

SALES OF DRUGS FOR URINARY TRACT INFECTIONS

The need for Furadantin or competitive drugs was apparently much more restricted than many of the other drugs studied.

During the four weeks covered by the prescription audits a total of only 40 prescriptions on the five drugs were filled and 14 of these were for the two analgesics, Pyridium and Serenium. The dollar value totaled \$211 for the five drugs. The 40 prescriptions were written by 20 physicians.

On an annual basis this amounted to approximately 520 prescriptions and about a \$2750 market not counting refills or direct dispensing. Analgesics excluded, the annual totals would have come down to about 340 prescriptions and \$2200.

Sales of these products are too small to justify comparisons of the four audit periods.

FURADANTIN SALES

Only 13 Furadantin prescriptions were filled during the four periods under audit, but because this product was relatively expensive (it was reduced in price in March 1955) the dollar value was nevertheless substantial.

The price of these 13 prescriptions was \$148. This meant that Furadantin made up 33%

of the prescriptions for the five drugs and 70% of their dollar volume. In terms of annual sales this became about 170 prescriptions and \$1925, exclusive of refills and whatever amount may have been dispensed by the one physician who said he had dispensed this drug.

PROFESSIONAL EVALUATION OF FURADANTIN

Furadantin was not as controversial a drug nor perhaps so spectacular as some of the drugs reported in this study so it had not had as many articles written about it.

A professional bibliography starting in 1952 and including some of the early 1955 articles had 79 listings, however.

And 13 papers in which nitrofurantoin occupied a major portion of the discussion had been read at medical meetings from 1952 through 1954.

CONCENTRATION OF FURADANTIN PRESCRIPTIONS

A total of 26 Fond du Lac area physicians reported that they had prescribed Furadantin at some time but only five of them appear in the four prescription audits.

Two of these doctors accounted for 10 of the 13 prescriptions—Internist "A" and Specialist "A." These two doctors were directly responsible for 87% of the Furadantin dollar volume. The other three doctors are another internist and two general practitioners with special interest in obstetrics and gynecology.

Four-Week Furadantin prescriptions

	Number	Price
Total	13	\$149
Internist "A"	7	\$103
Specialist "A"	3	26
Three other prescribers	3	20

The above figures (although not large) seem to establish the fact that in the Fond du Lac area, at least, Furadantin was a specialist's drug. This was a fact that Eaton evidently realized when it elected to stress it most strongly among urologists.

SOURCES OF INFORMATION ABOUT FURADANTIN

The most unique feature of the Furadantin story in Fond du Lac is the apparent influence that other prescribers attribute to Specialist "A."

One prescriber in every three states that Specialist "A" recommended Furadantin to him.

"Where did you happen to get the information about Furadantin which led you to prescribe it?"

21 Furadantin
prescribers

Specialist "A"	7
Detail man	7
Journal articles	6
Direct mail	4
Hospital staff meetings	2
Medical journal advertising	1
National conventions	1
County meetings	1

Specialist "A" himself said that he learned of the drug at a national convention. He was also sampled and later was detailed, too. Internist "A" credited journal articles for telling him of Furadantin. He was never detailed or sampled.

Of the 26 prescribing doctors, 18 were detailed and 17 received samples. Of the 29 non-prescribers, only 9 were detailed and 11 received samples.

Most of the 26 prescribers did not get around to prescribing the drug until the latter part of 1954. Specialist "A" first prescribed it in June 1954 and Internist "A" began using it in August or September of that year.

Other comparisons of Furadantin prescribers and non-prescribers as to source of information are unproductive and will be passed over here.

NATIONAL PROMOTION OF FURADANTIN

Dollar estimates of the amount of Furadantin advertising and promotion are not readily at hand, but some idea of the cost may be obtained through the indicated use of the various media.

At the time of the study about 150 different pieces of direct mail had been sent out—

12 mailings were made in 1953 to urologists only.

110 mailings were made in 1954 to urologists, pediatricians, and general practitioners.

25 mailings were made in the first quarter of 1956 to the above groups plus obstetricians and gynecologists.

Some mailings were also sent to druggists, technicians, and hospitals.

Furadantin was detailed nationally, although not until October 1954 in the Fond du Lac area.

A sizeable part of the advertising budget was devoted to journal advertising. The 1954 journal schedule is shown here as an example—

American Journal of Medicine	12 insertions
Annals of Internal Medicine	12 insertions
California Medicine	12 insertions
GP	12 insertions
Journal of the A.M.A.	60 insertions
Journal of Urology	12 insertions
Medical Examiner	17 insertions

Medical Times	12 insertions
Modern Medicine	12 insertions
World Medical Journal	1 insertion
New York State Journal of Medicine	12 insertions
Journal of Pediatrics	7 insertions
American Druggist	10 insertions

Samples of Furadantin had been sent to or left with selected physicians—about half (28) of those in the Fond du Lac area recalled receiving samples.

Eaton helped defray expenses of scientific exhibits at four national conventions of urologists and the profession, and at one meeting of the New York Academy of Medicine. In addition, from the introduction of Furadantin up to the time of this study, Eaton had shown commercial exhibits at 66 medical conventions.

SUPPORT FOR FURADANTIN IN MEDICAL JOURNALS

As Furadantin was not as controversial a drug nor perhaps as spectacular as some of the other drugs studied, it hadn't had as many articles written about it.

A professional bibliography starting in 1952 and including some of the early 1955 articles lists 79 papers.

In addition, 13 papers in which nitrofurantoin occupied a major portion of the discussion had been read at medical meetings from 1952 through 1954.

It is probable that there was little public influence brought to bear upon the profession regarding this drug.

**CORRELATION WITH SOURCES
OF INFORMATION ON FURADANTIN**

**"Where did you happen to get the information about
Furadantin which led you to prescribe it?"**

21 prescribers

7

medical journal articles and advertising

4

direct mail

1

national conventions

7

specialist A*

7

detail men

3

others including county meetings and hospital staff meetings

(Some physicians gave more than one source of information)

***The unique feature of the Furadantin story in Fond du Lac is
the apparent influence that prescribers of the drug attribute to a specialist
(specialist A) in the community.**

CHARACTER OF FURADANTIN JOURNAL ADVERTISING

Eaton selected a few publications and ran Furadantin ads in high frequency in these journals. Copy stressed rapid action and a symbol was developed (urine glass) to demonstrate the best product benefit visually.

use **FURADANTIN** first...

IN URINARY

TRACT INFECTIONS

for rapid clearing
of the
urine



In 30 minutes: antibacterial concentrations in the urine

In 24 hours: the urine is frequently clear

In 3 to 5 days: complete clearing of pus cells from the urine

In 7 days: sterilization of the urine in the majority of cases

With Furadantin there is no proctitis, pruritus ani, or crystalluria.

Average adult dosage: Four 100 mg. tablets daily, taken with meals and with food or milk before retiring.

50 and 100 mg. tablets.

Oral Suspension, 5 mg. per cc.

EATON LABORATORIES
NORWICH, NEW YORK



FURADANTIN®

brand of nitrofurantoin, Eaton

INTERVIEW PROFILE—SPECIALIST B

Specialist B is one of the few Fond du Lac doctors who is on the staff of the hospital only and is not affiliated with a clinic. He has been practicing, wholly in Fond du Lac, for about 25 years. He says that he attends most of the county medical society meetings, a couple of state meetings each year, and every meeting of his specialty group in Milwaukee.

An average prescriber (40 or so prescriptions a week) he has used only two of the five audited drugs, Furadantin and Achromycin. He credits his use of both drugs equally to medical journal articles and journal advertising. He has never been detailed on Achromycin and claims never to have been sampled on any of the five products under investigation in this study.

Specialist B is a staunch supporter of journal advertising and of company periodicals. He subscribes to and reads three journals and says that the company periodicals "are much preferred to detail men." He grants audiences to detail men only when he has "free time—and that is rare."

He reserves his strongest criticism for direct mail, saying that over 90 per cent of it goes into his wastebasket unread. Such mail that he selects to read is chosen primarily by company name.

COMMENTS ON JOURNAL ADVERTISING

Just as in other media, some Fond du Lac area doctors appear to rely heavily upon advertising in medical journals while others say that they ignore it.

Some of the favorable comments—

Part-time Specialist "A":

"I am truly a cover-to-cover reader of the journals and so I have to read all of the ads."

Part-time Specialist "D":

"To me there is no real distinction between the ads in the journals and the scientific articles. I read the journals a lot, so I pick up a good deal of scientific information on products."

General Practitioner "C":

"I like journal ads—particularly those with pictures, charts and graphs. An attractive ad helps a good deal to stimulate my interest in a product."

Eye Doctor "C":

"The advertising in the professional publications is a more reliable source once a detail man has made me aware of the existence of a product."

Some comments about auxiliary effect of journal advertisements—

Internist "B":

"I don't often notice them except for very new products which I have not heard about before. Seeing the ad lets me ask questions of the detail man his next time around."

General Practitioner "K":

"I read them if they deal with a product I am interested in and which I have heard about somewhere else."

Part-time Specialist "G":

"Such ads are a reminder to me, because they raise a certain amount of skepticism about whether a drug will do what it claims to do."

And some comments from those who accept journal advertising with reservations—

Surgeon "E":

"They are a valuable source, but I resent advertising which is non-professional. What the average doctor is looking for is a drug to do a specific job, so if the advertising gives technical detail without ballyhoo he is satisfied."

Eye Doctor "D":

"It is often too long before definite data are out on a drug so sometimes I try a product from specifications in the ads, but I don't like to do this unless it is not going to be at all risky."

Finally, the inevitable disclaimers about advertising—

General Practitioner "M":

"I never look at the ads too much."

Surgeon "F":

"I rarely look at the journal ads."

General Practitioner "H":

"I never read journal advertising."

(A.M.A. Fond du Lac Study, 1956)

SECTION III _ Chapter 3. The Story of Geigy's Butazolidin

THE NONHORMONAL ANTIARTHRITICS

Butazolidin and the drugs included for study with it are labeled here as antiarthritics although they have other uses as well. The basic active ingredient in the other four drugs is a salicylate, while Butazolidin is the trade name for phenylbutazone.

These drugs of course compete with cortisone, corticotropin (ACTH) and related products but are of synthetic, nonhormonal origin and may be considered here as a separate family.

Sodium salicylate is an official drug. Sodium Salicylate Enseals is a Lilly product.

Pabalate contains sodium salicylate, para-aminobenzoic acid and ascorbic acid. It is a Robins product.

Pabalate-Sodium Free is also a Robins item in which potassium replaces sodium. It is intended for use in place of Pabalate where sodium intake must be restricted.

Pabirin is a product of Smith-Dorsey. It contains aspirin, para-aminobenzoic acid and ascorbic acid. It is also available in capsule form with codeine.

Butazolidin was the latest of these products to appear. It came on the market in May 1952, four years after phenylbutazone was first synthesized in the Geigy laboratories. No estimate is available of the amount of research funds which went into developing the product, but a total of five years was spent working on it before it was marketed.

NATIONAL PROMOTION OF BUTAZOLIDIN

In the first seven or eight months on the market, the national advertising and promotion cost for Butazolidin amounted roughly to \$420,000.

The following are the amounts spent from May to the end of 1952—

The largest advertising expense incurred was for direct mail. The 21 mailings made in 1952 came to a total cost of about\$190,000

Detailing was of secondary importance as the company had only 14 representatives at the time, and these were located primarily on the east and west coasts. At no time was there a detail man for the Fond du Lac area. The 1952 costs are estimated at\$140,000

Ads were run in eleven medical journals during 1952 at a cost of about \$45,000

Sampling was done in three mailings in 1952..... \$40,000

Exhibits were made at medical meetings in four states (not Wisconsin) \$6,000

Very little marketing research was done on Butazolidin. No test markets or sample surveys were used. The market was studied "in general but without a formal research program."

PROFESSIONAL EVALUATION OF BUTAZOLIDIN (phenylbutazone)

Like most of the antiarthritic drugs, Butazolidin has occasional tendencies toward undesirable side reactions in individual cases. The possibility of such limitations in comparison with the marked therapeutic effects has given rise to a large number of professional communications.

At the time of the study, a bibliography was available listing over 500 references to writings about phenylbutazone, or Butazolidin, specifically. These articles, letters to editors, etc. were divided roughly three-to-one in foreign and United States publications, showing the wide interest in this drug.

No estimate has been made of the number of papers presented on this product at professional meetings but it is no doubt substantial.

GENERAL PUBLIC INFLUENCE

Some newspaper publicity had appeared on Butazolidin, but perhaps its most important general public notice was by word of mouth.

It is possible that some public demand was created by its discussion by the American Rheumatism Association.

No public relations program was established.

NONHORMONAL ANTIARTHRITIC SALES

These five antiarthritic drugs* together appear to have a fairly steady or even slightly increasing market in the Fond du Lac area, and a widespread appeal to the doctors of the area.

During the four weeks of the prescription audits a total of 28 of the 55 doctors prescribed one or more of the five drugs in this group, writing a total of 96 prescriptions which sold at \$225. On an annual basis this would amount to about 1250 original prescriptions and a \$2900 market, exclusive of refills and direct dispensing.

Both the number and dollar value of the prescriptions were larger during the last week of the audits than for earlier weeks.

*Original Prescriptions
5 drugs*

<i>Week of Audit</i>	<i>Number</i>	<i>Price</i>
May 1954	23	\$59
September 1954	20	\$49
January 1955	21	\$45
May 1955	32	\$72

*Butazolidin, Pabirin, Pabalate, Pabalate-Sodium Free and sodium salicylate.

BUTAZOLIDIN SALES

During the prescription audit periods, a total of 22 prescriptions for Butazolidin were filled. These prescriptions were written by only six doctors, whereas 22 of them reported that they had prescribed it at some time.

The price of the 22 Butazolidin prescriptions came to \$93, and indicates that prescriptions for this drug were priced higher than for the salicylates (although considerably lower than for the hormonal products). Thus, the Butazolidin prescriptions made up about a fourth (23%) of the total number of prescriptions for the five drugs and two-fifths (41%) of their total retail dollar volume.

In annual sales the above rate of Butazolidin prescriptions translates into about 285 prescriptions and \$1200 at retail, exclusive of refills and direct dispensing.

Or, looked at another way, if the 55 Fond du Lac area physicians are considered to share 1/3000th of the national promotion, exclusive of detailing, then this market's share of the cost projected for the first year might have been about \$150. This may be compared with this later year's retail sale figure of \$1200 for original prescriptions filled.

CONCENTRATION OF BUTAZOLIDIN PRESCRIPTIONS

It is important to note that 13 of the 22 Butazolidin prescriptions filled during the four audit periods were written by one general practitioner, G.P. "G."

And he probably was not always the heaviest prescriber of Butazolidin. One pharmacist stated that "it is not a big number today, but used to be. When Dr. _____ was alive last year we used to buy in the thousands; now we buy it in the hundreds."

G.P. "G" accounted for \$48 of the \$93 worth of Butazolidin prescriptions during the audit periods, while the next largest prescriber (G.P. "A") in his three prescriptions accounted for only \$19 of the total.

Unlike Serpasil, Butazolidin apparently was a general practitioner's drug in Fond du Lac. The four top prescribers of Butazolidin and of the competitive drugs were all general practitioners.

SOURCES OF INFORMATION ABOUT BUTAZOLIDIN

Because the sources of information about Butazolidin were limited so far as Fond du Lac physicians were concerned, they report only four sources which originally led them to prescribe it.

The two sources most often mentioned were journal articles and journal advertising.

"Where did you happen to get the information which led you to prescribe Butazolidin?"

**21 Butazolidin
prescribers**

Papers and articles in journals	12
Medical journal advertising	11
Direct mail	4
Other physicians	2

G.P. "G" named two sources—journal articles and direct mail—as prompting him to write his first prescription.

Most Fond du Lac area physicians (36) indicated that they had never received samples of Butazolidin.

12 of the 21 prescribers and

7 of the 34 nonprescribers recalled having been sampled

G.P. "G" was not among the earliest prescribers of this drug. Nine of the 21 doctors who had prescribed Butazolidin began using it prior to 1954, but G.P. "G" waited until the first part of that year.

GENERAL SOURCES OF INFORMATION

Butazolidin prescribers are almost indistinguishable from other Fond du Lac physicians in their ratings of general sources of information about new pharmaceutical products.

In proportion, they mention detail men and journal articles about as often as nonprescribers do.

"Which of these methods do you find most important to you personally in learning about a new drug?"

	21 Butazolidin prescribers	34 non- prescribers
Detail men	8	12
Papers, articles in journals	7	12
Journal advertising	2	2
Direct mail	2	2
National conventions	—	2
County meetings	1	1
Staff meetings	—	2
Reference books	1	—
Postgraduate courses	—	1

However, in their evaluations of the commercial media, Butazolidin prescribers do reveal some differences from nonprescribers.

The prescribers appear to be relatively impressed by commercial sources of information, except that far fewer of them are critical of journal advertising.

"Which of the four sources of information from manufacturers do you find most worthwhile for learning about new products?"

	21 Butazolidin prescribers	34 non- prescribers
Detailing	13	18
Company periodicals	2	5
Journal advertising	1	4
Direct mail	—	5
No choice	5	2

"Which do you consider least worthwhile to you personally?"

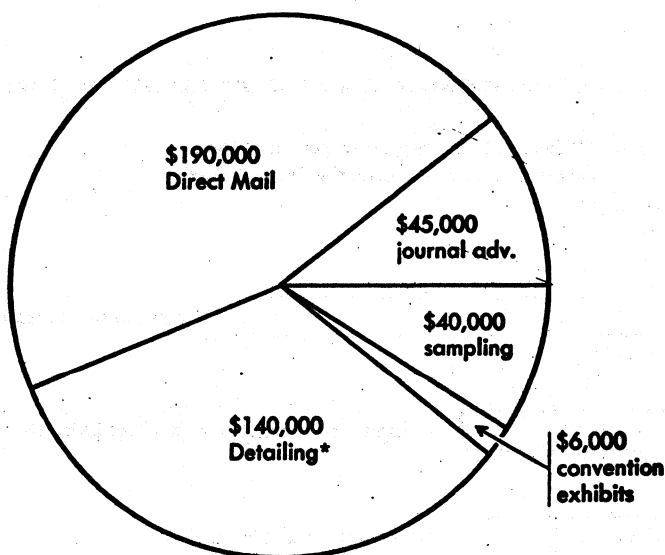
	21 Butazolidin prescribers	34 non- prescribers
Direct mail	11	19
Journal advertising	4	12
Detailing	4	1
Company periodicals	—	1
No choice	2	1

The largest prescriber of Butazolidin, G.P. "G," thought that detailing was the most worthwhile.

MARKETING MIX FOR BUTAZOLIDIN

In the first seven or eight months of its existence on the market, the national advertising and promotion cost for Butazolidin amounted roughly to \$420,000.

The following are the amounts spent from May to the end of the first year of promotion.



*14 detail men located primarily on the east and west coasts. *At no time* has there been a detail man in the Fond du Lac area.

MEDICAL ARTICLES AND BUTAZOLIDIN

At the time of the study, a bibliography was available listing over 500 references to the use of phenylbutazone (Butazolidin). These articles were divided roughly three-to-one among foreign and United States publications, showing the wide interest in the drug.

Some newspaper publicity had appeared on Butazolidin; perhaps its most important public notice had been by word of mouth. It is possible that some public demand had been created by discussion through the American Rheumatism Association and by articles written by medical columnists. The drug is restricted to use on prescription only.

SOURCES OF INFORMATION ABOUT BUTAZOLIDIN

"Where did you happen to get the information which led you to prescribe Butazolidin?"

21**Butazolidin prescribers****12****Papers and articles in medical journals****11****Medical journal advertising****4****direct mail****2****other physicians**

**some physicians named more than
one source of information**

GENERAL SOURCES OF INFORMATION

Butazolidin prescribers are almost indistinguishable from other Fond du Lac physicians in their ratings of general sources of information about new pharmaceutical products.

"Which of these methods do you find most important to you personally in learning about a new drug?"

	21 Butazolidin prescribers	34 nonprescribers
Detail men	8	12
Journal articles*	7	12
Journal adv.*	2	2
Direct mail	2	2
Conventions Natl.	—	2
County & Staff Meetings	1	3
Reference books	1	—
Postgrad. courses	—	1

*Journal articles and journal advertising combined lead all other methods of communication in telling physicians about new drugs. This is true of the prescriber and nonprescriber of Butazolidin.

INTERVIEW PROFILE, GENERAL OFFICE PRACTITIONER "A"

G.O.P. "A" is one of the older doctors in Fond du Lac—a former surgeon who has now restricted himself to general office practice. He remains one of the more frequent prescription writers, however, and is still a clinic and hospital staff member.

Like many other older doctors, his limited practice permits him to be more active in other professional activities. He attends national A.M.A. conventions, state conventions, county medical meetings and several surgical society meetings as well.

He regularly reads four of the leading medical journals, but he likes JAMA best and considers it the most valuable as well as the journal he feels most duty-bound to read. He says that journal articles are the most important sources of his information about new drugs, and journal advertising gave him the information which led to his first prescriptions of Achromycin. He first prescribed Serpasil after hearing about it at a convention and Butazolidin when a local doctor recommended it to him.

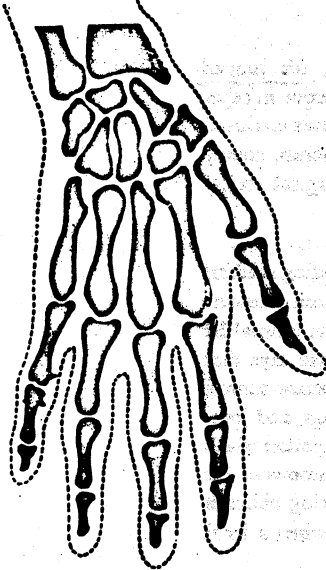
While he sees all detail men who call, he thinks of that method as the least worthwhile of the company media. He says that he teases them a little bit each time but he resents those who try to push their products too hard.

He reads about half of the house organs and very little of the direct mail that is sent to him. Once in a while a piece will catch his eye, usually because it reminds him of something from his earlier days—then he will save it.

He will seldom prescribe a new product but relies on his old stand-bys until sufficient technical data has been collected to indicate a desirable reason to make the change. He will wait a considerable time until definite, technical data does appear in the journals.

THE CHARACTER OF BUTAZOLIDIN ADVERTISING

Butazolidin advertising was characterized by the use of anatomical drawings and copy emphasizing action, efficacy and indications.



*in
arthritis
and allied
disorders*

Rapid Relief of Pain
usually within a few days

**Greater Freedom
and Ease of Movement**
functional improvement in a significant
percentage of cases

No Development of Tolerance
even when administered over
a prolonged period

BUTAZOLIDIN

(brand of phenylbutazone)

Its usefulness and efficacy substantiated by numerous published reports,
BUTAZOLIDIN has received the Seal of Acceptance of the Council on
Pharmacy and Chemistry of the American Medical Association for use in:

- Gouty Arthritis
- Rheumatoid Arthritis
- Psoriatic Arthritis
- Rheumatoid Spondylitis
- Painful Shoulder (including peritendinitis, capsulitis, bursitis and acute arthritis)

Since BUTAZOLIDIN is a potent agent, patients for therapy should be selected
with care; dosage should be judiciously controlled; and the patient should be regularly
observed so that treatment may be discontinued at the first sign of toxic reaction.

Descriptive literature available on request.

BUTAZOLIDIN® (brand of phenylbutazone), coated tablets of 100 mg.

 **GEIGY PHARMACEUTICALS**
Division of Geigy Chemical Corporation
220 Church Street, New York 14, N.Y.
In Canada: Geigy Pharmaceuticals, Montreal

READING OF HOUSE ORGANS

Fond du Lac area physicians receive company periodicals from pharmaceutical firms in even greater abundance than medical journals, and they look through or read these house organs in fairly high proportions.

The doctors were shown a list of eleven company periodicals. On the average each doctor said that he received nine of these publications, and that he usually read or looked through six or seven of them. While seven doctors say that they never look at company periodicals, 15 indicate that they look through all eleven.

"Which of these company periodicals do you happen to receive? Which of these do you usually read or look through?"

	<i>House organs received</i>	<i>Read or looked through</i>
Total doctors	55	55
All eleven	28	15
Nine or ten	12	9
Seven or eight	5	6
Five or six	5	8
Three or four	3	6
One or two	2	4
No house organs	—	7

Three company periodicals are each singled out by five or more doctors as doing the best job. They are:

Symposia of Ciba, named by 11 doctors

Therapeutic Notes of Parke, Davis, named by 10 doctors

What's New of Abbott, named by 5 doctors

SECTION III - Chapter 4. The Story of Lederle's Achromycin

DEVELOPMENT OF THE BROAD SPECTRUM ANTIBIOTICS

Soon after production of penicillin was begun during 1942 and 1943, wide attention was directed to discovering other antibiotics. For example, Dr. Benjamin M. Duggar joined the Lederle staff specifically to lead a program for screening potential antibiotics.

In a little over ten years the pharmaceutical industry isolated and studied more than 3500 different antibiotics, but low potency or high toxicity prevented use of almost all of them. The average of success has been about one new useable antibiotic a year.

The five antibiotic drugs included in the Fond du Lac study are "broad-spectrum," since they are active against both gram-negative and gram-positive bacteria, rickettsiae and certain viruses. The expression "broad-spectrum" dissociates these drugs as a class from such drugs as penicillin, which is active primarily against gram-positive bacteria.

The five drugs have a common derivation—from various species of the actinomycete mold, *Streptomyces*. Their chemical formulas, except that for Chloromycetin, also are

very similar as evidenced by their generic names, and Tetracycline is actually the same as Achromycin. Because exact dates of scientific discoveries are difficult to establish, the most useful dates are those of introductory marketing:

Aureomycin or chlortetracycline
(Lederle) December 1948

Chloromycetin or chloramphenicol
(Parke, Davis) March 1949

Terramycin or oxytetracycline
(Pfizer) March 1950

Achromycin or tetracycline
(Lederle) November 1953

Tetracycline or tetracycline
(Pfizer) February 1954

Because of their wide range of applicable use the five drugs come in a variety of forms. Aureomycin, for example, is available in 20 forms while Achromycin comes in 11 forms ...including capsules, tablets, drops, ointment, powder, and vials for intramuscular and intravenous injection.

NATIONAL PROMOTION OF ACHROMYCIN

Achromycin was launched with a very heavy advertising budget in its first year—somewhere in the neighborhood of \$2,500,000. Most of this advertising was of the blanketing type; for example, every physician in the country received on an average of two Achromycin mailings each week.

Heavy outlays were made for other media, especially detailing—

Detailing \$1,026,000
including literature and samples (\$85,500 a month)

Direct mail \$ 851,000

105 mailings to full list of
M.D.'s

7 dental mailings

2 druggist mailings

Medical journal advertising \$ 470,000

monthly insertions in Modern Medicine, Medical Economics, regional journals, all state journals, 116 county journals, and most specialty journals. 26 insertions in the journal of the American Medical Association

Exhibits at medical meetings \$ 100,000
200 during the year

(plus sales promotion devices such as pens, tongue depressors, and brushes)

Despite the fact that at least six years were spent on research to develop this drug and that so much money was spent to promote it, no research of any kind was undertaken to determine the potential market, advertising appropriation, media, etc. Of course, it could be argued that Lederle already had a wealth of experience on Aureomycin and other products to go on; but even so, a marketing research department would have been needed to best utilize this information.

PROFESSIONAL EVALUATIONS OF ACHROMYCIN (TETRACYCLINE)

It can be said, with reasonable justification, that the former success of penicillin and Aureomycin had the professional world eagerly awaiting Achromycin, especially since it was reported to be effective over a wider range and to be somewhat better tolerated.

A partial bibliography of only the first year's writings on Achromycin shows 118 titles, and the number of papers read at medical meetings is also impressive.

GENERAL PUBLIC INFLUENCE

The influence of the public on physicians with respect to Achromycin may or may not have been of much importance.

On the one hand, as one of the "wonder drugs" Achromycin had received its share of attention in the lay press; and the public should have been more aware of it than of any other drug.

On the other hand, physicians were made thoroughly aware of Achromycin early enough so that any mention of this drug by patients would have been like "carrying coal to Newcastle." Then, too, many people probably did not distinguish between Aureomycin and Achromycin.

ACHROMYCIN DETAILING IN THE FOND DU LAC AREA

The report of the Lederle detail man indicates how intensive the detailing on Achromycin was:

He had some 300 doctors in his territory and managed to see 150 or 160 of them a month, giving the heavy prescribers the most attention. Thus, he saw some doctors three times a month, some once a month and some just once in a while. He visited the largest volume druggist every week, the least busy one once a year. He spent a day a week in Fond du Lac and one day a month in Chilton.

On his first visit for Achromycin, he checked with the pharmacies to make certain that they had received their initial supply of the 250 mg. capsule.

Later, when other Achromycin products were added to the line, he used different methods of detailing for different doctors. With one doctor he would show the capsules and tablets and leave samples of them. As new dosage forms were introduced he might concentrate on the cherry flavored oral suspension and leave a sample of that. If one doctor showed little interest in a particular product form, the detail man would show him another. In most cases he found that the doctors already knew of Achromycin from journals and direct mail.

BROAD SPECTRUM SALES

The five broad spectrum drugs as a group had by far the widest usage among Fond du Lac physicians of any drugs studied, both in number of prescriptions written and in dollar volume.

During the four prescription audit weeks, for example, 41 of the 55 physicians each wrote prescriptions for one or more of the five antibiotics. On an average, these prescribers wrote $3\frac{1}{2}$ broad spectrum prescriptions a week, at a cost to their patients of about \$4.40 a prescription.

On an annual basis, this would add up to about 7500 original prescriptions and \$33,000 for the Fond du Lac market alone, exclusive of refills and direct dispensing by physicians.

Demand for drugs in this group was well established in May 1954, at the time of our first prescription audit.

Sales continued at a fairly steady rate except for a spurt in the winter months, as represented by our January audit week.

Week of audit	Original prescriptions	
	5 drugs	
	Number	Price
May 1954	129	\$504
September 1954	128	\$632
January 1955	202	\$841
May 1955	118	\$567

ACHROMYCIN SALES

Achromycin is a very broad-based drug, and 50 of the 55 doctors reported having prescribed it. The only physicians who did not were two EENT men, an anesthesiologist, a radiologist and a pathologist. During the four audit periods 260 prescriptions were filled in the Fond du Lac area over signatures of 33 physicians—an average of two a week per prescriber.

The total price of these Achromycin prescriptions was \$1224. This figure represents almost half (49%) of the total for the

broad spectrum drugs. Annual projection of these figures adds up to 3400 prescriptions and \$16,000 at retail for Achromycin alone—again not counting refills or direct dispensing.

The Fond du Lac area's pro rata share of the first year's advertising budget for Achromycin would have amounted to about \$850. This means that despite the heavy promotion in total dollars the Achromycin campaign was relatively inexpensive.

SALES OF COMPETITIVE DRUGS

The four audit weeks represent a very interesting period in the histories of these five drugs.

Aureomycin, far from being replaced by Achromycin, was still second in sales in Fond du Lac as late as May 1955.

Chloromycetin, which had suffered a serious setback apparently because of reports of blood dyscrasias, was making a comeback at the end of the period due to appearance of more reassuring reports.

Tetracycline, another brand of tetracycline, was not at any time an important factor in the market.

Here are the number of prescriptions filled for Achromycin and its four competitors during the audit weeks:

Week of audit	Original prescriptions of				
	Achro- mycin	Aureo- mycin	Terra- mycin	Chloro- mycetin	Tetra- cyn
May 1954	57	51	17	1	3
September 1954	67	37	12	4	8
January 1955	81	51	30	33	7
May 1955	55	32	8	22	1

BREADTH OF ACHROMYCIN PRESCRIPTIONS

For most of the drugs reported in this study the breadth of usage was narrow, only some of the physicians having prescribed them. At the same time usage of the other drugs had depth, in that one or two or three physicians relied very heavily upon them.

The Achromycin situation was different. Achromycin enjoyed wide breadth of usage, having been prescribed by almost all doctors who prescribed any drugs at all, and had not quite so much depth in that one or two doctors did not write the majority of prescriptions.

The heaviest prescriber of Achromycin wrote 21% of the prescriptions, while it took the top five prescribers to account for 54% of them and for 45% of the dollar volume.

*Four-week
Achromycin prescriptions*

	<i>Number</i>	<i>Price</i>
Total	260	\$1224
G.P. "F"	55	\$ 195
P.T. "A"	30	111
P.T. "D"	23	104
P.T. "G"	20	91
G.P. "C"	14	60
Spec. "A"	13	66
G.P. "K"	13	56
P.T. "F"	12	62
G.P. "A"	11	59
G.P. "I"	8	38
23 other prescribers	61	382

The initials assigned to the ten doctors listed above indicate the wide applications of Achromycin and that it is not a specialist's drug.

G.P. — general practitioner

P.T. — part-time specialist

Spec. — specialist

SOURCES OF INFORMATION ABOUT ACHROMYCIN

Three out of five Fond du Lac doctors said that the Lederle detail man was instrumental in getting them to prescribe Achromycin.

Forty-seven of the 55 doctors recalled having been detailed on the drug and 30 of these said that they prescribed it based on information which he gave them. All five of the heaviest prescribers said that the detail man got them to prescribe Achromycin. Incidentally, only four doctors indicated that they received no Achromycin samples.

"Where did you happen to get the information about Achromycin which led you to prescribe it?"

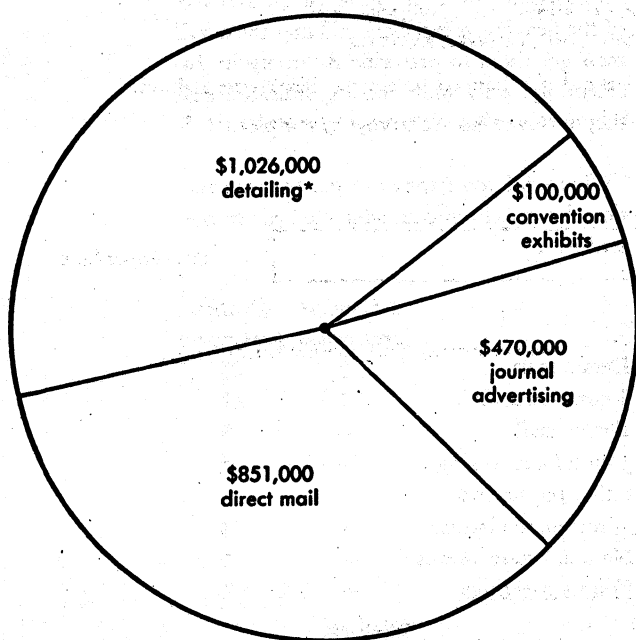
	<i>5 heaviest prescribers</i>	<i>45 other prescribers</i>
Detail man	5	25
Journal articles	1	11
Direct mail	—	5
Journal advertising	—	4
Other physicians' recommendations	—	3
National conventions	—	1
County meetings	—	1

(some physicians named more than one source of information)

Evidence of the quick acceptance of this drug is the fact that 32 of the physicians who prescribed it said they had used it within the first two months after its release.

THE ACHROMYCIN MARKETING MIX

The first year's national advertising and promotion effort for Achromycin cost in rough figures about \$2,500,000. Advertising was addressed to the mass physician audience; in the early stages of promotion every physician in the country received on an average of two Achromycin mailings each week.



*includes literature and samples for the detail men

SUPPORT FOR ACHROMYCIN IN MEDICAL JOURNALS

It seems justifiable to say that the previous success of penicillin and Aureomycin made the professional world eager for such a drug as Achromycin, since it was reported to be effective over a wider range and to be somewhat better tolerated.

A partial bibliography of just the first year's writings on Achromycin shows 118 articles, and the numbers of papers read at medical meetings is also impressive.

CORRELATION WITH SOURCES OF INFORMATION ON ACHROMYCIN

"Where did you happen to get the information about Achromycin which led you to prescribe it?"*

45

Total Prescribers

16

Journal articles and Journal advertising

1

conventions

5

direct mail

30

detail men

4

other sources including county meetings, staff meetings

*some physicians named more than one source of information

CHARACTER OF ACHROMYCIN JOURNAL ADVERTISING

Achromycin ads were run in a long list of publications, at high frequency, and for month after month. The idea was to "sell" the Achromycin name. Detail men reported that many doctors already knew about Achromycin when they first called upon them. This is the character of the advertising that did it.

new broad-spectrum antibiotic

ACHROMYCIN

**broader tolerance
greater stability
faster diffusion**

Lederle

LEDERLE LABORATORIES DIVISION, Pearl River, New York

ACHROMYCIN, a new broad-spectrum antibiotic developed by the Lederle Research Team, has demonstrated notable effectiveness in clinical trials.

Achromycin has already been administered to thousands of patients, proving its safety and effectiveness in a wide variety of clinical situations. It provides:

- more rapid diffusion in body tissues and fluids
- broader tolerance
- greater stability
- faster diffusion

ACHROMYCIN is available in the following forms:

CAPSULES	100 mg	500 mg	1000 mg
TABLETS	100 mg	500 mg	1000 mg
INJECTION	100 mg	500 mg	1000 mg

Other dosage forms will become available as supply in various countries.

INTERVIEW PROFILE—PART-TIME SPECIALIST "E"

P.T. "E" is one of the heavy prescribers, writing more than 100 prescriptions a week. He has been practicing medicine for more than 20 years in Fond du Lac, and is on the staff of the hospital as well as being active in one of the smaller clinics. He seldom if ever attends any national conventions or meetings of other doctor groups, but is present at most local medical society meetings and attends some state medical conventions.

This doctor professes to pay little attention to pharmaceutical promotion, admitting detail men from only three or four of the larger companies and discarding all direct mail and most house organs.

When pressed to name the most worthwhile source of information from manufacturers, he chooses company periodicals. However, he does not mention this source for either of the two audited drugs which he has prescribed.

He considers that papers and articles in medical journals are the most important means of his learning about new drugs. And, although he rates medical journal advertising as not very worthwhile, he credits such advertising with causing him to write his initial prescription of Achromycin. He takes six of the leading journals and reads three of them, including J.A.M.A., regularly.

He is one of the few doctors who admit that pharmacists may be an informative source. In fact, a local druggist first suggested that he use Serpasil.

READERSHIP OF MEDICAL JOURNALS IN FOND DU LAC

The most commonly received as well as the most often read medical publications in the Fond du Lac area are the *Journal of the American Medical Association* and *Medical Economics*.

Here are the top eight journals according to the number of mentions on both scores—

Total doctors	Received	Read or looked through
	55 %	55 %
J.A.M.A.	47—85.4	35—78.7
Medical Economics	47—85.4	35—78.7
Modern Medicine	39—70.9	22—56.4
Medical Times	24—43.6	10—41.6
Current Medical Digest	21—38.1	13—61.9
GP	19—34.3	17—89.5
Surgery, Gynecology and Obstetrics	14—25.4	10—71.4
Annals of Surgery	11—20.0	7—63.6

A somewhat larger number of doctors claimed regular readership than those reporting having read a journal within the last 30 days. For comparison with the 35 shown above for *J.A.M.A.*, a total of 41 said that they read at least half of the *J.A.M.A.* issues.

The top three journals in number of mentions as the most valuable were *J.A.M.A.* with 13 mentions, *GP* with 7 and *Modern Medicine* with 6. The two that doctors said they enjoyed reading most were *Medical Economics* with 17 mentions and *J.A.M.A.* with 10. *J.A.M.A.* was the only publication about which at least five doctors said they felt "duty bound" to read.

SECTION III Chapter 5. The Story of UPJOHN's PamineDEVELOPMENT OF THE
RECENT ANTICHOLINERGIC DRUGS

Pamine and the other drugs included for study in this group are useful in the treatment of peptic ulcer and gastrointestinal disorders.

Banthine (methantheline bromide) was introduced by Searle in 1950. It was the first of a new type of anticholinergics. Like the ones to follow, it is basically an antispasmodic and is believed to have some effect in reducing secretion of hydrochloric acid.

Within the next two or three years the other products studied came on the market. The order may not be as shown here.

Prantal (diphenamil methylsulfate) was introduced by Schering.

Antrenyl (oxyphenonium bromide) was brought out by Ciba.

Co-Elorine (tricyclamol sulfate and amobarbital) was a comparable Lilly product.

Pro-Banthine (propantheline bromide) is a Searle improvement of its original Banthine, having the advantages of the original product with almost none of its side actions. It was first marketed in February 1953.

Pamine (methscopolamine bromide) was one of the last products to be added, in July 1953. It is the result of three years of research at Upjohn and cost over \$200,000.

Demand for this group of drugs appears to have fluctuated only slightly, but the total price of prescriptions showed more variation:

*4-week prescriptions
Anticholinergic group*

<i>Week of audit</i>	<i>Number</i>	<i>Price</i>
May 1954	11	\$38
September 1954	17	\$63
January 1955	14	\$52
May 1955	12	\$28

BREADTH OF ANTICHOLINERGIC USE

This group of drugs is another that does not show extremely heavy concentration of usage by just one or two physicians.

For example, the five top prescribers of these anticholinergics account for less than half of the number of prescriptions, whereas in some of the other groups a single doctor may have been responsible for a majority of the prescriptions.

4-week prescriptions
Anticholinergic group

	Number	Price
Total	54	\$181
Surgeon "B"	8	\$ 24
Internist "A"	5	\$ 23
Surgeon "A"	4	\$ 17
G.P. "B"	4	\$ 17
P.T. "G"	4	\$ 13
Internist "C"	3	\$ 10
P.T. "H"	3	\$ 8
G.P. "E"	3	\$ 5
14 other prescribers	20	\$ 64

One fact disclosed by the above listing is that these drugs have been adopted rather heavily by surgeons. Not only are two specialists in surgery shown in the eight top prescribers but also the two part-time specialists both have special interest in surgery.

P.T. — part-time specialist

PAMINE, BANTHINE AND PRO-BANTHINE SALES

Pro-Banthine was the most used of this class of drugs in the Fond du Lac area during the audit periods, followed by Banthine and then Pamine in third place.

Pro-Banthine and Pro-Banthine/Phenobarbital were prescribed 39 times; Banthine and Banthine/Phenobarbital, 10 times; and Pamine and Pamine/Phenobarbital, 5 times (by three doctors).

ANTICHOLINERGIC SALES

Of the five groups of drugs singled out for investigation in the Fond du Lac study, the anticholinergics were used the least.

During the four audit weeks only 54 prescriptions for this group were filled over the signatures of 22 doctors. These prescriptions sold for \$181. This would mean about 700 prescriptions a year at roughly \$2350, exclusive of refills and direct dispensing by physicians.

Most of these products have since been manufactured in combination with phenobarbital for its sedative action. No distinctions between Pamine and Pamine/Phenobarbital and of similar combined forms of the other drugs will be made here.

NATIONAL PROMOTION OF PAMINE

Upwards of a million dollars had been spent on the promotion of Pamine at the start of the Fond du Lac study.

By far the greater part of these efforts were spent on detailing the new product. Detailing was done in two stages—intensively for the first two months after introduction and again intensively for two months the following year—

Detailing	\$850,000
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Major detailing effort two months in 1953 and two months in 1954

Medical journal advertising (Up to May 1955)	\$153,000
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Direct mail (Up to May 1955)	\$ 59,000
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No commercial exhibits were prepared on Pamine for medical conventions.

Sampling of Pamine was not so lavish as that of other products. For example, the detail man left no samples with pharmacists, because of Upjohn's pre-stocking policy. Physicians were offered a sample supply sufficient for one, or possibly two, prescriptions.

Studies of market potential were made at Upjohn but no sample surveys or test markets were used.

PAMINE DETAILING IN THE FOND DU LAC AREA

It was necessary to interview three different Upjohn detail men to learn just how Pamine was detailed in this area because one man is assigned to Fond du Lac and another to Chilton and there had been a replacement.

The original representatives each had spent about 16 hours studying the drug, half of this time in group lectures.

The Fond du Lac detail man spent one week of each month there, and estimates that the equivalent of a full two weeks was devoted to Pamine although he details more than one item at a visit. He would spend about five minutes talking about the drug with a physician and approximately two minutes with a pharmacist.

The original detail man for Chilton spent as much time at the two pharmacies as he did with the five physicians there. He divided his time about 20 to 30 minutes with each pharmacist and 5 to 15 minutes with each physician. He was in Chilton one day every month and called on every doctor and both drug stores each time. He accomplished his detailing of Pamine there the first day that he worked on it. He did mention it later but did not have to go into elaborate detailing of the drug and its uses.

As he recalled it, the physicians were not conversant with the drug before he introduced it, but the pharmacists had read about it in their journal.

The replacement detail man confirmed that Pamine was known to the Chilton doctors when he took over although he refreshed their memories when needed.

Both of the Chilton representatives mentioned that they thought technical reprints on Pamine had been most effective in getting Chilton doctors to utilize the drug.

PROFESSIONAL EVALUATIONS OF PAMINE (METHSCOPOLAMINE BROMIDE)

Pamine attracted less experimental attention than the other products in the study and was less productive of professional articles and papers.

Through April 1955 a bibliography compiled at Upjohn included 13 titles, while 5 papers had been read at national and local medical meetings.

A scientific exhibit had been shown at the San Francisco Meeting of the A.M.A. in June 1954.

Not a single prescription was filled for the other three drugs, Antrenyl, Co-Elorine and Prantal, during any of the four audit weeks—another indication perhaps that the anticholinergic market was not very active.

Week of audit	Number of original prescriptions		
	Pro-Banthine	Banthine	Pamine
Total	39	10	5
May 1954	11	—	—
September 1954	10	6	1
January 1955	9	3	2
May 1955	9	1	2

The total price of the five Pamine prescriptions was \$14. On an annual basis (although it is hazardous to project such small figures) this would amount to some 65 prescriptions retailing at roughly \$180, not counting prescription refills and direct dispensing by the six doctors who reported dispensing Pamine.

At this rate, if the Fond du Lac situation were at all general, it would take a long time for the manufacturer to recover his promotional expenses. The Fond du Lac area's 1/3000th share of those expenses amounted to more than \$300.

SOURCES OF INFORMATION ABOUT PAMINE

Most of the seventeen Fond du Lac area doctors who said they prescribed Pamine gave credit to detail men for prompting them to use the drug.

None of the three who credited other sources were detailed. All but one of the 17 received samples.

"Where did you happen to get the information about Pamine which led you to prescribe it?"

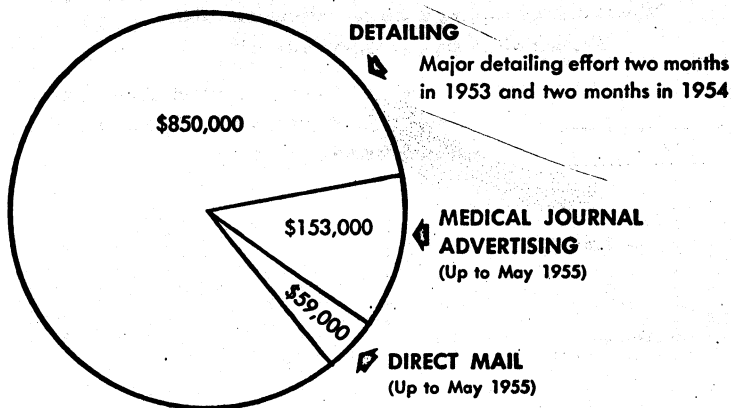
	<i>17 Pamine prescribers</i>
Detail men	14
Journal articles	3

A total of 26 doctors recalled having been detailed on Pamine, while 27 remembered receiving samples of it.

THE PAMINE MARKETING MIX

Upwards of a million dollars had been spent on the promotion of Pamine at the start of the Fond du Lac study.

By far the greater part of this effort was spent on detailing the new product. Detailing was done in two stages—intensively for the first two months after introduction and again intensively for two months the following year—



No commercial exhibits were prepared on Pamine for medical conventions.

Sampling of Pamine was not so lavish as that of other products. For example, the detail man left no samples with pharmacists, because of Upjohn's pre-stocking policy. Physicians were offered a sample supply sufficient for one, or possibly two, prescriptions.

SUPPORT FOR PAMINE IN MEDICAL JOURNALS

Pamine attracted less experimental attention than the other products included in the study and fewer professional articles and papers were published.

Through April 1955 a bibliography compiled at Upjohn included 13 titles, while 5 papers had been read at national and local medical meetings.

A scientific exhibit had been shown at the San Francisco Meeting of the A.M.A. in June 1954.

**CORRELATION WITH SOURCES
OF INFORMATION ON PAMINE**

"Where did you happen to get the information about
Pamine which led you to prescribe it?"

17**Total Prescribers****3*****journal articles****0****conventions****0****direct mail****14****detail men****0****other sources including county meetings, staff meetings**

*these doctors were not detailed

CHARACTER OF PAMINE JOURNAL ADVERTISING

Upjohn ran multiple half pages on Pamine in each publication for a 3-month saturation period. Then the journal program was cut back to one page once a month. Ads emphasized the length of Pamine antacid action and product name.

Pamine
BROMIDE

REGISTERED TRADEMARK FOR THE UPJOHN GROUP
OF MEDICAL-INDUSTRIAL GROUPS, INC.

Ulcer protection that lasts all night

Pamine
Tablets
Each tablet contains
Pamine 250 mg
Bottles of 100 and 500

Upjohn
The Upjohn Company
Kalamazoo, Michigan

INTERVIEW PROFILE - INTERNIST "C"

Internist "C" is a young doctor who has been practicing medicine only a few years. He is on the staff of the hospital and a clinic, attends all county medical society meetings, a monthly conference in Oshkosh, some state conventions, and other special meetings.

The most significant attitude of Internist "C" is his heavy reliance on medical journals and his complete rejection of direct mail. He throws out everything that looks like advertising whether it is house organs or other pieces.

He does talk with all detail men who visit him and considers detailing of some aid to him, although he says that detail men merely repeat what they have memorized and really add nothing that is not in the literature. He accepts samples and will use them, particularly for patients whom he knows cannot afford expensive prescriptions. Sometimes detailing and sampling give him the final push which encourages him to try a product at a particular time.

He places strong emphasis upon the desirability of direct articles in the literature, and states that ordinarily he uses a new drug only after reading an evaluation by a known authority. He does not trust clinical tests reported to him by detail men since he does not know the doctors that they quote or their reputations.

He states that he was led to prescribe four of the five audited drugs from information given in journal articles. The fifth one, he first used after learning about it at a medical convention. He receives a number of medical journals and reads those on internal medicine most thoroughly.

PHYSICIAN COMMENTS ABOUT JOURNAL ARTICLES

Speaking broadly, it appears that to many of the physicians in Fond du Lac, professional articles seem to be the most reliable source of new product information—or that such articles would be the most reliable source if they could be published sooner.

Some doctors will wait for journal publication before using a new drug—

Internist "C":

"The most desirable source by far is direct articles in the literature. Ordinarily I will use a new drug only after reading an evaluation by a known authority."

Surgeon "C":

"I am interested only in reports on clinical tests as a basis for my decision to use a drug or not."

G.P. "R":

"One good article on a new drug product will do more to convince me that I should try it than unlimited detailing and advertising will do."

G.O.P. "A":

"I will wait for a considerable length of time before trying a product until technical data appears in the journals."

But others feel that they either cannot wait or cannot take the time for professional articles—

Surgeon "F":

"Characteristically, I go to the table of contents first and then directly to the article that interests me. Sometimes I search through the literature for technical material, but I know that many physicians do not have the time

for that sort of searching. I will trust a reprint of an article more than the literature put out by the pharmaceutical house."

Eye Doctor "A":

"Journal articles are the best source of data in the long run. It is a very long time before they are out, however, so the only practical thing is to rely on detailing and whatever other data is immediately available."

G.P. "E":

"I have a conflict here. I trust professional evaluation above any other source, but at the same time I do not have sufficient reading time to dig through the journals."

Journal articles also come in for their share of criticism—

Surgeon "E":

"The value of professional articles hinges directly upon the name of the author and his professional reputation. I have a suspicion of statistics since they can prove almost anything depending upon the way they are applied. This places most professional writings on a par with pharmaceutical house literature and advertising."

G.P. "H":

"I have one complaint about the use of chemical and generic names. The individual physician has to make the tie-up with the particular brand or trade name. This is confusing since a doctor has to know that a product is available, where to get it and what to call it. If you prescribe by generic name, the druggist may even call you back to ask for the trade name."

1997, 1998, 1999, 2000, 2001, 2002, 2003, 2004, 2005, 2006, 2007, 2008, 2009, 2010, 2011, 2012, 2013, 2014, 2015, 2016, 2017, 2018, 2019, 2020, 2021, 2022, 2023, 2024, 2025, 2026, 2027, 2028, 2029, 2030, 2031, 2032, 2033, 2034, 2035, 2036, 2037, 2038, 2039, 2040, 2041, 2042, 2043, 2044, 2045, 2046, 2047, 2048, 2049, 2050, 2051, 2052, 2053, 2054, 2055, 2056, 2057, 2058, 2059, 2060, 2061, 2062, 2063, 2064, 2065, 2066, 2067, 2068, 2069, 2070, 2071, 2072, 2073, 2074, 2075, 2076, 2077, 2078, 2079, 2080, 2081, 2082, 2083, 2084, 2085, 2086, 2087, 2088, 2089, 2090, 2091, 2092, 2093, 2094, 2095, 2096, 2097, 2098, 2099, 2100, 2101, 2102, 2103, 2104, 2105, 2106, 2107, 2108, 2109, 2110, 2111, 2112, 2113, 2114, 2115, 2116, 2117, 2118, 2119, 2120, 2121, 2122, 2123, 2124, 2125, 2126, 2127, 2128, 2129, 2130, 2131, 2132, 2133, 2134, 2135, 2136, 2137, 2138, 2139, 2140, 2141, 2142, 2143, 2144, 2145, 2146, 2147, 2148, 2149, 2150, 2151, 2152, 2153, 2154, 2155, 2156, 2157, 2158, 2159, 2160, 2161, 2162, 2163, 2164, 2165, 2166, 2167, 2168, 2169, 2170, 2171, 2172, 2173, 2174, 2175, 2176, 2177, 2178, 2179, 2180, 2181, 2182, 2183, 2184, 2185, 2186, 2187, 2188, 2189, 2190, 2191, 2192, 2193, 2194, 2195, 2196, 2197, 2198, 2199, 2200, 2201, 2202, 2203, 2204, 2205, 2206, 2207, 2208, 2209, 2210, 2211, 2212, 2213, 2214, 2215, 2216, 2217, 2218, 2219, 2220, 2221, 2222, 2223, 2224, 2225, 2226, 2227, 2228, 2229, 2230, 2231, 2232, 2233, 2234, 2235, 2236, 2237, 2238, 2239, 2240, 2241, 2242, 2243, 2244, 2245, 2246, 2247, 2248, 2249, 2250, 2251, 2252, 2253, 2254, 2255, 2256, 2257, 2258, 2259, 2260, 2261, 2262, 2263, 2264, 2265, 2266, 2267, 2268, 2269, 2270, 2271, 2272, 2273, 2274, 2275, 2276, 2277, 2278, 2279, 2280, 2281, 2282, 2283, 2284, 2285, 2286, 2287, 2288, 2289, 2290, 2291, 2292, 2293, 2294, 2295, 2296, 2297, 2298, 2299, 2300, 2301, 2302, 2303, 2304, 2305, 2306, 2307, 2308, 2309, 2310, 2311, 2312, 2313, 2314, 2315, 2316, 2317, 2318, 2319, 2320, 2321, 2322, 2323, 2324, 2325, 2326, 2327, 2328, 2329, 2330, 2331, 2332, 2333, 2334, 2335, 2336, 2337, 2338, 2339, 2340, 2341, 2342, 2343, 2344, 2345, 2346, 2347, 2348, 2349, 2350, 2351, 2352, 2353, 2354, 2355, 2356, 2357, 2358, 2359, 2360, 2361, 2362, 2363, 2364, 2365, 2366, 2367, 2368, 2369, 2370, 2371, 2372, 2373, 2374, 2375, 2376, 2377, 2378, 2379, 2380, 2381, 2382, 2383, 2384, 2385, 2386, 2387, 2388, 2389, 2390, 2391, 2392, 2393, 2394, 2395, 2396, 2397, 2398, 2399, 2400, 2401, 2402, 2403, 2404, 2405, 2406, 2407, 2408, 2409, 2410, 2411, 2412, 2413, 2414, 2415, 2416, 2417, 2418, 2419, 2420, 2421, 2422, 2423, 2424, 2425, 2426, 2427, 2428, 2429, 2430, 2431, 2432, 2433, 2434, 2435, 2436, 2437, 2438, 2439, 2440, 2441, 2442, 2443, 2444, 2445, 2446, 2447, 2448, 2449, 2450, 2451, 2452, 2453, 2454, 2455, 2456, 2457, 2458, 2459, 2460, 2461, 2462, 2463, 2464, 2465, 2466, 2467, 2468, 2469, 2470, 2471, 2472, 2473, 2474, 2475, 2476, 2477, 2478, 2479, 2480, 2481, 2482, 2483, 2484, 2485, 2486, 2487, 2488, 2489, 2490, 2491, 2492, 2493, 2494, 2495, 2496, 2497, 2498, 2499, 2500, 2501, 2502, 2503, 2504, 2505, 2506, 2507, 2508, 2509, 2510, 2511, 2512, 2513, 2514, 2515, 2516, 2517, 2518, 2519, 2520, 2521, 2522, 2523, 2524, 2525, 2526, 2527, 2528, 2529, 2530, 2531, 2532, 2533, 2534, 2535, 2536, 2537, 2538, 2539, 2540, 2541, 2542, 2543, 2544, 2545, 2546, 2547, 2548, 2549, 2550, 2551, 2552, 2553, 2554, 2555, 2556, 2557, 2558, 2559, 2560, 2561, 2562, 2563, 2564, 2565, 2566, 2567, 2568, 2569, 2570, 2571, 2572, 2573, 2574, 2575, 2576, 2577, 2578, 2579, 2580, 2581, 2582, 2583, 2584, 2585, 2586, 2587, 2588, 2589, 2590, 2591, 2592, 2593, 2594, 2595, 2596, 2597, 2598, 2599, 2600, 2601, 2602, 2603, 2604, 2605, 2606, 2607, 2608, 2609, 2610, 2611, 2612, 2613, 2614, 2615, 2616, 2617, 2618, 2619, 2620, 2621, 2622, 2623, 2624, 2625, 2626, 2627, 2628, 2629, 2630, 2631, 2632, 2633, 2634, 2635, 2636, 2637, 2638, 2639, 2640, 2641, 2642, 2643, 2644, 2645, 2646, 2647, 2648, 2649, 2650, 2651, 2652, 2653, 2654, 2655, 2656, 2657, 2658, 2659, 2660, 2661, 2662, 2663, 2664, 2665, 2666, 2667, 2668, 2669, 2670, 2671, 2672, 2673, 2674, 2675, 2676, 2677, 2678, 26

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 gewöhnliche Funktion mit anderen auf die von
 den anderen abgeleitet, so dass ein bestimmter
 ...

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