

## EXECUTIVE SUMMARY

### 1. PRODUCT

- 1.1 Sulfamoxole is one of the sulfonamide group of drugs, belonging to the pharmaceutical category of antimicrobials. These drugs as a class are active against a large spectrum of both gram positive and gram negative organisms. Sulfamoxole has actions and uses similar to that of the more extensively used sulfa drug sulphamethoxazole.
- 1.2 Chemically sulphamoxole is sulphadimethyl oxazole and has to be given by mouth in dose of 500 mg. twice daily. With the discovery of the good synergistic effect of the combination of sulfamethaxazole and trimethoprim (Cotrimazol), similar studies with sulfamoxole and trimethoprim also had shown similar synergistic effects and this combination is being used more than sulfamoxole as a single drug.
- 1.3 Sulfamoxole in its combination formulations with trimethoprim (co-trifamole) are used extensively in France, Germany, Italy, Sweden, Belgium, S. Africa and in a small way in India and South-Korea. It has been incorporated in French Pharmacopoea and in Extra-Pharmacopoea. This drug is not included in the WHO's list published so far (*viz.*) 1985, 1988 and 1990.

### 2. PROCESS

The process for the manufacture of Sulfamoxole used in India is the same as that developed by BASF (Germany) and manufactured by its sister company Nordmark Arzneimittel GmbH. M/s German Remedies is the only company manufacturing this in India at present in collaboration with Nordmark.

- 2.1 The indigenously available Acetyl Sulfanilic acid chloride is treated with Calcium cyanamide to get acetyl Sulfocynamids calcium, which on condensation with acetyl methyl carbinol (Acetoin), gives the acetyl sulfamoxole and this on hydrolysis yields sulfamoxole. The process is very simple, requiring no imported or sophisticated equipments.
- 2.2 The process has been well studied by M/s. German Remedies and they have indiginised the imported technology to bring the product equivalent to the French Pharmacopoeal Standards. The technology followed by M/s German Remedies is the same as that of Nordmark, which is the major other company manufacturing this product in the world. Calcium cyanamide and Butynol solution (50%) are the only two raw materials imported by M/s German Remedies. However, some R&D effort can be put in by one of the National Laboratories to perfect the process of producing Acetoin from Diacetyl.

### 3. PRODUCTION IN INDIA AND THE REQUIREMENT PROJECTIONS

- 3.1 M/s. German Remedies has been marketing this range of products for the last ten years and they are finding it difficult to make the product acceptable to the medical profession in a big way, while Sulfamethoxazole and its formulations are steadily increasing in the clinical use. The use of Sulfamoxole is declining as can be seen in Table-I.

**Table 1 : Sulfamethoxazole and Sulfamoxole bulk drug production**

Item	Unit	1986-87	1988-89	1989-90
Sulfamethoxazole	Tons	535.42	1445.56	1565.43
Sulfamoxole	Tons	76.99	92.90	88.90

Source: -IDMA Bulletin, 21st June 1990-page 384

It can be noted that while Sulfamethoxazole production and demand is sharply increasing Sulfamoxole production and demand is quite small.

3.2 Further if we are to consider the consumption of Sulfamoxole for use in formulations within India it is less than 30 Tons a year according to the Market Research reports of ORG Baroda. The small extra production depends upon the export needs, which also is not very significant. Eventhough it is very effective broad spectrum drug particularly in combination with trimethoprim, it is not having significant market share because it is marketed in India by only one Company and that Company does not consider this as their major product. They are having high priced and more profitable product in their range and hence the promotional efforts on this product range is relatively less. If this product range is formulated and marketed by a larger number of Companies, as is being done with Sulfamethoxazole formulations, this product range also can have higher market share. This will be possible only if Sulfamoxole bulk is made available in large quantities to other formulators. Manufacture and supply of Sulfamoxole by bulk drug manufacturers like Indian Drug and Pharmaceuticals Ltd., Hyderabad can help to increase the Sulfamoxole market.

3.3 The Indian requirements of this product according to the analysis of ORG'S Market research reports will not be more than 30 Tons per year and the exports also can be only around 50 to 60 Tons per year, according to the present trend of sales.

It will be worthwhile to mention here that M/s. Cipla, Bombay also took a license for the manufacture of 10 ton/year Sulfamoxole in early 1980. In 1985-86, they could produce and sell 3.143 tons and in 1986-87 it declined to 0.83 tons. Because of low market potential and the small capacity with high imported raw material cost, made them to stop their production.

## 4 CONCLUSIONS

- 4.1 Sulfamoxole is an effective and useful sulpha drug particularly in combination with Trimethoprim. If properly promoted it can take a greater share of the Sulfa-Trimethoprim market.
- 4.2 Sulfamoxole formulations are not having comparable market share in relation to Sulfamethoxazole formulations. Therefore, the only Indian Company is unable to utilise its full capacity of 250 Tons per year. The maximum production, of late is around 70 to 90 Tons per year. This low sales may be due to a very poor promotion effort by the Company, probably due to not giving priority for this product for the reasons of their own. They have more important products for promotional efforts.
- 4.3 Of this production only 25 to 30 Tons appear to be used for formulations in Indian Market. The production appears to be mainly related to the export, which also is not steady since this product is used only in a very few countries in the world. Major countries like USA, UK, Canada etc., are not using this product and hence a big future for this product can not be envisaged.

It may also be mentioned here that one main Raw Material namely Butynol is the monopoly item of BASF (Germany) and that makes it difficult for any other Indian company to start production in a big way in competition with M/s. German Remedies. However, for the manufacture of acetoin, Butynol route can be substituted by making it from Diacetyl.; therefore Butynol availability need not be a limiting factor for the manufacturer of Sulfamoxole. The process for producing acetoin from Diacetyl is given in the report.

- 4.4 This product is not included in the WHO's list of essential drugs. The technology is simple, not involving any sophistication. The present bulk price is around Rs. 465/Kg which is quite comparable with other sulfa drugs in India. The company manufacturing this item in

our country is importing calcium cyanamide and Butynol solution and exporting a small quantity of this item to take care of import expenses.

## 5 RECOMMENDATIONS

- 5.1 No special R&D is needed nor any special efforts are required for increasing the production by using Butynol to Acetoin method. The alternate method of developing a good process for the production of Diacetyl and Diacetyl to Acetoin can be taken up by one of the National laboratories, particularly Central Drug Research Institute, Lucknow.
- 5.2 Sulfamoxole in combination with trimethoprim is known to have wider spectrum of effectiveness and this aspect may be well exploited in promotion work. Larger number of Companies may start formulating and marketing this product range. The limiting factor for its growth appears to be more due to lack of availability of Sulfamoxole to other formulators, rather than any lack of effectiveness of the drug.
- 5.3 The high clinical efficacy of Sulfamoxole-Trimethoprim combination in the treatment of various infections has been well documented in the monograph "Current concepts in Antibacterial Chemotherapy-Sulfamoxole/Trimethoprim (Co-Trifamole)" by Royal Society of Medicine, London, based upon the Symposium held at its International congress in 1979. Market potential of this combination may be tried.