonin type 2 (5-HT2) antagonism. Antagonism at receptors other than D2 and 5HT2 may explain some of the other effects of Risperdal. In general, improvement of negative symptoms and lessened risk of EPS are thought to result from blockade of serotonin $5HT_2$ receptors. Improvement of positive symptoms is thought to result from blockade of dopamine D_2 receptors in the limbic system.

2. Risperdal is a selective monoaminergic antagonist with high affinity for the serotonin type 2 (5HT2), dopamine type 2 (D2), alpha 1 and alpha 2 adrenergic, and H1 histaminergic receptors. Risperdal antagonizes other receptors, but with lower potency. Risperdal has low to moderate affinity for the serotonin 5HT1C, 5HT1D, and 5HT1A receptors, weak affinity for the dopamine D1 and haloperidol-sensitive sigma site, and no affinity for cholinergic muscarinic or beta 1 and beta 2 adrenergic receptors.

PHARMACOKINETICS

1. Risperdal is well absorbed. It is extensively metabolized in the liver by cytochrome P450 IID6 to a major active metabolite, 9-hydroxyrisperidone, which is the predominant circulating specie, and appears approximately equi-effective with Risperdal with respect to receptor binding activity and some effects in animals. Consequently, the clinical effect of the drug likely results from the combined concentrations of Risperdal plus 9-hydroxyrisperidone.

2. Food does not affect either the rate or extent of absorption of Risperdal thus, the drug can be given with or without meals.

3. Following oral administration of Risperdal solution or tablet, mean peak plasma concentrations occurred at about 1 hour. Peak 9-hydroxyrisperidone occurred at about 3 hours in extensive metabolizers, and 17 hours in poor metabolizers. The apparent half-life of Risperdal was three hours (CV=30%) in extensive metabolizers and 20 hours (CV=40%) in poor metabolizers. The apparent half-life of 9-hydroxyrisperidone was about 21 hours (CV=20%) in extensive metabolizers and 30 hours (CV=25%) in poor metabolizers.

4. Steady-state concentrations of Risperdal are reached in 1 day in extensive metabolizers and would be expected to reach steady-state in about 5 days in poor metabolizers. Steady-state concentrations of 9-hydroxyrisperidone are reached in 5-6 days (measured in extensive metabolizers).

5. Risperdal and 9-hydroxyrisperidone are approximately equi-effective, thus, the sum of their concentrations is pertinent. The pharmacokinetic of the sum of Risperdal and 9-hydroxyrisperidone, after single and multiple doses, were similar in extensive and poor metabolizers, with an overall mean elimination half-life of about 20 hours.

6. The plasma protein binding of Risperdal was about 90% over the in vitro concentration range of 0.5 to 200 ng/mL and increased with increasing concentrations of alpha1-acid glycoprotein. The plasma binding of 9-hydroxyrisperidone was 77%. Neither the parent nor the metabolite displaced each other from the plasma binding sites.

EFFICACY IN SPECIFIC DISEASES/INDICATIONS

A. Schizophrenia:

North American Trial:

The clinical efficacy of Risperdal was documented in over 500 patients in the North American trial. The data from the North American Trial formed the basis for the approval of Risperdal by the Food and Drug Administration (FDA). The North American trial was split into United States (Marder, 1994) and Canadian investigators (Chouinard, 1993) for publication purposes.

1. Marder (1994)

Marder (1994) conducted an 8-week multi-center double-blind study to compare the safety and efficacy of Risperdal 2, 6,10 or 16 mg/day, haloperidol 20 mg/day and placebo in 388 schizophrenic patients. The main efficacy measures included the Positive and Negative Syndrome Scale (PANSS) and the Clinical Global Impression (CGI) scale.

2. Chouinard (1993)

Chouinard (1993) conducted an 8-week multi-center parallel-group double-blind study of 135 chronic schizophrenic patients who were randomized to Risperdal 2, 6, 10, 16 mg/day, haloperidol 20 mg/day or placebo. Efficacy measures included the Positive and Negative Syndrome Scale (PANSS) and the Clinical Global Impression (CGI) of Severity of Illness and Improvement.

3. Results

The combined results of the North American Trial are reported below:

Clinical Improvement: On both the total PANSS and total (PANSS and CGI) scales, Risperdal at a dose of 6 mg was superior to placebo and haloperidol 20 mg in the percentage of patients with clinical improvement.

Positive Symptoms: On the PANSS positive subscale, Risperdal at a dose of 6 mg was superior to placebo and haloperidol 20 mg.

Negative Symptoms: On the PANSS negative subscale, Risperdal at a dose of 6 mg was superior to placebo and haloperidol 20 mg.

B. Geriatric Patients

The results of numerous open trials and case reports in which Risperdal was evaluated in geriatric patients have recently been reported. In general, lower doses of Risperdal were reported in these studies.

A review of published reports is provided below. In addition, a summary of these reports is presented in Table 1.

1. Aronson et al. reported the results of a retrospective study of 32 patients with diagnoses of behavioral disturbances in dementia (BDD), schizophrenia, bipolar, major depressive disorder with psychotic features and delusions disorder. The patients, with a mean age of 74.3 years, received Risperdal at a mean dose of 2.72 mg/day for a mean duration of 6.6 months. Improvement was reported in 31 of the 32 patients. Based on the Clinical Global Impression (CGI) score which was used to assess efficacy, 24 patients were reported to improve to a clinical significant degree. No patients had to discontinue treatment and none reported adverse effects.

2. In an open-label study conducted by Berman et al. in 10 schizophrenic patients with a mean age of 71 years who received Risperdal, statistically significant improvement in psychiatric scores was reported on the PANSS total (positive and negative symptom scale; p=0.002), negative (p=0.03) and general symptoms (p=0.02). Statistically significant improvement was also reported on cognitive scores (Mini-Mental State Exam, Digit symbol; $p < 0.05$). No changes in vital signs or ECG were reported. Preexisting agitation, constipation, sleep problems and restlessness persisted in some patients. No patient reported significant EPS. One case of syndrome of inappropriate secretion of antidiuretic hormone, which resolved after discontinuation of risperidone, was reported in one patient.

3. Frenchman et al. conducted a chart review of 186 geriatric patients ($\geq$ 65 years) with Alzheimer's dementia, senile dementia NOS, or organic brain syndrome. Sixty patients had been treated with Risperdal (mean 1 mg/day), 83 with haloperidol (mean 2 mg/day) and 43 with thioridazine (mean 33 mg/day). Ninety-five percent of patients who received Risperdal had improvement in their target symptoms which included violence, shouting, delusions, paranoia, pacing and mixed behaviors. Sixty-six percent and 65% of patients who received haloperidol and thioridazine respectively had improvement in their target symptoms. EPS was reported in fewer patients who received Risperdal (7%) than haloperidol (22%) and thioridazine (18%).

4. Gierz et al. presented in a poster, the pooled results of three open-label studies conducted in 35 older patients with schizophrenia, organic delusional disorder, bipolar and dementias of different etiologies. The ranges of the mean age and Risperdal dose for the three studies were respectively 55.6-71 years and 1.75-5.64 mg/day. Sixty percent (21/35) of the patients were considered to improve considerably with only 6% showing signs of worsening of symptoms. Side effects which occurred in some patients were considered tolerable.

5. In a poster, Goldberg reported the use of Risperdal in dementia-related disturbed behavior in nursing home residents. Sixty-four patients with dementia-related behavioral disturbances were treated with low doses of Risperdal (0.25-0.5 mg twice daily) for 6 months. Their ages ranged from 43-98 years with a mean of 80.4 years. The patients' behavior was recorded on questionnaires by the nursing staff for up to 6 months. Symptoms that showed the greatest improvements included agitation, verbal outbursts, physical aggression, depressed mood, anxiety, and abnormal movements. In general, Risperdal was well-tolerated and reported to be very helpful in 26 (41%) patients, moderately helpful in 17 (27%), slightly helpful in 10 (16%), and not helpful in 11 (17%) patients.

6. In a letter to the editor, Jeanblanc and Davis reported the use of Risperdal in five elderly patients (4 with dementia of the Alzheimer's type and 1 with vascular dementia). The age range was 70-91 years. A marked reduction or elimination of the patients' dementia-related agitation or violent behavior was observed within 7-10 days at Risperdal doses of 1.5-2.5 mg/day. Mild extrapyramidal symptoms were reported in two patients.

7. Kopala and Honer reported the use of Risperdal (1.5 mg) for persistent vocalizations in two elderly patients (92 and 78 years) with combined Alzheimer-vascular dementia. Vocalizations were reported to decrease to less than 20% of baseline ratings with Risperdal. Moreover, a decrease in Extrapyramidal System Rating Scale (ESRS) score was noted in one patient with dyskinesia.

8. Lacro et al. reported the results of 4 pooled open-label independent studies involving 47 patients (mean age 67.9) with schizophrenia, dementia, delusional disorder and mood disorder with psychotic features who receive Risperdal at a mean dose of 3.2 mg/day for a mean duration of 10.8 weeks. Target symptoms which included psychotic symptoms and severe behavioral disturbances were reported to improve in 85% of the patients after Risperdal was initiated. Statistically significant ($p < 0.01$) improvement in cognitive function (mean scores on the Mini-mental State Exam) was also reported in a subsample of 19 patients. Adverse effects reported included hypotension (5), sedation (5), salivation (3) and EPS (1).

9. Lavretsky et al. conducted a 10-week open-label study of Risperdal for the treatment of agitation in 15 elderly patients (mean 78 years) with dementia. The range of Risperdal dose was 0.5-3.0 mg. All patients who received Risperdal were improved or very much improved at 10 weeks based on the Clinical Global Impression scale (CGI). After 2 weeks of treatment, 50% of patients were reported to improve on the Overt Aggression Scale (OAS) while 50% improvement was reported on the Cohen-Mansfield Agitation Inventory (CMAI) after 8 weeks of treatment with Risperdal. Four patients reported EPS. Mean

Mini-Mental State Exam (MMSE) scores decreased and Unified Parkinson's Disease Rating Scale (UPDRS) scores increased over 10 weeks.

10. In a letter to the editor published in the Lancet, Allen et al. described three patients with Lewy body dementia (LBD) who were treated with low dose Risperdal (0.5 to 1 mg per day). All three patients showed improvement in their behavioral and psychotic symptoms as measured by the Alzheimer's disease rating scale. Cognitive function either improved or stayed the same during Risperdal therapy.

11. Lee et al. reported the use of Risperdal in a 74-year-old female patient with senile dementia of Lewy body type (SDLBT). The patient received Risperdal 5 mg/day which was titrated over 10 days. Due to drowsiness and increased confusion, Risperdal was reduced to 1 mg BID. The patient's mental and cognitive state showed a gradual improvement after the dose reduction. In a letter to the editor, McKeith et al. cautioned about the possibility of sensitivity reactions to Risperdal in Lewy body dementia.

12. In a case series, Madhusoodanan et al. reported the efficacy of Risperdal in 11 geriatric patients (mean age 69.4) years with schizophrenia, schizoaffective, bipolar and senile dementia. The mean dose of Risperdal was 4.9 mg/day. Overall, 8 patients responded to Risperdal and 7 had marked decreases in their positive and negative symptoms. Decreases in EPS and tardive dyskinetic symptoms were also reported in 4 patients. Adverse events reported such as hypotension, orthostatic hypotension, somnolence, headache, abdominal cramps and dizziness were considered negligible.

13. Madhusoodanan et al. reported the results of a 12-week open multicenter study to evaluate the efficacy and safety of Risperdal used at a mean dose of 2.4 mg/day in 103 elderly (mean age 71 years) with schizophrenia and schizoaffective disorder. Statistically significant reductions in severity of symptoms were reported on the Positive and Negative Symptoms Scales (PANSS) total and subscales. When efficacy was assessed by the Clinical Global Impression Scale (CGI), 62% of the patients were reported to at least minimally improved at endpoint (11% very much improved, 24% much improved, 27% minimally improved). Patients who received Risperdal $\leq$ 3 mg/day (64% improved) were more likely to improve than > 3 mg/day (58% improved). The most frequently reported side effects were dizziness, insomnia, agitation, somnolence and injury. EPS was reported to decrease from baseline to endpoint.

14. In a letter to the editor, Meco et al. suggested that Risperdal (range 0.25-1.25) may be effective for hallucinations in six levodopa-treated elderly (mean age 71.17 years) patients with Parkinson's disease. No worsening of EPS was reported.

15. Raheja et al. reported the successful use of Risperdal in two geriatric (76 and 82 years) patients to control behavioral disorders. The Risperdal dose in the two patients was 3 mg/day.

16. Reyntjens et al. conducted a 5-week pilot study to evaluate the effect of Risperdal in forty geriatric patients with behavioral disturbances. Risperdal was

started at 0.5 mg BID and the dose was adjusted based on therapeutic response and side effects. The results suggested that Risperdal is an effective and well-tolerated drug for the management of behavioral symptoms in geriatric patients.

17. Zarate et al. conducted a retrospective study to evaluate the use of Risperdal in 122 elderly patients with diagnoses of dementia, mood and psychotic disorders. The mean dose of Risperdal was 1.6 mg. Risperidone was effective in 85% of the 108 patients who continued treatment based on the Clinical Global Impression Improvement Scale (CGI-I). The common adverse events reported included hypotension (29%), EPS (11%) and symptomatic orthostasis (10%).

18. Borison et al. reported on the use of Risperdal in 22 elderly patients with schizophrenia or dementia (Alzheimer's disease).

19. Czobor P, et al. reported on the positive effect of Risperdal on hostility in elderly with schizophrenia.

INDICATIONS, USES, DOSE RECOMMENDATIONS

1. Risperdal is indicated for the management of the manifestations of psychotic disorders.

2. ***Elderly:*** In general, a lower starting dose is recommended for an elderly patient, reflecting a decreased pharmacokinetic clearance in the elderly, as well as a greater frequency of decreased hepatic, renal or cardiac function, and a greater tendency to postural hypotension. In healthy elderly subjects renal clearance of both Risperdal and 9-hydroxyrisperidone was decreased, and elimination half-lives were prolonged compared to young healthy subjects. Dosing should be modified accordingly in the elderly patients.

3. The recommended **initial dose** is 0.5 mg BID in patients who are elderly or debilitated, patients with severe renal or hepatic impairment, and patients either predisposed to hypotension or for whom hypotension would pose a risk. **Dosage increases in these patients should be in increments of no more than 0.5 mg BID.** Increases to dosages about 1.5 mg BID should generally occur at intervals of at least 1 week. In some patients slower titration may be medically appropriate. Elderly or debilitated patients, and patients with renal impairment, may have less ability to eliminate Risperdal than normal adults may. Patients with impaired hepatic function may have increases in the free fraction of the Risperdal, possibly resulting in an enhanced effect. Patients with a predisposition to hypotensive reactions or for whom such reactions would pose a particular risk likewise need to be titrated cautiously and carefully monitored.

SAFETY ISSUES

1. The favorable safety profile of Risperdal demonstrated in 6-8 week short-term studies has been confirmed in seven 1-year safety studies involving over 1,100 patients. The most common side effects reported with Risperdal in short-term studies are insomnia, agitation, EPS, headache, anxiety, and rhinitis.
2. The long-term safety of Risperdal has been reported in 1,156 patients enrolled in seven 1-year clinical trials (Belcher, 1996). Adverse events reported in these 1-year trials were consistent with the findings from short-term double-blind studies. The range of the mean

dose of Risperdal in the long-term trials was 7.6-9.4 mg/day. Although the mean dose of Risperdal was higher than the doses used in practice (avg. dose for schizophrenia: 4.7 mg/day; all conditions: 3.2 mg/day) and found to be optimal in clinical trials (4-6 mg), the adverse events' profile of Risperdal from the long-term studies was similar to that reported in short-term pivotal trials.

Extrapyramidal symptoms/Tardive dyskinesia

3. Risperdal's potent effects at $5HT_{2A}$ receptors may be responsible for the low incidence of neurological adverse effects, such as EPS, associated with it use. Importantly, Risperdal at a dose of $\leq$ 10 mg/day has demonstrated an incidence of extrapyramidal symptoms (EPS) comparable to placebo (Risperdal product labeling). Marder (1994) reported that there were no significant differences in Extrapyramidal Symptom Rating Scale (ESRS) score between patients receiving placebo and Risperdal $\leq$ 6 mg.

4. In a study of 36 schizophrenic patients, Borison (1992) concluded that Risperdal decreased the signs of tardive dyskinesia. Chouinard (1995) determined that Risperdal had a significant beneficial effect on tardive dyskinesia in the Canadian Multi-center Risperdal study of 135 schizophrenic patients. In a post hoc analysis, Chouinard (1995) further examined the effects of Risperdal in patients with tardive dyskinesia from the Canadian Multi-center Risperdal study. The author reported that Risperdal at 6 mg/day had the most beneficial effect on tardive dyskinesia.

5. Brecher (1996) evaluated the long-term safety of Risperdal (mean dose 7.6-9.4 mg/day) in 1,156 patients enrolled in seven 1-year clinical trials. Only four cases (0.3%) of tardive dyskinesia were reported in the long-term studies.

Anticholingeric side effects

6. Risperdal's low affinity for muscarinic receptors is consistent with the relatively low incidence of anticholinergic adverse events reported in clinical trials conducted to evaluate its safety and efficacy. In these trials, the incidence of constipation was 3% in the placebo group and 7% in patients who received Risperdal in a dose of less than 10 mg/day, and 13% of patients who received 16 mg/day (Risperdal Product labeling). In a study conducted by Marder and Meibach (1994), the incidence of constipation was reported as 1.6% for both 2 and 6 mg daily doses of Risperdal.

Orthostatic hypotension

7. Risperdal may induce orthostatic hypotension especially during the initial dose-titration period, which is reflective of its alpha-adrenergic antagonistic properties. Orthostatic hypotension may be minimized, however, by following the recommended dose titration schedule. Syncope was reported in 0.2% (6/2670) of Risperdal-treated patients (Risperdal Product labeling).

Weight gain

8. Brecher (1996) reported a small weight gain with a mean increase in body weight per patient of 2.6 kg over the 1 year time period.

Sedation/Somnolence

9. The incidence of somnolence was reported as 3.2% and 3.1% respectively for 2 and 6 mg daily doses of Risperdal by Marder (1994) and is consistent with Risperdal's relatively low affinity for histamine H_1 receptors.

Laboratory monitoring

10. Laboratory monitoring, such as liver enzymes or white blood cell count is not required during Risperdal therapy since increased liver enzymes or white blood cells disorders have not consistently been reported in the pre-marketing studies or the post-marketing experience.

Other adverse effects

11. The most common adverse events reported in patients treated with Risperdal in pre-marketing clinical trials were insomnia, agitation, EPS, headache, anxiety, and rhinitis.

RISPERDAL SHORT AND LONG-TERM SAFETY

	Risperdal Safety Information	
Adverse Effects	**Short-term Safety**	**Long-term Safety**
Anticholinergic side effects	• No affinity for muscarinic cholinergic receptors • Minimal risk of anticholinergic side effects (e.g., constipation): • 3% placebo • 7% RIS ≤ 10 mg/day • 13% RIS 16 mg/day	• The rate of anticholinergic side effects is comparable to short-term studies
Extrapyramidal symptoms	• The incidence of EPS with Risperdal at doses ≤ 10 mg is comparable to placebo	• Long-term data indicates that the risk of EPS does not increase with extended use
Tardive dyskinesia	• Risperdal may have a beneficial effect on tardive dyskinesia in some patients	• Only four cases of (0.3%) of tardive dyskinesia reported in long-term studies
Somnolence	• Risperdal causes minimal somnolence at ≤ 10 mg/day • RIS ≤ 10 mg/day: 3 % • RIS 16 mg/day: 8% • Placebo: 1%	• The rate of somnolence is comparable to short-term studies
Weight gain	• The incidence of weight gain (≥ 7% of body weight) with Risperdal has been reported as 18% compared to 9% with placebo	• Weight gain data from long-term studies revealed a mean increase in body weight of 2.6 kg (range 1.8-3.3 kg) or 5.72 lb. (range 3.96-7.26 lb.). The mean duration of exposure was 213 days.

	Risperdal Safety Information	
Adverse Effects	**Short-term Safety**	**Long-term Safety**
Prolactin	• Greater plasma prolactin elevations than haloperidol • No correlation between prolactin-related adverse effects (e.g., gynecomastia, galactorrhea, oligomenorrhea, erectile and ejaculatory dysfunction) and prolactin levels in men and women	• Limited available data are similar to short-term data • Long-term study in progress
Electrocardiographic changes	• Mean QTc changes: Range –5.5 to + 2.7 msec Clinically insignificant	• Mean QTc changes: Range –0.9 to +4.4 msec Clinically insignificant
Liver enzymes monitoring	• No monitoring required	• No monitoring required
White blood cell monitoring	• No monitoring required	• No monitoring required

DRUG INTERACTIONS

1. There have been no systematic evaluations of interactions between Risperdal and other drugs, to date. Given the primary central nervous system effects of Risperdal, caution should be used when Risperdal is taken in combination with other centrally acting drugs or alcohol.

2. Risperdal may antagonize the effects of levodopa and dopamine agonists.

3. Chronic administration of carbamazepine with Risperdal may increase the clearance of Risperdal.

4. Chronic administration of clozapine with Risperdal may decrease the clearance of Risperdal.

DRUG ADMINISTRATION FACTORS

1. Risperdal 1 mg/ml oral solution has been approved by the Food and Drug Administration (FDA) and is commercially available.

2. Data submitted to the FDA demonstrated that the Risperdal 1mg/ml oral solution is bioequivalent to the 1 mg tablets. Gutierrez presented, in a poster, the results of an open-label, randomized, two-way crossover study comparing the bioavailability of Risperdal as a 1-mg tablet and 1-mg/ml oral solution in 23 healthy male subjects. The tablet and the oral solution were given as a single 1-mg dose and were separated by a 10-day washout period. The 90% confidence intervals on the relative bioavailability for Risperdal, 9-hydroxyrisperidone, and total Risperdal for Cmax and AUC were within the equivalence range of 80-120%. Both formulations are bioequivalent and were well tolerated.

3. The oral solution is supplied in 100 ml bottles with a calibrated (in milligrams and milliliters) pipette. The minimum calibrated volume is 0.25 mL, while the maximum calibrated volume is 3 mL.

4. **Tests indicate that Risperdal oral solution is compatible in the following beverages: water, coffee, orange juice, and low-fat milk; it is NOT compatible with either cola or tea.**

COST

1. Utilizing Risperdal as the branded anti-psychotic of choice in behavioral disturbances associated with dementia, in residents who have not responded or tolerated conventional antipsychotic agents, will provide cost savings to the payer of the pharmacy bill. When compared to other branded anti-psychotic currently available on the market (Zyprexa®).

SUMMARY

Risperdal possess several characteristics that make it a "select" agent for use in the geriatric population. Risperdal has been proven effective for the positive and negative symptoms of psychosis while exhibiting an excellent safety profile, unlike the older, first generation anti-psychotic agents. Risperdal can be administered by tablet or liquid, can be given in a twice daily regimen, and, when compared to the other branded anti-psychotic, provides a cost savings to the payer of the pharmacy bill. For these reasons we are initiating an intervention program to:

1. **Initiate anti-psychotic therapy with Risperdal when a new, atypical agent is selected for use.**

2. **Suggest Risperdal as the anti-psychotic of choice when a resident has experienced adverse effects or therapeutic failure with a trial of a conventional anti-psychotic.**

REFERENCES

Available for review.

CONVENTIONAL VS. ATYPICAL ANTIPSYCHOTICS

The new atypical antipsychotic agents include clozapine (Clozaril®), risperidone (Risperdal®) and olanzapine (Zyprexa®). Although there is no universally accepted definition for atypicality, in general an atypical antipsychotic has a higher 5HT2 (serotonin 2) to D2 (dopamine 2) ratio resulting in less extrapyramidal symptoms and improved efficacy against the negative symptoms associated with schizophrenia. In addition, the atypical antipsychotic drugs carry a lower risk of tardive dyskinesia than the conventional antipsychotic agents.

Mechanism of action...

1. The conventional antipyschotics primarily block the *dopamine* D_2 receptors
2. The atypical antipsychotics block the *dopamine* D_2 and *serotonin* $5HT_2$ receptors to various degrees
3. The atypical antipsychotics have higher $5HT_2$ to D_2 ratios than the conventional antipsychotics

Safety...

1. The conventional antipsychotics, especially the high-potency agents, frequently cause extrapyramidal side effects such as pseudoparkinsonism, acute dystonia, and akathisia
2. The atypical antipsychotics cause less extrapyramidal side effects due to a higher $5HT_2$ to D_2 ratio
3. The atypical antiphsychotic agents have a lower risk of tardive dyskinesia

RISPERDAL...

* **Extra Pyramidal Symptoms**
Short-term studies have shown that the incidence of EPS with Risperdal at doses ≤ 10 mg/day is comparable to placebo
- **Placebo: 16%**
- **RIS ≤ 10 mg/day: 17%**
- **RIS 16 mg: 34%**

Long-term data indicates that the risk of EPS does not increase with extended use

* **Tardive dyskinesia**
- **Low incidence (0.3%) in long-term studies**
- **Risperdal may have a beneficial effect on tardive dyskinesia**

References

1. Kane JM. Schizophrenia. N Engl J Med 1996;334(1):34-41.
2. Love RC. Novel versus conventional antipsychotic drugs. Pharmacotherapy 196;16 (1 Pt 2):16S-10S.
3. Risby BR, Donnigan D, et al. Formulary considerations for treating psychiatric disorders: Schizophrenia. Formulary 1997;32:142-55.

Table 1: Summary of Published Reports on the Use of Risperidone in the Geriatric Population

Study	Patients	Risperidone Dosing	Efficacy Results	S
Aronson et al. Retrospective	n=32; mean age 74.3 years Behavioral disturbances in dementia, schizophrenia, bipolar, major depressive disorder with psychotic features, delusional disorders	mean=2.72 mg/day Duration 6.6 months	Improved CGI (31) Clinically significant improve-ment CGI scores (24)	N
Berman et al. Open-label	n=10; mean age 71 years Schizophrenia	Maximum 6 mg/day	Statistically significant improvement in psychiatric scores: PANSS total (p=0.002), negative (p=0.03), general score (p=0.02) Statistically significant improvement on cognitive scores (MMSE, Digit Symbol; p<0.05)	P c r N E S s (
Frenchman et al. Retrospective	n=186; ≥ 65 years Alzheimer's disease, senile dementia, organic brain syndrome	RIS: 1 mg/day Haloperidol: 2 mg/day Thioridazine: 33 mg/day	Target symptoms improvement: RIS: 95% Haloperidol: 66% Thioridazine: 65%	E R H T
Gierz et al. Open-label	n=35: Age: 55.6-71 years Schizophrenia, organic delusional disorder, bipolar, dementias	range: 1.75-5.64	60% improved considerably (21/35)	6 s S
Jeanblanc & Davis Case reports	n=5; Age: 70-91 years Alzheimer's and vascular dementia	1.5-2.5 mg/day	Marked reduction in dementia-related agitation/violence in all patients	N
Kopala and Honer Case reports	n=2; Age=92-78 Combined Alzheimer-vascular dementia	1.5 mg	Vocalizations decreased by 20% of baseline ratings Decrease in ESRS score in one patient with dyskinesia	N
Lacro et al. Pooled open studies	n=47; mean age 67.9 Schizophrenia, dementia, delusional disorder, mood disorder with psychotic features	mean 3.2 mg/day 10.8 weeks	Target symptom improvement in 85% of patients MMSE improved in subsample of 19 patients, p<0.01	H S S E
Lavretsky et al. Open-label	n=64; mean age 78 Agitation in dementia	range 0.5-3.0 mg	All patients improved or very much improved via CGI at 10 weeks CMAI: 50% improvement after 8 weeks OAS: 50% improvement after 2 weeks	E 1 1
Allen et al. Case reports	n=3; Age 66-78 Lewy body dementia	range 0.5-1 mg/day	All three patients improved in their behavioral and psychotic symptoms via Alzheimer's rating scale Cognitive function improved or stayed the same	
Lee et al. Case reports	n=1; 74 years Lewy body type dementia	1 mg bd	Gradual improvement in mental and cognitive state	D
Madhusoodanan	n=11; mean age 69.4	4.9 mg/day	8 patients responded	N

Et al. Case reports	Schizophrenia, schizoaffective, bipolar, senile dementia		7 had marked decrease in positive and negative symptoms Decrease in preexisting EPS and tardive dyskinesia (4)	H O S a
Madhusoodanan Et al. Open-label, Multi-center	n=103; mean age 71 Schizophrenia and schizo-affective	2.4 mg/day	Statistically significant reductions in PANSS total and subscales 62% minimally improved via CGI Patients who received RIS $\leq$ 3 mg/day (64% improved) more likely to improve than > 3 mg/day (58% improved)	e D s E t
Meco et al. Letter to the Editor	n=6; mean 71.17 years Hallucinations / parkinson's disease	range 0.25-1.25 mg/day	Effective for hallucinations in L-dopa-treated patients	N
Raheja et al. Case reports	n=2; 76, 82 years Behavorial disorders	3 mg/day	Symptoms improvement in both patients	N
Reyntjens et al. Open-label	n=40; Behavioral disturbances	Starting dose 0.5 mg bid Titrated based on response and side effects	Effective for the management of behavioral disturbances	N
Zarate et al. Retrospective	n=122; $\geq$ 65 years old Dementia, mood and psychotic disorders	mean 1.6 mg/day	Effective in 85% of patients via CGI-I	H E O

CONFIDENTIAL

Risperidone (Risperdal)
Information for Omnicare Pharmacists

Information for Dispensing Pharmacists

Dispensing pharmacists have the unique opportunity to perform clinical interventions prior to dispensing a prescription. The following scripts were developed to facilitate the appropriate intervention prospectively .

Scenario #1
A new prescription for an atypical antipsychotic is received

We have received a new prescription for [Name of atypical antipsychotic, dosage, and frequency].
As Risperdal is the only atypical that has been studied in the elderly for controlling behaviors and also offers a significant price advantage for the payer when compared to other atypical antipsychotics I would recommend Risperdal [dosage and frequency] in this resident.

Scenario #2
A resident is already taking an antipsychotic drug and a new prescription for Artane or Cogentin or Symmetrel has been added due to abnormal movement side effects from a typical antipsychotic

(Do not initiate this interchange if the resident has Parkinson's Disease - if the diagnosis is unclear, or unavailable, check medication regimen for the presence of Parkinson's medications)

Risperdal has been studied in the elderly for controlling behaviors associated with geriatric dementia and/or psychotic disorder and has significantly less side effects compared to conventional antipsychotic agents. This resident is receiving (antipsychotic name /dose) and [] appears to have been added to address extra-pyramidal side effects. Recommend reassessing the continuation of [name of typical antipsychotic] and/or initiating Risperdal __mg__times daily

Scenario #3
A resident is receiving a typical antipsychotic drug and a prescription to increase the dosage of Artane or Cogentin or Symmetrel is received.

(Do not initiate this interchange if the resident has Parkinson's Disease - if the diagnosis is unclear, or unavailable, check medication regimen for the presence of Parkinson's medications)

Risperdal has been studied in the elderly for controlling behaviors associated with geriatric dementia and/or psychotic disorder and has significantly less side effects compared to conventional antipsychotic agents. This resident is receiving (antipsychotic name /dose) and the dose of [] has been increased to address extra-pyramidal side effects. Recommend reassessing the continuation of [name of typical antipsychotic] and/or initiating Risperdal __mg__times daily.

Information for Consultant Pharmacists

Consultant Pharmacists are optimally positioned to discuss the clinical benefits of a therapy with physicians and nurses. The following scripts were developed to assist the consultant pharmacist to discuss the appropriate use of Risperdal.

Scenario #1
Initiating Risperdal therapy when an atypical antipsychotic is already being prescribed.

As Risperdal is the only atypical that has been studied in the elderly for controlling behaviors and also offers a significant price advantage for the payer when compared to other atypical antipsychotics I would recommend Risperdal [dosage and frequency] in this resident.

Scenario #2
Initiating Risperdal therapy when a typical antipsychotic is being prescribed.

[Name of resident] is currently receiving [name, dosage, and frequency of the present typical antipsychotic]. As you are aware, [name of drug] is associated with significant side effects, which could include extrapyramidal side effects (EPS), tardive dyskinesia (TD), as well as anticholinergic side effects. [Name of Drug] side effect profile is also associated with an increased incidence of falls and fractures. Due to the potential for these adverse effects, I would recommend changing [name of drug] to Risperdal (dosage and frequency).

Scenario #3

Interchanging Risperdal when resident is receiving a typical antipsychotic and an anticholinergic agent (Cogentin, Artane and Symmetrel) is being prescribed to control extrapyramidal side effects.

Resident is currently receiving [name, dosage, frequency of the present typical antipsychotic] and [name of anticholinergic] to control EPS symptoms. Due to the presence of this adverse drug reaction, I

recommend that this therapy be modified to the use of Risperdal [dosage and frequency].

Drug Regimen Review Comments

Resident is exhibiting inappropriate behavior warranting the use of an antipsychotic and is presently receiving a typical agent.

This resident is receiving [name, strength, dose drug] for [diagnosis / behavior] and continues to have documentation of this behavior. Recommend discontinuing/tapering [name of drug] and initiating Risperdal ___mg ___times per day. Risperdal has been studied in the elderly for controlling behaviors associated with geriatric dementia and/or psychotic disorder and has a lesser side effect profile compared to conventional antipsychotics.

Resident is exhibiting inappropriate behavior warranting the use of an antipsychotic and is presently receiving an atypical agent.

This resident is receiving [name, strength, dose drug] for [diagnosis/ behavior]. Recommend discontinuing/ tapering [name of drug] and initiating Risperdal ___mg ___times per day. Risperdal has been studied in the elderly for controlling behaviors associated with geriatric dementia and/or psychotic disorder and significantly reduces the cost to the payer of the pharmacy bill.

An anticholinergic drug has been added due to side effects from a typical antipsychotic.

[Name of anticholinergic] apparently has been added to address apparent EPS side effects of [name of typical antipsychotic]. Recommend discontinuing/tapering [name of typical antipsychotic and name of anticholinergic] and initiating Risperdal __mg__times daily. Risperdal has been studied in the elderly for controlling behaviors associated with geriatric dementia and/or psychotic disorder and has a lesser side effect profile compared to conventional antipsychotics.

Resident has an anticholinergic dosage increase and is receiving a typical antipsychotic

[Anticholinergic drug] dosage has been increased apparently to address EPS side effects of [name of typical antipsychotic]. Recommend discontinuing/tapering [name of typical antipsychotic and name of anticholinergic] and initiating Risperdal __mg__times daily. Risperdal has been studied in the elderly for controlling behaviors associated

with geriatric dementia and/or psychotic disorder and has a lesser side effect profile compared to conventional antipsychotics.

Typical antipsychotic therapy for a resident with Parkinson's Disease

This resident has a diagnosis of Parkinson's Disease and is receiving [name of typical antipsychotic]. This therapy may exacerbate symptoms and reduce the effectiveness of Parkinson's therapy. Recommend discontinuing/tapering this therapy and initiating Risperdal __mg ___times per day. Risperdal has been studied in the elderly for controlling behaviors associated with geriatric dementia and/or psychotic disorder and has a lesser side effect profile compared to conventional antipsychotics.

An atypical (non-Risperdal) antipsychotic is being utilized

This resident is receiving [atypical antipsychotic]. Recommend discontinuing /tapering and initiating Risperdal ___mg ___times daily. Risperdal has been studied in the elderly for controlling behaviors associated with geriatric dementia and/or psychotic disorder and costs less than other atypical agents.

A conventional antipsychotic is being utilized and the resident is exhibiting signs of tardive dyskinesia or extrapyramidal symptoms.

This resident is currently receiving [name, dosage, and frequency of the present atypical antipsychotic]. Recommend a change to Risperdal because this resident is experiencing side effects of muscle and facial expressions, lip and peripheral area puckering, and choreic movements according to nurses notes and last AIMS test dated _____. Atypical antipsychotics, such as Risperdal, have less potential for producing extrapyramidal symptoms.

The mnemonic SWITCH can be a good reminder for changing therapy:

S start atypical agent at low dose
W with draw conventional agent slowly using standard tapering
I involve resident by providing drug information, if applicable
T titrate atypical agent as recommended until therapeutic effect reached
C challenge adverse effects, if needed
H halt conventional therapy

COMPARATIVE POTENCIES OF ANTIPSYCHOTICS

Generic/Brand	Potency Index Antipsychotic Daily dose**		**Risperdal equivalent/day**
risperidone/Risperdal	1	***	***
haloperidol/Haldol	1	2mg	2/1 = 2mg /day or 1mg bid
thioridazine/Mellaril	20	75mg	75/20 = 3.75mg/day or 2mg bid
perphenazine/Trilafon	4	4mg	4/4 = 1mg/day or 0.5mg bid
thiothixene/Navane	2	4mg	4/2 = 2mg/day or 1mg bid
olanzapine/Zyprexa	5*	10mg	10/5 = 2mg/day or 1mg bid
quetiapine/Seroquel	100*	150mg	150/100= 1.5 mg/day or 1 mg bid

Risperdal has been selected as the antipsychotic of choice in behavioral disturbances associated with dementia and/or psychotic disorders, ***in residents who have not responded or tolerated conventional antipsychotic agents or who are beginning therapy with as atypical agent*. Risperdal should be suggested as the antipsychotic of choice when a resident has experienced adverse effects or therapeutic failure with a trial of a conventional antipsychotic.

Risperdal can be administered by tablet or liquid, can be given in a twice daily regimen or due a long half life, some residents may be candidates for daily dosing, and provides a cost savings to the payer of the pharmacy bill. When antipsychotic therapy with a new, atypical agent is indicated, Risperdal should be recommended.

*The potency index was derived by assigning a value of 1 to the most potent agents, based on the American Psychiatric Association's Practice Guideline for the Treatment of Residents with Alzheimer's Disease and Other Dementias of Late Life. The remaining less potent agents were then assigned an index based on initial dosing information contained in this practice guideline. The use of olanzapine (Zyprexa) and quetiapine (Seroquel) was not addressed in the APA Practice Guideline. Thus, the conversion factor was based on dosing information. While immediate discontinuation of the previous antipsychotic may be acceptable for some residents, more gradual discontinuation may be most appropriate for other residents. In all cases, the period of overlapping antipsychotic administration should be minimized.

Risperdal Dosing Conversions

Haldol to Risperdal
To be done on a mg for mg basis. If receiving Haldol 2mg/day, convert to Risperdal 2 mg/day (i.e. 1 mg BID).

Mellaril to Risperdal
Divide daily Mellaril dose by potency index (20) to get daily dose of Risperdal (i.e. Mellaril 50mg/day divided by 20 equals 2.5 mg/day of Risperdal)

Trilafon to Risperdal
Divide daily Trilafon dose by potency index (4) to get daily dose of Risperdal
(i.e. Trilafon 4 mg/day divided by 4 equals 1 mg/day of Risperdal)

Navane to Risperdal
Divide daily Navane dose by potency index (2) to get daily dose of Risperdal
(i.e. Navane 4 mg/day divided by 2 equals 2 mg/day of Risperdal)

Zyprexa to Risperdal
Divide daily Zyprexa dose by potency index (5) to get daily dose of Risperdal (i.e. Zyprexa 10mg/day divided by 5 equals 2 mg/day of Risperdal)

Seroquel to Risperdal
Divide daily Seroquel dose by potency index (100) to get daily dose of Risperdal
(i.e. Seroquel 150/day divided by 1.5 mg = 2 mg of Risperdal.

Note: These dosage conversions are based upon a recent psychiatric practice guideline for the elderly and a manufacturer's package insert, not upon data from randomized, double blind clinical trials. Behavioral manifestations of dementia and/or psychotic disorders in the long-term care setting are highly variable, and clinical judgment is necessary both before and after initiating a conversion to Risperdal on each resident.

Stepwise Approach For Switching From a Conventional Antipsychotic to Risperidone[4,5]

1. Begin starting dose of risperidone once daily at bedtime to the existing regimen
2. Wait at least 5-7 days

3. Reduce dosage of current agent over several weeks, while gradually increasing risperidone to "target dose".
4. Reduce any concomitant anticholinergic or antiparkinsonism medication over several weeks

- There are no recommendations regarding conversion from other atypical medications to risperidone, however, a gradual conversion such as this would seem reasonable.

References

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4. Aronson, SM. Use of Newer Antipsychotic Agents For Behavioral Symptoms in Pharm 1996 (Suppl D); 11:12-15.

OMNICARE , Inc.

Omnicare, Inc., headquartered in Covington, Kentucky, is a leading geriatric pharmaceutical care company. Currently serving approximately 628,000 residents in more than 8,800 long-term care facilities in 43 states. Omnicare is the nations largest provider of professional pharmacy, related with health care providers. In addition, Omnicare is the fifth largest global contract research organization ("CRO") providing comprehensive clinical research services for the pharmaceutical and biotechnology industries in 23 countries.

Omnicare employs over 1,000 pharmacists. Approximately 500 Omnicare pharmacists go into facilities as consultant pharmacists. These pharmacists consult with physicians on proper medications and help initiative health management programs.

Omnicare publishes a formulary guide for all its provider sites on an annual basis. This book is called The "Geriatric Pharmaceutical Care Guidelines" and is published in conjunction with the University of Sciences in Philadelphia. The University, based on clinical evaluation suggests medications in over 100 therapeutic drug categories to be positioned in preferred, acceptable, or unacceptable categories . Omnicare will then take this information, and add a cost component (cost to the payer) to be added to the positioning.

During 1997, The Johnson &Johnson Long Term Care Business Group along with Johnson and Johnson Health Care Systems signed a performance based contract with Omnicare, Inc. The contract provided for a performance driven tiered rebate to be implemented for Johnson & Johnson strategic brand pharmaceutical products including Ultram, Duragesic, Propulsid, Procrit, Risperdal, Levaquin, and Floxin.

Currently, Omnicare is running two initiatives for products produced at Janssen and Ortho-McNeil. Risperdal has generated an all time market share high of 55.5% throughout the 1st quarter of 2000. This market share represents Omnicares ability in persuading physicians to write Risperdal in the areas of Behavioral Disturbances associated with Dementia.

Omnicare also has an initiative under way for the antibiotic Levaquin for Urinary Tract Infections and Community Acquired Pneumonia. At the end of the first quarter, Levaquin reached an all time high market share of 67.02%. Once again, demonstrating Omnicare's ability to persuade physicians to write the most efficacious medication based on clinical evidence.

The partnership has grown beyond product interventions. Omnicare's Clinical Research Organizations have been involved with past clinical studies and offers potential in a geriatric specific environment for products such as Reminyl.

Janssen and Omnicare have also piloted an e-commerce initiative that would demonstrate Omnicare's abilities in persuading physicians to write medications in a less structured assisted care living environment. There are also meetings currently underway that would look at a partnership approach in the European sector, in addressing the same type of product interventions with Janssen Cilag in England.

Omnicare, Inc. has demonstrated its ability to partner in a true sense of the word and has generated well over 100 million dollars of Johnson & Johnson pharmaceuticals annually.

OMNICARE MEMORANDUM
Professional Services

DATE: November 23, 2001

FROM: Mark E. Lehman
Chief Clinical Officer

Lisa R. Welford
Director, Clinical Operations

TO: Omnicare Operations Managers
Omnicare Consultant Coordinators
(copy and distribute to all Omnicare Consultants)

RE: Risperdal Fax Campaign

CC: Tim Bien
Gary Erwin
RVP's
RCD's

Beginning November 5th and ending November 20th, Omnicare Senior Health Outcomes, a subsidiary of Omnicare Inc., initiated a national program to highlight the superior safety and effectiveness of atypical versus conventional antipsychotics in the resident populations we serve. Omnicare's goal was to focus efforts on those residents who may benefit by conversion from a conventional antipsychotic agent, such as haloperidol, mesoridazine (Serentil®), thioridazine, or fluphenazine to Risperdal®.

Using a national prescription claims database, residents receiving conventional antipsychotics and who may potentially benefit from conversion to Risperdal® were identified. Physicians received a letter via facsimile, or a telephone call and a letter via mail, asking for conversion to Risperdal® therapy.

Upon being presented with sound scientific evidence, a significant number of physicians agreed to the conversion from a conventional antipsychotic to Risperdal®. This interchange occurred across all patient population types. **A significant number of physicians also responded by agreeing to "consider Risperdal® for the resident at the next visit."**

Each Omnicare consultant should have received a copy of the patient specific responses generated by this fax campaign. There must continue to be ongoing communication between consultant pharmacists and those physicians who agreed to re-evaluate. Consultants should have discussions with physicians who indicated they would be open to

reconsidering therapy and be armed with the appropriate clinical information. Comments should be generated and may be modified to include the following language:

"Recently you received clinical information regarding the safety and effectiveness of atypical antipsychotics vs. conventional agents. Your response indicated the need for further evaluation of this resident." Insert comment i.e. BD11

Comment

This resident is receiving $
(Haldol/Loxitane/Stelazine/Trilafon/Prolixin/Orap/Mellaril/Thorazine/Serentil/Navane/Moban/Etrafon/Triavil).

Recommendation

Please consider changing to risperidone (Risperdal) 0.5mg, as the risk of development of EPS with $ is high, and risperidone should adequately control behaviors while exhibiting a much more favorable side effect profile.

It is imperative that each and every resident on a conventional antipsychotic be re-evaluated for appropriate conversion to an atypical antipsychotic, with Risperdal® being the more cost effective GPCG "preferred" alternative. In addition, residents excluded from the formal fax initiative should not be excluded from ongoing formal consultant pharmacist evaluation for potential conversion to Risperdal® where clinically appropriate.

Many of our physicians have indicated their willingness to re-evaluate or convert residents to more appropriate antipsychotic therapy. Please make it a priority to maintain the momentum generated by the dissemination of this significant clinical information.

Thank you in advance for your follow-up in this important clinical initiative.

PAL Template Updated 6/1/00

OMNICARE PHYSICIAN AUTHORIZATION LETTER TEMPLATE

Dear Physician:

By checking the options below and signing this document you will authorize Omnicare pharmacists to modify existing orders and dispense the following alternative medications based on interchange protocols. This process promotes medication management which is therapeutically beneficial or equal and forwards cost effectiveness to the payer whenever possible. It will also reduce the number of individual drug regimen review comments. Conversion protocols will be implemented as noted below.

YES NO

ACE INHIBITOR INTERCHANGE

(Interchange to occur at point of dispensing or via consultant based on availability of appropriate diagnosis)

- **Zestril®** will be dispensed in lieu of other ACE inhibitors
  Monitoring will be initiated as follows:
  - BP q shift x 72 hours then weekly.
  - Serum potassium and creatinine/BUN should be checked periodically after initiating or modifying therapy and status will be monitored by consultant pharmacist.

  **Capoten® (captopril) will not be interchanged when unaccompanied by a diagnosis or with a documented diagnosis of diabetic nephropathy.*

ADALAT CC INTERCHANGE

(Interchange to occur via consultant based on medical record review if order is unaccompanied by a diagnosis)

- **Adalat CC®** will be dispensed in lieu of an equivalent dose of Procardia XL® for a diagnosis of hypertension only.

ATYPICAL ANTIPSYCHOTIC INTERCHANGE

(If interchange occurs prospectively, antipsychotic interchange may be done *only* for new orders on existing residents defined as those in the facility for five days or longer. If retrospective, the consultant pharmacist may use their clinical judgment based upon the availability of resident specific data.)

Risperdal® (risperidone) will be dispensed in lieu of Zyprexa® and Seroquel® for a diagnosis of Dementia (Alzheimer's /OMS) only, with a starting dose of Risperdal® 0.5mg QD.

COX-2 INHIBITOR INTERCHANGE

(Interchange to occur at point of dispensing)

- **Celebrex® (celecoxib) will be dispensed in lieu of an equivalent dose of Vioxx®**

FLUOROQUINOLONE INTERCHANGE

(Interchange to occur at point of dispensing)

- **Levaquin®** (levofloxacin) will be dispensed in lieu of an equivalent dose of other fluoroquinolones. This interchange excludes Noroxin®. Trovan® may only be interchanged after diagnosis verification.

HMG CO-A REDUCTASE INHIBITOR INTERCHANGE

(Interchange to occur at point of dispensing)

- **Lipitor®** will be dispensed in lieu of **Pravachol®, Zocor® and Mevacor®.**
  - All doses (except Zocor® 40mg) will be converted to Lipitor® 10 mg daily.
  - Zocor® 40mg will be converted to Lipitor® 20 mg.

  Note: Mevacor® 10mg will be excluded from the interchange process due to lack of demonstrated cost savings associated with this conversion.)

_____ _____ **H2 RECEPTOR ANTAGONIST INTERCHANGE**

(Interchange to occur at point of dispensing)

- **Omnicare Select H2 Receptor Antagonist of Choice** will be dispensed in lieu of other solid and liquid H2 Receptor antagonists. (Note: Cimetidine will not be eligible to be selected as Omnicare's H2 of Choice due to it's inferior clinical ranking in Omnicare's Geriatric Pharmaceutical Care Guidelines.)

_____ _____ **LEVOTHYROXINE INTERCHANGE**

(Interchange to occur via consultant based on medical record review)

- **Levothyroxine of Choice** will be dispensed in lieu of Synthroid® on a mg per mg basis. Following a change from one manufacturer to another, consultants must monitor the need for and/or request appropriate follow-up thyroid monitoring according to the combined clinical judgment of the pharmacist and physician.

_____ _____ **POTASSIUM CHLORIDE INTERCHANGE**

(Interchange to occur at the point of dispensing)

- **Sustained Release Potassium Preparation of Choice** will be dispensed in lieu of other sustained release potassium preparations on a mEq. per mEq. basis.

_____ _____ **PROTON PUMP INHIBITOR INTERCHANGE**

(Interchange to occur at the point of dispensing)

- **Proton Pump Inhibitor of Choice** will be dispensed in lieu of an equivalent dose of other PPI's.

_____ _____

PHYSICIAN SIGNATURE **DATE**

OMNICARE, INC.
Approved Interchange Protocols*

I. ACE INHIBITOR INTERCHANGE:

selected agent: Zestril® (lisinopril)

TOTAL DAILY DOSES IN MG ARE INDICATED: *if prescribed dosing regimen is not described below, prescriber clarification must be obtained.

ZESTRIL	MONOPRIL	VASOTEC	ACCUPRIL	LOTENSIN	ALTACE	CAPOTEN	MAVIK	UNIVASC
DOSED QD								
5	5	5	5	5	N/A	25	1	3.75
10	10	10	10	10	2.5	50	2	7.5
20	20	20	20	20	5	100	4	15
40	40	40	40	40	10	200	8	30

Note: Conversion tables are guidelines only. As individual resident specific data becomes available, i.e. during consultant review, clinical judgment supersedes.

II. H2 RECEPTOR ANTAGONIST INTERCHANGE:

selected agent: H2 of Choice

H2 DOSING EQUIVALENTS:

cimetidine (Tagamet®)	famotidine (Pepcid®)	nizatidine (Axid®)	ranitidine (Zantac®)
400mg HS	20mg HS	150mg HS	150mg HS
800mg HS	40mg HS	300mg HS	300mg HS
400mg BID	20mg BID	150mg BID	150mg BID
300mg QID	20 mg BID	150mg BID	150mg BID
400mg QID(GERD)	40mg BID	150mg BID	150mg BID
800mg BID (GERD)	40mg BID	150mg BID	150mg BID
N/A	N/A	300mg BID (GERD)	300mg BID

III. FLUOROQUINOLONE INTERCHANGE

selected agent: Levaquin (levofloxacin)

FLUOROQUINOLONE	DOSAGE FORM	DOSE & DOSING FREQUENCY	EQUIVALENT LEVOFLOXACIN (LEVAQUIN®) DOSE & DOSING FREQUENCY for CrCl > 50 ml/min
Ciprofloxacin (Cipro®)	PO	250mg Q 12 hrs	250mg Q 24 hrs
	IV	200mg Q 12 hrs	250mg Q 24 hrs
	PO	500mg Q 12 hrs	500mg Q 24 hrs
	IV	400mg Q 12 hrs	500mg Q 24 hrs
Gatifloxacin (Tequin®)	PO	400 mg QD	500 mg Q24 hrs
Enoxacin (Penetrex®)	PO	200mg Q 12 hrs	250mg Q 24 hrs
	PO	400mg Q 12 hrs	250mg Q 24 hrs
Lomefloxacin (Maxaquin®)	PO	400mg QD	500mg Q 24 hrs
Moxifloxacin (Avelox®)	PO	400 mg QD	500 mg Q24hrs.
Ofloxacin (Floxin®)	PO	200mg Q 12 hrs	250mg Q 24 hrs
	IV	200mg Q 12 hrs	250mg Q 24 hrs
	PO	300mg Q 12 hrs	500mg Q 24 hrs
	IV	300mg Q 12 hrs	500mg Q 24 hrs
	PO	400mg Q 12 hrs	500mg Q 24 hrs
	IV	400mg Q 12 hrs	500mg Q 24 hrs
Sparfloxacin (Zagam®)	PO	200mg QD	500mg Q 24 hrs

IV. PROTON PUMP INHIBITOR INTERCHANGE

selected agent: PPI of Choice

Prilosec®	Prevacid ®	Aciphex®
10mg	15mg	20 mg
20mg	30mg*	20 mg
40mg	30mg	20 mg
60mg	60mg	60 mg

*upon retrospective review, if consultant determines that resident is in maintenance, dose reduction recommendation may be made.

V. HMG CO-A REDUCTASE INHIBITOR INTERCHANGE

selected agent: Lipitor®

Pravachol®	10mg	LIPITOR® 10mg
	20mg	LIPITOR® 10mg
	40mg	LIPITOR® 10mg
Mevacor®	20mg	LIPITOR® 10mg
	40mg	LIPITOR® 10mg
Zocor ®	10mg	LIPITOR® 10mg
	20mg	LIPITOR® 10 mg
	40mg	*LIPITOR® 20mg*

VI. COX-2 INTERCHANGE

selected agent: Celebrex®

VIOXX ®	CELEBREX®
12.5 mg po QD	200 mg po QD
25 mg po QD	200 mg po QD

- **See pertinent Patient Specific Therapeutic Interchange (PSTI) document for specific documentation.**

Unknown

From: Cummins, Bruce [JAN]
Sent: Friday, June 28, 2002 8:50 AM
To: Forsthoefel, Tim [OMP]
Cc: Farley, Brett [JAN]; Thurmond, Tracey [OMP]
Subject: RE: Omnicare Levaquin initiative

Tim,

This is an ideal situation where all of the pieces of the puzzle come together. Certain states allow for interchange letters to be sent to physicians which authorizes a substitution based on clinical data, formulary, etc..... to take place at the pharmacy level when a pharmacists receive a prescription for a competitive medication. If the physician signs the authorization, the pharmacist will switch the medication at the pharmacy. The state of Missouri had the same program available, however a little over a year ago the "State Board of Pharmacy" intervened and lobbied for removing the authorization and it is no longer available to use in Missouri

Where we have the opportunity, we are doing in partnership with our external customer - Omnicare.

Regards,

Bruce

-----Original Message-----
From: Forsthoefel, Tim [OMP]
Sent: Friday, June 21, 2002 12:47 PM
To: Gamgort, James [OMP]; Russell, Dale [OMP]; Kennedy, Sara [OMP]; Grewcock, David [OMP]; Cummins, Bruce [JAN]; Thurmond, Tracey [OMP]
Cc: Butler, Dave [JANUS]; Graham, Roger [OMP]; Farley, Brett [JAN]; Ball, Gary [OMP]
Subject: FW: Omnicare Levaquin initiative

Dale- Sara - David:

19% share gain in 5 months due to Omnicare pharmacist's physician calling.

Bruce/Tracey --- have all regions of Omnicare implemented? Any other National Accounts that have "gaps" in similar behavior modeling?

Outstanding! Tim

-----Original Message-----
From: Schwans, Roxanne [JAN]
Sent: Wednesday, June 19, 2002 12:04 AM
To: Farley, Brett [JAN]
Cc: Butler, Dave [JANUS]
Subject: Omnicare Levaquin initiative

Hi Brett,
I wanted to share some great news. In January of this year I worked with Cedar Rapids, IA to do Therapeutic interchange letters for Levaquin. They implemented them in Jan while they had a share of 70%. Then in March of '02 they started calling the physicians back. They would fill one script of Cipro and then call the doctor and if they would not return the call after 2 days then they would stay on Cipro but the majority of the physicians would call back and let Omnicare know it was ok to switch to Levaquin. So in May of 02 they have a share of 89% while Cipro is down to 11%.
Great news.
Roxie

Roxanne Schwans
J and J Long Term Care Business Manager

REDACTED

Long-Term Care Group

JANSSEN ORTHO-McNEIL ORTHO BIOTECH LIFESCAN

LTC Group Monthly Report
July 2001

Issue and Solutions

1. Omnicare makes the decision to give Zyprexa co-preferred status with Risperdal in its geriatric guidelines. *Solution* Reevaluate and negotiate a new agreement
2. The Assisted Living Initiative is growing rapidly and may require additional resources. *Solution:* Allocate funds in 2001-2002 fiscal year budget.
3. A promotional letter sponsored by Lilly been sent out to physicians nationally concerning drugs that prolong the QT interval. There are several drugs listed from all companies except Lilly. The letter does include Risperdal. *Solution*: LTCBM's are trying to secure a copy of this letter to deliver to the Risperdal brand team.
4. Develop broader relationships at the Nursing Home Corporate level. *Solution:* Develop programs specifically targeted for each individual chain account. Beverly and HIS have named Risperdal as their "Preferred Antipsychotic".
5. Consultant Pharmacists are requesting CME material on audiotape so they can participate in these educational programs when they are driving to their accounts. *Solution:* Work with brand teams to develop audiocassette tapes to pilot with consultant pharmacist.

Highlights

Janssen

RISPERDAL®

- NCS HealthCare, Beachwood, Ohio mails out letter to all of their NCS HealthCare pharmacy sites restating Risperdal as their "preferred" antipsychotic and introduced an accelerated initiative for 11 of their "high dollar potential" antipsychotic sites.
- Risperdal "Pilot Round Table" discussions have now been secured for the following Omnicare sites. Roeschens, Jacobs, Home, and Interlock. The first program has been successfully completed in Chicago with Home following on August 13th and Roeschens on September 6th. Interlock will be re-scheduled and additional six programs will be targeted for Specialized Livonia, Value HealthCare, Evergreen, Shore, Westhaven, and Lo-Med Pharmacies.
- American Pharmaceutical Services/Risperdal Initiative - This month APS will send out a letter to identified HV prescribing antipsychotic physicians stating the Risperdal is their preferred antipsychotic. Additionally, APS ran a list of High Volume prescribing antipsychotic physicians for each of their branches. List was forwarded to Janssen EC for call plan targeting. Feedback from EC is that this list has been very helpful and feel will help them increase Risperdal use with APS branches.
- Jacobs Healthcare (16,000 beds) and Lawrence Weber (12,000 beds) started a PAL initiative with Risperdal in the month of May. The authorization letter requests a substitution to Risperdal from any new prescription of Zyprexa or Seroquel.
- Neighborcare has asked to have 900 copies of FADAMA (Katz) article distributed to consultant pharmacists and bench pharmacists throughout the country.

REMINYL®

- Working with Assisted Living Federation of America (ALFA) on implementing a DSM partnership program with 7,000 AL providers.
- Reminyl Clinical Update to Beverly Enterprises (Tony Hughes, Clinical Director of Pharmacy Operations and John Ferguson, Director of Training) with Steve Stansilav. Looking at opportunities to partner with Training for CSO representatives and Beverly AD sites.
- Alterra Corporation requested 50,000 branded pieces for the Sharing Care Program.
  They plan to drive this program in the following ways:
  - Sales representatives will distribute to potential customers/
  - Alterra will distribute during trade shows and family night programs.
  - Alterra captured a list of 750,000 individuals that are potential candidates for assisted living. We are negotiating budget for them to include Sharing Care program in mailing to these individuals.
  - Greater NY Healthcare Facilities Association learn message on Reminyl. Approximately 125 nurses attended.

ACIPHEX®

- Met with NCS to discuss possible Aciphex coexist strategy. Customer currently at 85% share with Prevacid®. This may make potential agreement difficult due to "cliff" and the inability for JPI to make up lost rebate revenue. Customer agreed to further discussion and investigation.

DURAGESIC®

- A successful speaker program was conducted by Hob Osterlund, RN to over 90 Pharmerica customers. She is a great speaker and great advocate for Duragesic.
- ChemRx put out a conversion message to nursing homes to switch from Oxycontin to Duragesic
- Two Auburn Pharmacy School programs are scheduled for August 3 and August 10, 2001. Programs will reach about 300 key pharmacists.
- NeighborCare will conduct programs on "Pain in the Elderly beginning in the 1st Quarter of 2002. These "Plan for the Future" educational programs, held nationwide, should be a great opportunity to help promote Duragesic.

OMP

LEVAQUIN®

- ChemRx E-Box campaign has achieved 60-70% E-Box conversion from CIPRO to LEVAQUIN.
- AAPI CME program at national convention was well attended and impactful.
- Omnicare agrees to send PAL letters as well as a universal mailing in August/September to promote Levaquin for the upcoming respiratory season.

- American Pharmaceutical services provides physician prescribing information for each of their branches that identifies high volume antibiotic physicians and prescribing patterns. This information disseminated to OMP for rep targeting. LTCBM will follow-up with OMP on a District Manager level to discuss lists and targeting.

ULTRAM®

- Dr. Michael Slick Pharm D, FASCP spoke on the Myths and Realities of Pain Management to Medilife in Colorado.
- New CE tape series on Joint Commission Guidelines on Chronic Pain are being rolled out to LTCPP customers. Response has been excellent and LTC pharmacists have confirmed that they must offer Pain management education in each facility at least once per year.
- American Pharmaceutical Services will launch an Ultram intervention beginning in July. They will target propoxyphene. On June 15th we conducted the first of six regional consultant pharmacy educational programs.

OBI

PROCRIT®

- PharMerica identifying oncology patients within Skilled Nursing Facilities (SNF's) setting for Procrit intervention.

LifeScan®

- LifeScan contract was signed by Gerimed. Program will start in the 4th quarter.
- MHA signed LifeScan contract worth up to$1.7MM annually
- Innovatix signed tiered pricing program contract for CAM members. Innovatix has innovative systems to provide market share data continuously.

Long-Term Care Group

JANSSEN • ORTHO BIOTECH • ORTHO-McNEIL • LIFESCAN

LTC Group Monthly Report

January, 2002

Highlights

- A national teleconference was scheduled for 125 dementia residences that Alterra services. Each residence will participate in the program and at each location there will be about 5 healthcare professionals. Potential to reach 600 healthcare professionals with a Risperdal message. Marc Agronin, MD will be the presenter.
- PBI signed the LifeScan amendment to the contract.
- PharMerica - Developed a national mailing to skilled nursing facilities and physicians outlining the benefits of Ultram over Propoxyphene.
- NCS HealthCare, Beachwood, OH mails Risperdal "preferred" letter to 4,000 attending physicians.
- In-services were held in NE to educate Nurses, MD's and Pharmacists on Reminyl. There were over 250 health care professionals at these in-services. Great discussion was held around the expectations of ACI's. Reminyl was shown to have a proven one- year success in maintaining baseline scores.
- Levaquin featured at NCS, Phoenix formulary management workshop.
- Coordinated Ultracet in-services for dispensing and consulting pharmacists at the following accounts:
  - PharMerica Minneapolis
  - NCS Decatur
  - Enloe Drug Decatur
- Forging partnership with Marriott Senior Living Services. Determined 14 pilot sites for Reminyl/Risperdal programs and implemented process with LTC managers.

Long-Term Care Group

JANSSEN ORTHO-McNEIL ORTHO BIOTECH LIFESCAN

LTC Group Monthly Report

JANSSEN

RISPERDAL®

- Developed a CD/ROM and newsletter with PharMerica around PPS issues and the benefits of Risperdal for skilled nursing facilities.
- ALPHA National Meeting – Weston, FL – Introduced Risperdal teletopics for their AL facilities to combat Zyprexa.
- Florida EC/LTC - Partnering on business plan to target top independent LTCPPs in the State of Florida for Risperdal preferred status. Currently 4 independent pharmacies have approximately $4.0 million in total potential with average of 36% Risperdal MS.
- In-services completed at independent CAM, Skilled Care Pharmacy. Skilled Care has three top 30 pharmacies in Southern California.
- Business review at NCS Van Nuys identified three key facilities for Risperdal focus in first quarter.
- Omnicare is very supportive of the Chicagoland MI initiative on a local and national level. They will partner with us to first determine how to influence this market and second drive Risperdal utilization in this market segment. Jacobs HealthCare, Chicago, IL (Services approx. 3,000 MI patients) is in the planning process to grow their business with the mental illness market segment that are cared for in the LTC environment.
- Met with Lisa Welford (OmniCare Director, Clinical Operations). She stressed that Risperdal is their primary intervention. They are targeting all new and existing classical APS prescriptions for conversion to Risperdal. She is helping coordinate a business planning meeting, which will take place in February, between LTC Group and Omnicare Regional Clinical Directors to discuss and develop action plans on how to maximize this intervention within each of their regions.
- PharMerica Conference Call with Texas Lead Consultants to discuss strategies for getting to the key Zyprexa writers. Each Lead had a 15 minute slot to discuss needs.
- NCS HealthCare, Beachwood, OH reports 59.4 Risperdal market share for 3Q01. This is their highest quarterly share recorded to date.

REMINYL®

- Reminyl pilot program for Marriott Senior Living has been scheduled for March 9th in Voorhees, NJ. Will be working with ElderCare and other JPI FSFs to draw top decile ALZ prescribers. The meeting with be co-sponsored by the Virtua Health Sysytem of Southern NJ.
- Submitted AD information/background information to Marriott Senior Living Services marketing, as second article will be included in their e-newsletter.

Long-Term Care Group

JANSSEN ORTHO-McNEIL ORTHO BIOTECH LIFESCAN

LTC Group Monthly Report

- Atria assisted living centers based in Louisville, KY reviewed a Reminyl initiative.
- CA Medi-Cal team met in January to continue preparation for Medi-Cal launch. Currently developing Medi-Cal prescriber list for dissemination to ElderCare teams.
- Omnicare Minnesota requested educational programs to educate and influence physicians prescribing and not prescribing ACI's.
- Met with Fred Wendt, IHS Clinical Director to continue our discussion of a proposed venture to educate his Medical Directors, Don's, and nursing staff on AD.

DURAGESIC®

- Set up "Substance Abuse" Teletopics for pharmacists at the NeighborCare in Moorestown, NJ for February 14th. Doing the lunch in-service with Joann Price, ElderCare rep.
- Worked with AMDA to development and support "train the trainer" tools for AMDAs Pain CPGs.
- Shore/Omnicare-Cost comparison literature and educational prompt distributed to key sites.
- ElderCare/LTCBM identified Professional Pharmacy, in Phoenix as top Duragesic potential account in region. Set up in-service and identified top customer for sales in-service activity.
- Duragesic pain assessment program held in conjunction with NeighborCare at Skyline Home/ Glendale Community Hospital.
- Roeschens Omnicare – Milwaukee - Developing educational programs that would target this site's NH customers and educate them on recognizing, assessing, and treating chronic pain in the elderly. All programs will position Duragesic appropriately and motivate them to recommend Duragesic to attending physicians.

OMP

LEVAQUIN®

- Omnicare - New England - Levaquin inservice programs for skilled nursing facilities
- PharMerica, Longwood, Flordia – Coordinating with OMP for two Levaquin educational programs for 1Q 2002, in Ocala and Longwood, Florida
- LTCBM AI/AN RBD Meeting - Business review demonstrated high tab shares in Tier 1 accounts, but low shares at independent CAM's. PrimeCare, the largest account in the LA area as a pilot account for special focus.

Long-Term Care Group

JANSSEN ORTHO-McNEIL ORTHO BIOTECH LIFESCAN

LTC Group Monthly Report

- NCS, Van Nuys continues to drive share over 70%
- Maude Babbington will present on Maximizing Internal Interventions with Levaquin to 20 pharmacy managers and directors from the Western and Mid Western regions on Feb 7th.
- Lisa Welford (Omnicare – Director, Clinical Operations) stressed that Levaquin is one of their primary interventions. They are targeting all prescriptions for Cipro for conversion to Levaquin.
- NCS HealthCare, Beachwood, OH reports 60.4 Levaquin market share for 3Q01. This account has remained above 60% for the last four quarters.
- NCS HealthCare, Beachwood, OH targets attending physicians with a Levaquin "PAL" letter mailing. This letter is designed to secure blanket authorization to switch Cipro prescriptions to Levaquin.

ULTRACET®

- PharMerica (Texas) consultants requested Ultracet be added to the SNF E-Box. They maintain their commitment to convert Darvocet patients.
- Good Samaritans of SD has scheduled a two part pain program. It will be broadcast to all of their sites via satellite. This will be provided to approximately 500 participants.

DITROPAN XL®

- Considerable interest concerning contract opportunities with Ditropan XL. Many providers and NH requesting in-services on incontinence.
- Met with Lisa Welford (Omnicare National Clinical Director). She stressed that identification of potential incontinence therapy patients and converting patients from generic oxybutinin to Ditropan XL is one of their current interventions.
- Coordinated Ditropan XL in-services for dispensing and consulting pharmacists at the following accounts:
  - PharMerica Minneapolis
  - NCS Decatur
  - Enloe Drug Decatur
- Presentations conducted at the OMP SeniorCare RBD/DM and regional meetings on LTC/OMP Senior Partnerships and business plans.

OBP

PROCRIT®

- Beverly Nursing Home Corporation, Arkansas – Partnering with OBI in the ERI population to improve patient QOL issues.

Long-Term Care Group

JANSSEN ORTHO-McNEIL ORTHO BIOTECH LIFESCAN

LTC Group Monthly Report

- Chem Rx – Working with OBP account team on Chem Rx-Procrit service contract agreement
- J&J LTC Group coordinating with OBP Strategic accounts group for Home Health Care (HHC) programs that can be initiated at HHC sites by LTC Managers.

LifeScan®

- Meeting was held at LifeScan to finialize the training session for the Long Term Care Group on Feburary 20. LifeScan has added several folks to their team including a Marketing Person with sole responsibility to LTC
- LifeScan Contract for Kindred Healthcare - Meeting was held with all principles at LifeScan to develop a new Health Care Compliant contract for Kindred Health Care. This business represents $3.8 Million in annual sales and is one of the largest individual contracts for LifeScan products.
- LifeScan GPO CAM Program - A meeting was held in January with GeriMed (LTC GPO) to investigate opportunities to build on business opportunities through the LifeScan LTC GPO Cam agreement.

Long-Term Care Group

JANSSEN ORTHO-McNEIL ORTHO BIOTECH LIFESCAN

LTC Group Monthly Report

Programs

RISPERDAL	**Alliance Speaker Programs**	
	Arista Programs	
	Professional Services Program	
	HOV Programs (2)	
	Regional Ad Boards (4)	
	Multi-disciplinary Summits	
	Teletopics	
	Video Lunch/Learn	
	Inservices	
REMINYL	**Speaker Programs**	
	Teleconferences	
	HOV Programs (10)	
	Regional Ad Boards (8)	
	Professional Services	
	Inservices	
DURAGESIC	**Speaker Programs**	
	Professional Services	
	Teletopics	
	Inservices	
ULTRACET	**Speaker Programs**	
	Professional Services	
	Teletopics	
	Inservices	
LEVAQUIN	**Speaker Programs**	
	Professional Services	
	Teletopics	
	Inservices	
DITROPAN XL	**Speaker Programs**	
	Professional Services	
	Teletopics	
	Inservices	
PROCRIT	**Speaker Programs**	
	Professional Services	
	Teletopics	
	Inservices	

Long-Term Care Group

JANSSEN ORTHO-McNEIL ORTHO BIOTECH LIFESCAN

LTC Group Monthly Report

Omnicare- Current Analysis & Recommendations 9/25/01

Current Situation

- OMP cliff offer of 67% for Levaquin PO share rejected by Omnicare on 9/18
- Response very strong- Dan Maloney VP, Contracting said this would force him to contact Bayer, BMS
- Dan Maloney left me VM & E-mails on 918, 9/21 wanting to have further discussions around Levaquin
- Phone conversation with Dan Maloney on 9/24/01. Wanted to know if we were firm on 67% and if so then he was going to contact Bayer to investigate contract potential. Said his risk/reward was too great with a 67% cliff. Claimed Omnicare has not had any contract discussions with Bayer or BMS up to this point. Said Omnicare would be willing to work with OMP/J&J on UTI targeting around Cipro. Latest Omnicare figures for July month had Cipro at 28% share
- Dan maintained that Omnicare could do nothing around the USP Clinical monograph. Claims Omnicare does not even inform vendors when there drugs are being reviewed by USP. He said the only reason Mark Lehman shared this with us in mid-July was because of the strong business relationship with J&J.
- I made it clear to Dan that Levaquin & Risperdal were linked and we had to get both of these situations resolved in order to still have an agreement with Omnicare.
- Joel Gemunder, President of Omnicare contacted David Norton, Pres. Of Janssen on Friday, Sept 18 to say that Omnicare would continue to support Risperdal.

Market Comparisons

A. Current Long Term Care Contract Matrix

Product	Product	Transition Period	Tier 1	Tier 2	Tier 3	Tier 4	Tier 5	Activ I Re
JANSSEN	DURAGESIC®		55.0% 2.0%	60.0% 4.0%	65.0% 8.0%	70.0% 10.0%		S
	ACIPHEX®	**12 Months** 8.0%	<15.0% 0.0%	15.0% 8.0%	25.0% 10.0%			S
	RISPERDAL®		35% 6.0%	38% 9.0%	>=42% 11.0%			S
Ortho McNeil Pharmaceutical	LEVAQUIN® TABLETS	**3.5% transition rebate for first 6 months not tied to share**	<50% 0.0%	50% 14.0%				S
	Available for first 12 months of contract only	If 40% share is attained in first 12 months, rebate increases to 6% for the remaining X of first 12 months						
	LEVAQUIN® IV		<15% 12.0%	25% 18.0%	40% 24.0%	60% 36.0%		S
	ULTRAM®		At / Above Baseline 1.0%	10.0% 2.0%	15.0% 3.0%	20.0% 4.0%	25.0% 6.0%	S
			Formulary Access					

Ortho Bio Tech	PROCRIT							
McNeil Consumer Products	All Products		No Requirement					
Ortho Dermatological	All Products		No Requirement					

- **Omnicare currently receives a 15% rebate on Levaquin PO for a share ≥ to 50%**
- **Omnicare currently operates off the old Levaquin IV matrix with < 50% at 0%, ≥ 50% to 70% equals 5%, > 70% equals 7% rebate**

B. Basic Hospital Contract Matrix

PDOT DEFINED MARKET SHARE TABLE					
Quinolone Defined Market Share	*LEVAQUIN Defined Market Share*	*250mg IV*	*500mg IV*	*750mg IV*	*LEVAQUIN Tablet Discount Tiers*
5.1-10%	0-5%	$16.00	$32.00	$33.00	GPO Price
10.1-20%	5.1-10%	$16.00	$31.00	$33.00	GPO Price
20.1-40%	10.1-15%	$16.00	$29.00	$33.00	GPO Price
40.1-60%	15.1-25%	$13.00	$27.00	$31.00	GPO + 1%
60.1-70%	25.1-35%	$12.00	$23.00	$30.00	GPO + 2%
70.1-80%	35.1-45%	$11.00	$21.00	$28.00	GPO + 3%
80.1-90%	45.1-55%	$10.00	$19.00	$27.00	GPO + 4%
90.1%+	55.1%+	$9.00	$17.00	$26.00	GPO + 5%

- **Must achieve a 90% share in quinolone only market to achieve a 15% TOS discount for Levaquin PO. Keep in mind the 90% is based on additive figure for IV & PO Levaquin**

C. Managed Care Contracts for Levaquin PO

1. To my knowledge we only have one Managed Care contract where we are the exclusive quinolone with the major accounts – Inter-Mountain Healthcare
2. Levaquin PO is generally in a position where we are one of two quinolones being contracted
3. For measurement purposes the National share for Levaquin PO in the quinolone market is apporx. 35.9% based on 2Q '01 share – Rebate performance is calculated on # of share points above National average
4. Rebate structure is generally based on 3 to 4 point spreads and range from 10% to 18% varying per Managed Care customer.

D. Market Segments – Comparisons of Market Share & Other Facts

➢ Retail TRX Weekly share Shares for last 12 weeks I Quinolone Only Market thru Sept. 12, 2002

Levaquin - 34.9%
Floxin - 1.7%
Cipro - 49.7%
Avelox - 4.1%
Tequin - 8.2%

- **Omnicare Market share for quinolones for Month July '01**

Avelox	**.3%**
Cipro	**28.0%**
Floxin	**.4%**
Levaquin	**69.3%**
Noroxin	**.7%**
Tequin	**1.4%**

1) **Levaquin Share in Omnicare almost double the National Retail Average**
2) **Cipro in Omnicare is about 77% below the National Retail Average**
3) **Tequin & Avelox in Omnicare are will below the National Retail Average**

- **Omnicare has grown Levaquin Share from 19.2% in 4th Quarter of '98 prior to the Levaquin Initiative to 66.4% in 2Q '01. In this same time period Cipro has gone from 80% + to the 28% range**
- **Comparing DDD Tab Sales in 1Q 2000 versus 1Q 2001:**
  LTC market Share (without Omnicare – represents appox. 33%) is showing largest share @ 36.2% up from 32.8%
  Hospital at 34.3% and decline verus 35.2% for prev. year
  Federal Sector show a big decline from 30.1% to 13.0%?

- **Key Point- LTC market has very limited OMP Sales Force support versus the Retail, Hospital, Federal Markets**
- **Market Share in the LTC market for Levaquin PO is driven by Physician Authorization Letters, very important due to the fact this is a prospective intervention. Education of dispensing pharmacists in the LTC area is important.**
- **My opinion --- We are getting a greater ROI for our rebate dollars in the LTC sector due to limited sales activity versus other market sectors**
- **Omnicare is the largest Tier I LTC provider that controls about 30% of the market**
- **Omnicare has demonstrated the greatest control and has the highest share for Levaquin PO on any Tier I LTC Provider**
- **Last four quarters of sales (2Q '00-1Q'01) for OMP products = $22,104,717**
- **Potential upside sales for Ultracet**
- **Potential upside with Ditropan XL**
- **We are in better position ever to drive $ sales within Omnicare due to Senior Care Sales Force**

Proposed Tier Options & Recommendations

MY belief --- Omnicare will reject a 67%, 65%, and 63% tier. They will go to Bayer to contract.
Rebates have been paid over the last four quarters based on the following:

2Q '00	3Q '00	4Q '00	1Q'01
61.4%	**63.1%**	**63.1%**	**66.4%**

Option # 1

Keep Share Cliff @ 67% -- Believe Omnicare will reject

Option #2

Establish Share Cliff @ 65% - Believe Omnicare will reject

Option #3

Establish Share Cliff @ 63% - Believe Omnicare will reject

Option # 4

Establish Share Cliff @ 60% -- Might possibly accept – still think very questionable

Option # 5

Establish new performance tiers that minimizes our financial risk if in fact they begin to move against us but provides financial incentive for Omnicare to stay with OMP & Levaquin PO

0- 49.9%	**0% rebate**
50% - 55%	**5% (currently paying 15% rebate)**
55.1- 59.9%	**8% (currently paying 15% rebate)**
60- 69.9%	**15% (currently paying 15 rebate)**
70.0% +	**16% (currently paying 15% -- this level has never been achieve, additional incentive)**

You can run a number of different options varying from # 5

My recommendations would be that # 5 is the best or a variation of this followed by option #4.

Unknown

From: Russell, Dale [OMP]
Sent: Friday, June 21, 2002 12:07 PM
To: Forsthoefel, Tim [OMP]
Subject: RE: Omnicare Levaquin initiative

Tim,

Incredible: good for us but scary on the power to do this.

Thanks,

-----Original Message-----
From: Forsthoefel, Tim [OMP]
Sent: Friday, June 21, 2002 12:47 PM
To: Gamgort, James [OMP]; Russell, Dale [OMP]; Kennedy, Sara [OMP]; Grewcock, David [OMP]; Cummins, Bruce [JAN]; Thurmond, Tracey [OMP]
Cc: Butler, Dave [JANUS]; Graham, Roger [OMP]; Farley, Brett [JAN]; Ball, Gary [OMP]
Subject: FW: Omnicare Levaquin initiative

Dale- Sara - David:

19% share gain in 5 months due to Omnicare pharmacist's physician calling.

Bruce/Tracey --- have all regions of Omnicare implemented? Any other National Accounts that have "gaps" in similar behavior modeling?

Outstanding! Tim

-----Original Message-----
From: Schwans, Roxanne [JAN]
Sent: Wednesday, June 19, 2002 12:04 AM
To: Farley, Brett [JAN]
Cc: Butler, Dave [JANUS]
Subject: Omnicare Levaquin initiative

Hi Brett,
I wanted to share some great news. In January of this year I worked with Cedar Rapids, IA to do Therapeutic interchange letters for Levaquin. They implemented them in Jan while they had a share of 70%. Then in March of '02 they started calling the physicians back. They would fill one script of Cipro and then call the doctor and if they would not return the call after 2 days then they would stay on Cipro but the majority of the physicians would call back and let Omnicare know it was ok to switch to Levaquin. So in May of 02 they have a share of 89% while Cipro is down to 11%.
Great news.
Roxie

Roxanne Schwans
J and J Long Term Care Business Manager
REDACTED

EXHIBIT F: MANAGER'S CHECKLIST FOR NON QUANTITATIVE REQUIREMENTS

Johnson & Johnson Health Care Systems Inc.
Non-Market Share Based Performance Requirement Checklist (To Be Completed by OMNICARE Every Quarter)

Company Name: Omnicare, Inc.
Quarter: SECOND QUARTER 2001
Number of Beds:
Formulary ID:

Please place an (X) in the appropriate column for all products that are on contract to signify compliance with contract terms.

Product Description	Formulary Status						No Active Intervention Program	General Active Intervention Program	Product Specific Active Intervention Program	Target List of "High" Prescribers of Competitive Agents to Supplier	Other [*]
	Equal	Exclusive	Formulary Access	Preferred	Restricted	Unrestricted					
DURAGESIC						X		X			
FLOXIN						X	X				
LEVAQUIN				X					X		
PROPULSID											
PROCRIT						X			X		
ACIPHEX						X				X	
RISPERDAL				X					X	X	
SPORANOX						X					
ULTRAM						X		X	X		
NIZORAL						X	X				

* Any other requirements specified in contract terms that are not listed herein.

Authorized Signature:
Name: DANIEL J MACCOY
Date: 7/23/01

Note:

1. This form must be filled out completely by Manager and sent to Supplier's Contract Administration group described on the cover page of this Agreement on a quarterly basis with rebate submissions. If checklist is not received, no payments will be made.
2. **Mandatory Brand Interchange** - If contract specifies a Mandatory Brand Interchange for any product, the required documentation per contract terms must be supplied on a quarterly basis with rebate submissions.
3. Contract terms grant Supplier a specific amount of time from the time rebate submissions are received (i.e. 60 days) to make payments. The count does not begin until a complete rebate submission is received. Completeness is defined as all the proper report formats and the above stated requirement.

EXHIBIT F: MANAGER'S CHECKLIST FOR NON QUANTITATIVE REQUIREMENTS

Johnson & Johnson Health Care Systems Inc.
Non-Market Share Based Performance Requirement Checklist (To Be Completed by OMNICARE Every Quarter)

Company Name: Omnicare, Inc.
Quarter: 2002 Q2
umber of Beds:
Formulary ID:

Please place an (X) in the appropriate column for all products that are on contract to signify compliance with contract terms.

Product Description	Formulary Status						No Active Intervention Program	General Active Intervention Program	Product Specific Active Intervention Program	Target List of "High" Prescribers of Competitive Agents to Supplier	Other (*)
	Equal	Exclusive	Formulary Access	Preferred	Restricted	Unrestricted					
DURAGESIC	✓		✓			✓		✓			
FLOXIN	✓		✓			✓					
LEVAQUIN			✓	✓					✓		
PROPULSID											
PROCRIT			✓						✓		
ACIPHEX	✓		✓					✓			
RISPERDAL			✓	✓					✓		
SPORANOX			✓			✓	✓				
ULTRAM			✓			✓		✓	✓		
DITROPAN XL	✓		✓			✓					
NIZORAL			✓			✓					
REMINYL			✓			✓					

* Any other requirements specified in contract terms that are not listed herein.

Authorized Signature: [signature]
Name: DAN MALONEY
Date: 4/22/02

Note:

1. This form must be filled out completely by Manager and sent to Supplier's Contract Administration group described on the cover page of this Agreement on a quarterly basis with rebate submissions. If checklist is not received, no payments will be made.
2. **Mandatory Brand Interchange** - If contract specifies a Mandatory Brand Interchange for any product, the required documentation per contract terms must be supplied on a quarterly basis with rebate submissions.
3. Contract terms grant Supplier a specific amount of time from the time rebate submissions are received (i.e. 60 days) to make payments. The count does not begin until a complete rebate submission is received. Completeness is defined as all the proper report formats and the above stated requirement.

REDACTED

NAME	ID	AGE	PROV	PAID	DATE	UNITS	DEANO	REFILL	DAYS	LOC	RX	NDC	DESC	STR	GENERIC
		89		$26.81	2/12/2002	60		1	30	3	1417858	50458030150	RISPERDAL	0.25MG	RISPERIDONE
		95		$27.62	1/17/2001	30		0	30	3	0919940	50458030150	RISPERDAL	0.25MG	RISPERIDONE
		95		$14.63	7/6/2001	30		0	30	3	1177178	50458030150	RISPERDAL	0.25MG	RISPERIDONE
		64		$177.81	4/25/2004	60		1	30	4	2765485	50458030250	RISPERDAL	0.5MG	RISPERIDONE
		55		$768.95	8/7/2003	270		0	90	5	2295671	50458030250	RISPERDAL	0.5MG	RISPERIDONE
		74		$244.25	4/4/2002	90		5	30	3	1338630	50458030250	RISPERDAL	0.5MG	RISPERIDONE
		65		$266.33	11/2/1999	60		0	30	3	0421932	50458033050	RISPERDAL	3MG	RISPERIDONE
		88		$72.66	10/15/1999	30		0	30	3	0406126	50458030050	RISPERDAL	1MG	RISPERIDONE
		86		$37.83	11/5/2000	15		1	30	3	0778366	50458030150	RISPERDAL	0.25MG	RISPERIDONE
		79		$71.40	8/20/1999	30		0	30	3	0358990	50458030250	RISPERDAL	0.5MG	RISPERIDONE
		77		$84.79	4/24/2003	30		5	30	3	1900163	50458030250	RISPERDAL	0.5MG	RISPERIDONE
		84		$146.50	4/17/2001	60		2	30	3	0970550	50458030250	RISPERDAL	0.5MG	RISPERIDONE

REDACTED

NAME	ID	AGE	PROV	PAID	DATE	UNITS	NDC	DEANO	REFILL	DAYS	LOC	RX	DESC	STR	GENERIC
		92		$16.47	8/23/2000	10	00045152550		0	10	3	0721435	LEVAQUIN	500MG	LEVOFLOXACIN
		78		$76.86	8/23/2000	10	00045152550		0	10	3	0720539	LEVAQUIN	500MG	LEVOFLOXACIN
		92		$54.70	8/23/2000	7	00045152550		0	7	3	0720654	LEVAQUIN	500MG	LEVOFLOXACIN
		74		$10.73	8/23/2000	7	00045152550		0	7	3	0721445	LEVAQUIN	500MG	LEVOFLOXACIN
		63		$200.27	4/19/2001	30	00045152050		0	30	3	1060521	LEVAQUIN	250MG	LEVOFLOXACIN
		84		$79.80	4/19/2001	10	00045152550		0	10	3	1059899	LEVAQUIN	500MG	LEVOFLOXACIN
		93		$30.85	4/19/2001	10	00045152550		0	10	3	1059603	LEVAQUIN	500MG	LEVOFLOXACIN