

Tracing new patterns

COMPUTER AIDED DRUG DESIGN • HIGH
THROUGHPUT SCREENING • COMBINATORIAL
CHEMISTRY • PHARMACOGENOMICS •
MICROARRAYS • SNP AND NEW TARGETS •
ALLELIC VARIATION • DNA VACCINES • SOLUBLE
RECEPTORS • MICROPHYSIOMETRY
• HEALTHCARE CUSTOMIZATION • GENETIC
IDENTITY • GENE MUTATIONS • GENE THERAPY
• POPULATION GENETICS • NANOTECHNOLOGY
• LIPOSOMAL TARGETED DRUG
• BIODEGRADABLE POLYMERS •
FORMING SYSTEM • MATRIX RELEASE
RELEASE • PRODRUGS • SOLID-STATE
INDICATIONS • CHIRAL CHEMISTRY • OFF LABEL
USES • NEW INDICATIONS • ANTI-HERPES DRUGS
• RECEPTORS • INFLAMMATORY MARKERS •
PLASMON RESONANCE • IMMUNE THERAPY •
NUCLEAR RECEPTORS • CHANNELS • CYTOKINES

ANNUAL REPORT 2001-2002



Tracing new patterns...

Explorer-like, following new leads, new ideas, new directions across an uncharted landscape.

Drug discovery research is the ultimate convergence science. Insight for research directions borrow liberally from innumerable fields, an approach or idea from one field is borrowed to find application in another.

There are numerous instances of such generous "flights of thought".

Consider for instance, synthetic chemistry. Process chemistry of the individual sequential reaction variety has little in common with modern day high throughput screening and parallel synthesis, automated technologies inspired by chip making processes. Over time this science itself is polished, refined and re-refined, so that it has very little in common with its precursor IT-based technology.

Or, consider for instance the cutting edge science of bioinformatics. Borrowing liberally from powerful information technology, the mammoth task of tracing the human genome sees light of day. From gene elucidation, a leap of understanding to gene comprehension. And then the path leads on to gene therapy, gene profiling, drug customization and beyond. Or bifurcates to proteomics and beyond. As always this charting of a new course, following clues, marks an opening on the road ahead.

On a simpler plane- consider new indications that originate from off label uses. From observation to a biological comprehension of the way it works. Through clinical trials to new in-clinic uses...Possibly a new treatment for a poorly addressed ailment. Another path, another solution giving way to persistent inquiry.

From following an idea, from the process of allowing it to meander and reshape itself along a wilful path, a whole new approach, a new tool emerges.

11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 41 42 43 44 45 46 47 48 49 50 51 52 53 54 55 56 57 58 59 60 61 62 63 64 65 66 67 68 69 70 71 72 73 74 75 76 77 78 79 80 81 82 83 84 85 86 87 88 89 90 91 92 93 94 95 96 97 98 99 100 101 102 103 104 105 106 107 108 109 110 111 112 113 114 115 116 117 118 119 120 121 122 123 124 125 126 127 128 129 130 131 132 133 134 135 136 137 138 139 140 141 142 143 144 145 146 147 148 149 150 151 152 153 154 155 156 157 158 159 160 161 162 163 164 165 166 167 168 169 170 171 172 173 174 175 176 177 178 179 180 181 182 183 184 185 186 187 188 189 190 191 192 193 194 195 196 197 198 199 200 201 202 203 204 205 206 207 208 209 210 211 212 213 214 215 216 217 218 219 220 221 222 223 224 225 226 227 228 229 230 231 232 233 234 235 236 237 238 239 240 241 242 243 244 245 246 247 248 249 250 251 252 253 254 255 256 257 258 259 260 261 262 263 264 265 266 267 268 269 270 271 272 273 274 275 276 277 278 279 280 281 282 283 284 285 286 287 288 289 290 291 292 293 294 295 296 297 298 299 300 301 302 303 304 305 306 307 308 309 310 311 312 313 314 315 316 317 318 319 320 321 322 323 324 325 326 327 328 329 330 331 332 333 334 335 336 337 338 339 340 341 342 343 344 345 346 347 348 349 350 351 352 353 354 355 356 357 358 359 360 361 362 363 364 365 366 367 368 369 370 371 372 373 374 375 376 377 378 379 380 381 382 383 384 385 386 387 388 389 390 391 392 393 394 395 396 397 398 399 400 401 402 403 404 405 406 407 408 409 410 411 412 413 414 415 416 417 418 419 420 421 422 423 424 425 426 427 428 429 430 431 432 433 434 435 436 437 438 439 440 441 442 443 444 445 446 447 448 449 450 451 452 453 454 455 456 457 458 459 460 461 462 463 464 465 466 467 468 469 470 471 472 473 474 475 476 477 478 479 480 481 482 483 484 485 486 487 488 489 490 491 492 493 494 495 496 497 498 499 500 501 502 503 504 505 506 507 508 509 510 511 512 513 514 515 516 517 518 519 520 521 522 523 524 525 526 527 528 529 530 531 532 533 534 535 536 537 538 539 540 541 542 543 544 545 546 547 548 549 550 551 552 553 554 555 556 557 558 559 560 561 562 563 564 565 566 567 568 569 570 571 572 573 574 575 576 577 578 579 580 581 582 583 584 585 586 587 588 589 590 591 592 593 594 595 596 597 598 599 600 601 602 603 604 605 606 607 608 609 610 611 612 613 614 615 616 617 618 619 620 621 622 623 624 625 626 627 628 629 630 631 632 633 634 635 636 637 638 639 640 641 642 643 644 645 646 647 648 649 650 651 652 653 654 655 656 657 658 659 660 661 662 663 664 665 666 667 668 669 670 671 672 673 674 675 676 677 678 679 680 681 682 683 684 685 686 687 688 689 690 691 692 693 694 695 696 697 698 699 700 701 702 703 704 705 706 707 708 709 710 711 712 713 714 715 716 717 718 719 720 721 722 723 724 725 726 727 728 729 730 731 732 733 734 735 736 737 738 739 740 741 742 743 744 745 746 747 748 749 750 751 752 753 754 755 756 757 758 759 760 761 762 763 764 765 766 767 768 769 770 771 772 773 774 775 776 777 778 779 780 781 782 783 784 785 786 787 788 789 790 791 792 793 794 795 796 797 798 799 800 801 802 803 804 805 806 807 808 809 810 811 812 813 814 815 816 817 818 819 820 821 822 823 824 825 826 827 828 829 830 831 832 833 834 835 836 837 838 839 840 841 842 843 844 845 846 847 848 849 850 851 852 853 854 855 856 857 858 859 860 861 862 863 864 865 866 867 868 869 870 871 872 873 874 875 876 877 878 879 880 881 882 883 884 885 886 887 888 889 890 891 892 893 894 895 896 897 898 899 900 901 902 903 904 905 906 907 908 909 910 911 912 913 914 915 916 917 918 919 920 921 922 923 924 925 926 927 928 929 930 931 932 933 934 935 936 937 938 939 940 941 942 943 944 945 946 947 948 949 950 951 952 953 954 955 956 957 958 959 960 961 962 963 964 965 966 967 968 969 970 971 972 973 974 975 976 977 978 979 980 981 982 983 984 985 986 987 988 989 990 991 992 993 994 995 996 997 998 999 1000

Over the course of the year, the domestic pharma market, barring some ups and downs, registered a 10-12% growth rate. Price cuts for new/revolutionary products, a trend that had begun last year, was witnessed with several interesting products this year too. But compensating for this was the more than double-digit rate of growth seen with speciality products. A substantial increase in the volumes of new products, particularly products that were now available at lower prices, was also seen. This is probably because the availability of newer therapies at a lesser per day cost of therapy prompts doctors to switch patients from older molecules, and offer them advantages such as efficacy, lower dose, and convenience, at a sensible price.

Growth in domestic formulations and speciality bulk actives were the main reasons for turnover growth for the year. SPARC helped to bring more than 35 new products to market, and helped us compete with new products based on our own bulk for an early to market and margin advantage.

The greatest single upside opportunity is from the fact that our plans for the international market have now finally begun to take shape- markets have been identified, existing product baskets pruned, new products are at various stages of registration. We are working to deliver repeatable two-digit growth in the international markets.

On the domestic front, March 2002 saw Sun Pharma firm at 5th rank- the same rank as last year. Prescription rankings with core customers improved in some new areas, remained the same in the key therapy areas, and dropped in some areas. One fact this underlines, is that the basics of building strong customer relationships remains unchanged, regardless of the therapy areas that this is applied to. Of course, there would need to be variation in strategy that is specific for the therapy areas addressed.

Beyond chemistry :
A new healthcare frame of reference?

summary

For the year, total income was up 22.3% backed by domestic formulation growth. Among divisions, which did well (some in excess of targets allocated), were Arian, Aztec, Synergy and Sun.

In order to meet increasing domestic market requirements, a new formulation plant at Dadra commenced operations. This is a large 5 acre site with built up area of 120,000 sq. ft. This plant was completed over a 10 month period- a record of sorts for a plant of this size and complexity. It has been built to comply with international regulatory standards like that of the USFDA and UKMCA.

Dosage form exports is the section of the business with the most exciting turnaround potential. The people, infrastructure and direction required for this business area to grow exponentially, have now been put into place. Currently we have a presence in 36 markets with 1025 active applications made and 255 approvals received in the last two years. Over the last few months, team strength has been increased to 90 professional representatives (both directly recruited and through agents), and managers/supervisory staff, many of them from the domestic marketing team, have also been put into place. Since the base itself is so small and the opportunity immense, this part of the business is expected to grow much faster over the next few years than it has in the past.

Cumulatively, across domestic and export markets, speciality bulk actives turnover was Rs.2467 mill, or 33% sales. Over the last year we have gradually discontinued the production and export of cephalexin bulk active- now a very little residual commodity bulk component remains in our speciality bulk business. Among the new speciality bulk actives recently launched, clopidogrel, mirtazapine and letrozole have been doing rather well.

(Rs. mill)

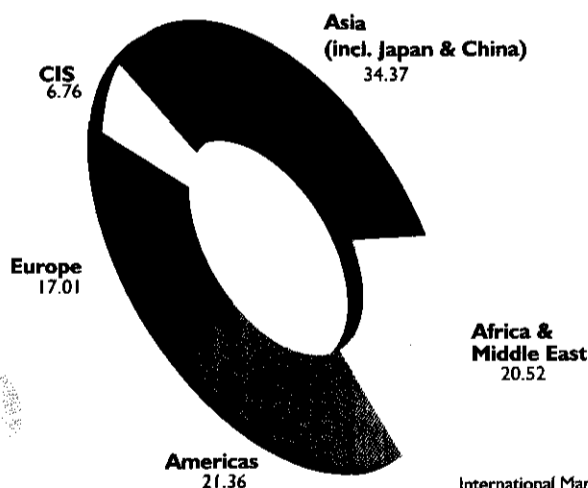
Sales Breakup by type	01-02	00-01
Domestic formulations	4660.8	3699.1
Domestic bulk	1397.7	1213.6
Others	22.7	20.9
Export formulations	283.6	337.5
Export bulk	1069.9	841.6
Export others	42.5	1.7

PSR team size by division

Synergy	97
Symbiosis	73
Aztec	152
Arian	149
Inca	58
Sun	265
Spectra	258
Solares	266
Milmet	93

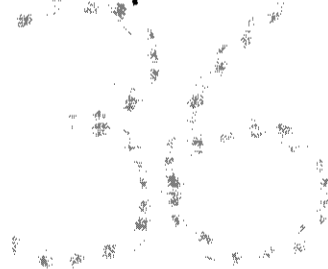
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Gravity assisted material flow at the Silvas 2 plant



International Markets:
A country specific strategy with speciality dosage forms and high value bulk actives (%)

presence





The Ahmednagar plant holds several approvals :
US FDA, ISO 9002, ISO 14001

The USFDA approved Ahmednagar plant received ISO9002 and ISO14001 certification this year. Panoli filed several US drug master files this year. Across both the plants, approximately 14 US drug master file and 12 European drug master file applications will be submitted this in 2002-03.

The facilities at Panoli and Ahmednagar will be increasingly used for the regulated markets that offer substantially higher margins. The facilities at Ankleshwar and at Chennai are being used for the domestic as well as traditional markets.

These market-specific bulk drug facilities will help us cater to the huge growth opportunity with bulk drugs in the less regulated as well as highly regulated markets.

ORG March 2002 states a growth rate in excess of 20%+ overall for the company, which continues to be twice that of the industry. Market share for the company was up to 2.80% from 2.61% last March, despite increasing competitive interest and consolidation in the industry. The company expects to reach a market share well in excess of 3% in the next two years.

CMARC : We notched a fairly consistent position in the core therapy areas. An encouraging uptrend was also seen in the newer therapy areas entered in the last few years post their acquisition. We are working to attain a top 3 position in all the primary therapy areas of our interest.

CMARC RANKS

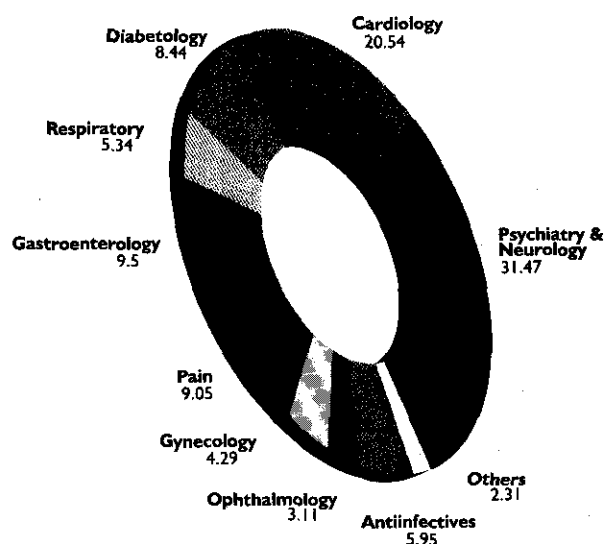
	MARCH-JUNE 01	JULY-OCT 01	NOV-FEB 02
Psychiatrists	1	1	1
Neurologists	1	1	1
Cardiologists	3	4	3
Gastroenterologists	3	2	3
Chest physicians	5	6	4
Consultant physicans	6	6	8
Orthopedics	3	4	6
Ophthamalogists	3	4	4
ENT Specialists	6	5	5
Diabetologists	8	6	6
Oncologists	8	11	7
Nephrologists	7	8	8
General Practitioners	22	22	23
Paediatricians	31	33	34
Surgeons	20	23	21
Gynaecologists	19	17	17

therapy review

The 5 core areas: psychiatry, neurology, cardiology, diabetology, gastroenterology: accounted for 69.95% of domestic prescription formulation sales. 6 brands continue to feature in the ORG list- although with a replacement- Coldact was replaced by Pantocid, an antiulcerant/proton pump inhibitor with a much longer residual life cycle.

In line with our record of aggressive new product introduction, of the 35 new products launched, 4 products featured among the best 30 new pharma launches in the country (2 products had featured on this list last year). A total of 48 products were placed among the top 3 by molecule.

A discussion of operations for each marketing division follows.



Based on March 2002 MAT Data (%)



SYNERGY

Synergy's market share moved from 18.72% to 18.47% of the participated market.

New

Oleanz Rapitabs
Bupron SR
Citopam
Liofen Intrathecal
Ropark

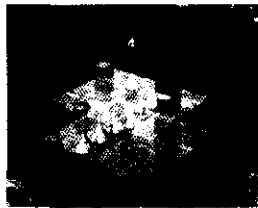
The high growth therapy areas of psychiatry and neurology continued to be areas that people commonly associate with the company- despite leadership in several other therapy areas like cardiology.

Synergy, backed by its strong record of new product introduction and lineage of customer relationships based on scientific and academic support, continued to be the top rated company with these customer groups. The markets in these two therapy areas continue to exhibit double-digit growth rates, primarily because of increasing awareness and competitive interest. Increasing competition helps switch patients from older therapies to newer molecules. Secondly, because these products are detailed more often, this increased "noise" level can help expand the market, particularly for lesser-recognized therapy areas like Parkinson's disease and schizophrenia.

Among Synergy's products, Oleanz and Lonazep, products that have been introduced in the last 2/3 years, have performed rather well.

Oleanz Rapitabs were introduced in order to offer better compliance as well as address a patient need. The illness and loss of understanding makes it difficult for some patients to appreciate the importance of taking medications regularly. Patients with schizophrenia tend to be fairly uncooperative when it comes to regularly taking medication, and instances where a patient spits out the tablet after appearing to swallow it, are very common. It is estimated that in 55% of relapse cases, simple non compliance-not taking the medicine at all- is the reason for relapse. Oleanz rapitabs help address this problem at a basic level-helping ensure that medication is atleast taken as prescribed. Oleanz rapitabs uses a porous matrix structure to ensure quick dissolution in the mouth.

Placebo appears to alter brain function in individuals with major depression



EEG studies show that changes caused by a placebo are different from changes that are caused by depression... patients who responded to placebo as versus patients who responded to medication showed different activity patterns in a part of the brain called the prefrontal cortex... This research could help develop treatments that are individualized, as well as new medication types.... This also helps to show that there are different pathways to improvement for depressed patients.

Leuchter A. et al, American Journal of Psychiatry, Jan 2002

(Rs. mill.)

	2002	2001
Participated market size	4402	3675
Division market share (%)	18.47	18.72

(Data from ORG March MAT for both the years)

BRAIN CHANGES

Magnetic resonance imaging shows structural brain abnormalities after the first psychotic episode. These abnormalities are not linked to the chronic illness or to its treatment. Brain volume was found to be larger and lateral ventricles increased in patients with chronic schizophrenia, more so if the patient had a development disturbance in childhood.

British Journal of Psychiatry, September 2000, Report on a study at the Institute of Psychiatry, London



The earlier new medicines are begun, the better...

Since patients at the beginning of treatment (freshers?) are extremely sensitive to treatment (unlike patients already on medication), they tend to be more responsive to newer antipsychotic medication than to older medicines. In a trial on new patients, clozapine was found to be better for new patients compared to older drugs like haloperidol.

Lieberman J. A., University of North Carolina, Findings presented at the Annual meeting of the American College of neuropsychopharmacology, Dec 2001

Antiepileptics, the area that contributes the largest chunk of Synergy sales continued to grow at double-digit rates. This is because of increasing usage of newer antiepileptics and antiepileptic use for non-epilepsy related problems such as mood disorders and pain. Even with available drugs, only about 70% epilepsy patients are adequately controlled. Newer antiepileptics such as Gabantin and Lonazep should help expand the number of responders to medication.

Citopam (citalopram), will perhaps make new product introduction history for Synergy- it had the fastest prescriber support among all antidepressants recently launched by the division. Daytime sleepiness and fatigue, commonly expressed as a "hangover" effect after antidepressant use, is less frequently seen with citalopram. Citalopram is used across a broad depression range right from resistant depression to relapse prevention. Recently, studies have been presented showing Citalopram to be safe and effective for use in children and adolescents, which is important since very few studies have been done testing efficacy and safety in children. This is an unaddressed segment- The American Academy of Child and Adolescent Psychiatry estimates that about 5% of the adolescent/pediatric population suffers from depression. Non psychiatry uses have ranged from fibromyalgia to nerve pain that is associated with diabetes.

Citalopram is also believed to begin acting quicker than older antidepressants (which may take from 4 to 6 weeks to begin showing an effect). This quicker action may mean a better quality of life for the depressed patient and more so, for his family. In the elderly depressed who are generally on medication from ailments ranging from GI problems to heart disease, its speed of onset and lack of interaction with other drugs are a definite plus point.

Riding the stress wave...



Stress, depression and Wall street

Psychology doctoral candidate Alden Cass is studying wall street by immersing himself in its culture, "an arcane world, dominated by money, fear and greed". This is a population that is underserved, undernoticed, he says. Of the sample of male brokers that he gathered from the top US brokerage houses, 23% of the men met the criteria for a clinical diagnosis of major depression vs 7% in the general population. Troubled by the high rate of depression in this population and the 11/9 impact on this community, Cass has now set up a firm that helps brokerages identify and treat brokers suffering from depression and anxiety...

From a Reuters news report, April 14, Business Standard

Fine movement is one of the first casualties in Parkinson's



One of the new products added to Synergy's therapeutic basket was the antiparkinson Ropark (ropinirole). This product is truly termed revolutionary for Parkinson's disease, and belongs to a new class of compounds called dopamine receptor agonists. These are believed to act by directly activating dopamine receptors. The medication in the treatment termed the gold standard for Parkinson's disease, levodopa, has an inherent drawback on long term use. At larger doses taken over a long time, it is believed to cause uncontrolled limb movement (dyskinesias). This is a limiting factor in therapy, and becomes a ceiling after which the dose cannot be increased. But by starting therapy with Ropinirole, it is possible to delay the use of levodopa till such time it becomes absolutely necessary. With more patients being detected at an early stage than ever before (early onset Parkinson's Disease), this medication effectively increases the timespan that a person with Parkinson's can take medication. Ropinirole is being studied in a number of indications such as restless leg syndrome, and certain kinds of treatment resistant depression.

Neurologists have now begun to favor dopamine agonists as the initial PD treatment. Over 76% of the neurologists surveyed by the American Parkinson's Disease Association opined that initial therapy with dopamine agonists helps delay levodopa therapy, and therefore dyskinesias...

52nd American Academy of Neurology proceedings

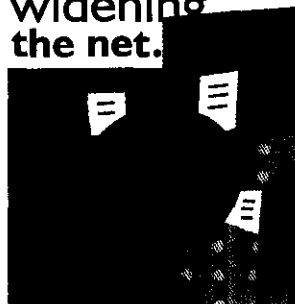


THE LUCKY MAN AND DYSKINESIAS

2 years ago, celebrity TV director Michel Fox created a medical research foundation acclaimed for its work supporting PD research, specifically in the area of dyskinesia reduction... About dyskinesias Mr. Fox says "his body is moving but his mind is perfectly calm" and .. that "I can't be still, until I can literally no longer keep still..." "These dyskinesias you are seeing, it comes from too much levodopa, its difficult to get an exact dose.. it's a trade off between being able to sit and talk in a fluid way or being halted and rigid..."

from a New York Times article on Michael Fox, May 14, 2002, "The Lucky Man puts his celebrity to work", Mary Duenwald

Panel recommendation- widening the net.



Perhaps everyone qualifies...

The US preventive services task force (an independent medical panel nominated by the US govt.) has recently recommended that ALL adults should be screened for depression during regular visits to their doctor, since more than half cases are either missed or mistreated. Often, depression is the hidden problem in a patient's symptoms....

US Preventive Services Task Force recommendations, Annals of Internal Medicine.



SYMBIOSIS

Symbiosis' market share moved from 10.83% to 12.52% of the participated market.

New

Topirol
Oxetol

With continuing success for older products used in the areas of psychiatry and neurology as well as increasing acceptance of newer molecules (some of which are competing brands/molecules for products from the Synergy product list), Symbiosis had a good year. With this parallel division competing in the same therapy area, both can promote products from the same therapy class to the same set of doctors.

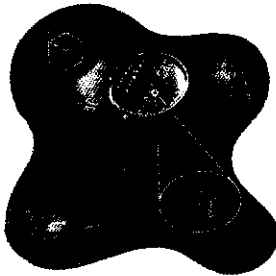
There is, as yet, no significant change in the list of the top products- Fluvoxin, Mirtaz, Lithosun and Sizodon continue to feature in the list and Verglob (immunoglobulin treated human serum albumin) entered this list.

Important among the products introduced this year were the antiepileptics Oxetol (oxcarbamazepine) and Topirol (Topiramate). These molecules address specific patient needs.

By some estimates, more than 20% of patients taking antiepileptic medication are inadequately treated. Another interesting estimate: 50% of patients currently taking antiepileptic medication suffer from side effects that limit treatment.

The medication in Oxetol (oxcarbamazepine) is a modification of the molecule carbamazepine (marketed by the Syergy division as Zeptol) which has been in use for over 2 decades. Since oxcarbamazepine uses a different set of pathways for metabolism, there is a lesser likelihood of drug interactions and side effects.

Oxetol is approved for use as monotherapy as well as an adjunct in adults and monotherapy in children. It is being studied for use in additional indications such as bipolar mood disorder, refractory seizures, trigeminal neuralgia.



Researchers identify gene responsible for intellectual disability and Epilepsy

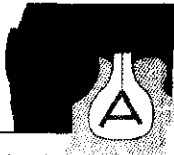
Dr. Josef Gecz, et al
Dept of Cytogenetics and Molecular Genetics, Womens' and Childrens' Hospital, Adelaide

Intellectual disability and epilepsy often occur together and both have a genetic cause. Researchers from the womens' and childrens' hospital in Adelaide have identified a major gene responsible for both the conditions.... "This gene is found on the X chromosome and is one of hundreds on that chromosome, which when mutated, can cause intellectual disability.. This particular gene is more of a master gene, controlling cognitive ability. The team is puzzled by the fact that the same mutation in the gene results in vastly different clinical outcomes. Genetic material from 9 different families from different parts of the world were studied, and all these pointed to mutations in the same gene...

	(Rs. mill.)	
	2002	2001
Participated market size	2433	2153
Division market share (%)	12.52	10.83

(Data from ORG March MAT for both the years)

EXPERT GUIDELINES TO TREAT EPILEPSY

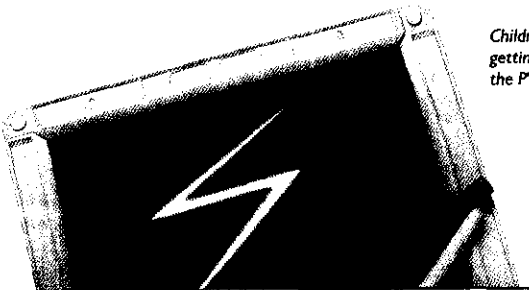


- Increased use of single antiepileptic medication before turning to combination therapy. Single drug use helps balance side effects and medication.
- Recognition that special groups such as women and older adults require different treatment strategies. Antiepileptic drugs can affect reproductive health in women of childbearing age. In older patients these medicines can impair cognitive ability, and cause dizziness and sedation. There is recognition of the fact that epilepsy cannot be treated with a "one size fits all" approach

Expert consensus guidelines to treat epilepsy, Morell M.et al., NY Presbyterian Hospital, NY, NY, Published in 'Epilepsy and Behavior', Nov 2001

Topirol is yet another new antiepileptic from Symbiosis. This medication is approved for use in patients with partial epilepsy who are inadequately controlled, or who do not respond to treatment (refractory)- or show difficulty in thought and learning because of their current medication. A significant indication of its safety profile is that it is approved for use in children aged 2 and older- one of the few drugs to be relatively free of learning and cognitive side effects. Topirol is believed to act by several mechanisms and hence show efficacy across a range of partial and generalized epilepsy.

In addition to its use as an epileptic, Topirol is being studied in bipolar mood disorders, where it reduces the severity of the manic symptoms. Unlike other standard medication used in bipolar mood disorders, such as lithium and carbamazepine, in some studies, Topirol was found to reduce weight.



Children's epilepsy: getting on with the P's and Q's

ARIAN

TLC for
the heart

Arian's market share moved from
11.38% to 11.56% of the participated market.

New Rebase

After the demonstration of success with the divisionalization of the Synergy division, this exercise in splitting divisions was extended to the Aztec division, and some of the products addressing cardiology/diabetology were split off to a new division called Arian.

With the formation of Arian, we are trying to ensure that tomorrow's likely star brands Pioglit, Repace H (both promoted by the Arian division) as well as Irovel and Cardivas (promoted by the Aztec division) are promoted adequately without losing focus, and without cannibalizing market share.

Arian has begun its existence with an impressive list of top brands - Glucored, Korandil, Pioglit and Repace H.

Repace and Repace H are now replacing older molecules like atenolol in the treatment of hypertension. In addition to lowering blood pressure, losartan, the medication in Repace, was shown to improve the heart's pumping action, and thus reduce the risk of congestive heart failure. As a complication of long standing uncontrolled hypertension, at times the left side of the heart becomes stiff (technically called left ventricular hypertrophy) and pumps too little blood, while the right side pumps normally, filling the lungs with blood, which can eventually lead to pulmonary edema and death.

An eye opening trial called LIFE*, compared atenolol, one of the most commonly used 1st line antihypertensives with losartan, the medication in Repace. Both medications lowered blood pressure, but losartan did more: as versus atenolol it reduced the likelihood of cardiovascular death and stroke by a significant number.

Even in a group of diabetics with hypertension which is otherwise a group at high risk for cardiac problems, losartan was more effective in reversing the stiffness and malfunction of the left ventricle.

DIABETES AND THE FEMALE GENDER...

Women with type 2 diabetes have dramatically increased risk of all kinds of coronary heart disease... in women who have had diabetes for more than 15 years, the risk is as high as that of previous heart disease. While the reason for increased atherogenesis in women is not completely known, in part this is related to lipid abnormalities, high TG, low levels of HDL (the good cholesterol). Diabetes has a more damaging effect on women than on men, since it eliminates the female hormone based advantage for death from heart disease.

Archives of Internal Medicine, 2001
"the Impact of Diabetes Mellitus on mortality from all causes and CHD in women after 20 years of followup"

	(Rs. mill.)	
	2002	2001
Participated market size	4862	3646
Division market share (%)	11.56	11.38

(Data from ORG March MAT for both the years)

The DEADLY quartet



- 1 Most adults with diabetes have modifiable risk factors, but are inadequately counseled by their doctors about these...
- 2 Hypertension occurs in 56% diabetics vs. in 22% non-diabetics
- 3 Elevated cholesterol occurs in 41% diabetics versus 20% non-diabetics
- 4 78% of diabetic adults were found obese as versus 21% of the non-diabetic population

Archives of Internal Medicine, 2002
"Modifiable Cardiovascular risk factors in Adults with diabetes prevalence and missed opportunity for physician counseling"



Pioglit, the antidiabetic we launched last year continues to do exceedingly well, because of its safety profile and control over blood sugar levels. Pioglitazone (the medication in Pioglit) received a boost after the EVIDENT* trial results were announced. This trial comparing pioglitazone and rosiglitazone, showed blood sugar control with both but pioglitazone offered additional cholesterol lowering effect. It increased the good cholesterol (HDL) while sharply cutting the extent of bad cholesterol (TC, LDL and TG). These results were critical -the most common cause of death in diabetics is cardiovascular.

Korandil (Nicorandil) is yet another of our recent products that is quietly settling into "gold standard level" for stable angina. Kornadil had sales in excess of Rs.35mill. In a UK trial called IONA®, nicorandil was found to possess cardioprotective properties in addition to anti-ischemic effects. Nicorandil so far, is the only drug to have improved outcomes in this class. It may change the way stable angina is treated altogether.

US trials are not too many- apparently in the US, in patients who have stable angina, rather than medication, revascularisation procedures (angioplasty/bypass with stenting) are preferred.

IONA®: Impact of nicorandil in Angina trial
LIFE®: Losartan intervention for end point reduction trial
EVIDENT®: Effects of Pioglitazone and Rosiglitazone on blood lipids and glycemic control of patients with type 2 diabetes trial

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AZTEC

Aztec's market share moved from 11.83% to 12.41% of the participated market.

New

Clopilet

Irovel H

Monosprin

Rezult M

Over the last year, there has been a significant change in the line up of products from the Aztec division as several star brands have emerged- now, other than Monotrate, all the brands in the top 5 are new products that have been introduced within the last few years. For instance, Clopilet (clopidogrel) was introduced only after April 2001 and within this short span has emerged as one of the best launches in the pharma industry and front runner for the division. A sharp price cut driven by competitive reasons in mid 2001 has only helped increase volumes, as patients are prescribed aspirin + clopidogrel combination, instead of aspirin.

New products and innovative campaigns such as a graphology analysis campaign, patient benefit campaign and diabetes detection camps have helped propel the division to a top slot with core customers.

Among major products that were launched last year, Cardivas and Aztor continue to move up the sales ratings backed by several trials that promote their use more quickly or in new indications.

Rushing life-giving bloodflow through clogged arteries



After an across the market price cut for atorvastatin brands, there has been a more than proportionate increase in the number of units sold, and Aztor has become the 2nd ranked brand among all atorvastatin molecules. Atorvastatin, the medication in Aztor received approval for new dosage strengths. This offers greater choice to the physician for titrating the drug as required. This supplements data from trials discussed last year- atorvastatin should be prescribed as quickly as possible after a heart attack, preferably within a 24-hour window.



(Rs. mill.)

	2002	2001
Participated market size	5590	4115
Division market share (%)	12.41	11.83

(Data from ORG March MAT for both the years)

STROKE FOLLOWS THE CLOCK

High risk early morning

The timing of stroke is similar to that of acute MI, MI and sudden cardiac death. Early morning is associated with a higher risk of onset of stroke symptoms irrespective of the type of stroke. A second peak period happens in the evenings

Archives of Neurology, 2002,59,44-53



Practice guideline update for unstable angina is a shot in arm for clopidogrel, statins

The American College of Cardiology and the American Heart Association recently published practice updates for unstable angina and NSTEMI, these updates recommendations from a year ago.

In addition to aspirin and heparin, all patients with unstable angina and NSTEMI must receive clopidogrel, since this limits the capacity of platelets to bind blood cells into clots

Statins are almost mandatory to treat elevated LDL cholesterol... starting statins early is crucial.

ACC and AHA guidelines March 15/2002, as announced online

Depression and Stroke



Depressive disorder is a risk factor for stroke that appears to be independent of additional cardiovascular risk factors. This was the finding from a 13 year follow up of a sample of 1700 households from Baltimore. People with depression were 2.6 times more likely to report stroke, this was after the researchers took into account heart disease, hypertension, diabetes and tobacco use... more research is required on this link....

Stroke /2002/32

