

Novantrone® Briefing Document

| | |
|------------------------------------------------------------------------------------------------------|----------------|
| Novantrone® (Mitoxantrone HCL) P&CNS Advisory Committee Briefing Document..... | 1 - 001 |
| Executive Summary | 1 - 002 |
| 1.0 Background on Multiple Sclerosis..... | 1 - 012 |
| 2.0 Mitoxantrone | 1 - 016 |
| 3.0 Clinical Development Program of Mitoxantrone in Multiple Sclerosis | 1 - 017 |
| 4.0 Efficacy of Mitoxantrone in Multiple Sclerosis..... | 1 - 020 |
| 5.0 Safety Results..... | 1 - 047 |
| 6.0 Benefit and Risk Assessment..... | 1 - 062 |
| 7.0 Post-Marketing Commitments..... | 1 - 066 |
| 8.0 Proposed Use of Mitoxantrone in Patients with MS | 1 - 066 |
| 9.0 References | 1 - 068 |
| Appendices..... | 1 - 070 |
| Appendix A: Extended Disability Status Scale (EDSS) | 1 - 070 |
| Appendix B: Ambulation Index (AI)..... | 1 - 072 |
| Appendix C: Standard Neurological Status (SNS) | 1 - 073 |
| Appendix D: Summary of Preclinical Studies in Experimental Allergic Encephalomyelitis (EAE) | 1 - 074 |
| Appendix E: Statistical Methodology for the Primary Efficacy Analysis in Study 901 | 1 - 077 |
| Appendix F: Summary of Sensitivity Analyses Conducted in Study 901 | 1 - 080 |
| Appendix G: Published Papers | 1 - 085 |

| Description | Volume - Page |
|-------------|---------------|
|-------------|---------------|

- Bastianello S, Pozzilli C, Millefiorini E, Trojano M, et al. 1994 . . 1 - 085
- De Castro S, Cartoni D, Millefiorini E, Funaro S, et al. 1995. 1 - 090
- Edan G, Miller D, Clanet M, Confavreux C, et al . 1997 1 - 096
- Hartung HP, Gonsette R, and the MIMS-Study Group.
Supplement 2, 1999 1 - 103
- Hartung HP, Gonsette R, and the MIMS-Study Group. 1998. 1 - 104
- Hartung HP, Gonsette R, and the MIMS-Study Group.
Supplement 1, 1999 1 - 105
- Krapf H, Morrissey SP, Zenker O, Gonsette R, at el. 1998. 1 - 106
- Millefiorini E, Gasperini C, Pozzilli C, D'Andrea F, et al. 1997 . . 1 - 107

NOVANTRONE® (Mitoxantrone HCl)
FOR PATIENTS WITH MULTIPLE SCLEROSIS
Briefing Document

Peripheral & Central Nervous System Drugs
FDA Advisory Committee
January 28, 2000

Immunex Corporation
51 University Street
Seattle, WA 98101

12/16/1999