

1. Record Nr.	UNINA9910965591903321
Titolo	Clinical applications of mifepristone (RU 486) and other antiprogestins : assessing the science and recommending a research agenda // Committee on Antiprogestins: Assessing the Science, Division of Health Promotion and Disease Prevention, Institute of Medicine ; Molla S. Donaldson ... [et al.], editors
Pubbl/distr/stampa	Washington, D.C., : National Academy Press, 1993
ISBN	9786610196029 9781280196027 1280196025 9780309598354 0309598354 9780585024783 0585024782
Edizione	[1st ed.]
Descrizione fisica	xi, 288 p. : ill
Altri autori (Persone)	BenetLeslie Z DonaldsonMolla S
Disciplina	615/.766
Soggetti	Mifepristone - Research Abortifacients - Research Progesterone - Antagonists - Research
Lingua di pubblicazione	Inglese
Formato	Materiale a stampa
Livello bibliografico	Monografia
Note generali	"Support for this project was provided by a grant from the Henry J. Kaiser Family Foundation, Menlo Park, California."--Verso T.p. Committee chairman: Leslie Z. Benet.
Nota di bibliografia	Includes bibliographical references and index.
Nota di contenuto	Clinical Applications of Mifepristone (RU 486) and Other Antiprogestins -- Copyright -- Preface -- Contents -- Summary -- CROSS-CUTTING RECOMMENDATIONS -- USES OF ANTIPROGESTINS: THE REPRODUCTIVE CYCLE -- Contraception -- Post-Coital Contraception -- Menses Induction -- Pregnancy Termination During the First Trimester -- Pregnancy Termination During the Second Trimester -- Cervical Ripening -- Labor Induction in Late Pregnancy -- OTHER POTENTIAL THERAPEUTIC USES OF ANTIPROGESTINS -- Endometriosis -- Uterine Leiomyomas (Fibroids) -- Breast Cancer -- Meningioma --

ANTIGLUCOCORTICOID EFFECTS OF ANTIPROGESTINS -- 1 Introduction -- BACKGROUND AND HISTORICAL PERSPECTIVES -- Finding an Antiprogesterin -- THE IOM REPORT -- CROSS-CUTTING RECOMMENDATIONS -- REFERENCES -- 2 Uses of Antiprogesterins: The Reproductive Cycle (Part I) -- CONTRACEPTION -- POST-COITAL CONTRACEPTION -- MENSES INDUCTION -- REFERENCES -- 3 Uses of Antiprogesterins: The Reproductive Cycle (Part II) -- PREGNANCY TERMINATION DURING THE FIRST TRIMESTER -- Health Services Research -- PREGNANCY TERMINATION DURING THE SECOND TRIMESTER -- CERVICAL RIPENING -- LABOR INDUCTION IN LATE PREGNANCY -- Fetal Demise -- SUMMARY -- REFERENCES -- 4 Other Therapeutic Uses of Antiprogesterins -- ENDOMETRIOSIS -- Utility of Mifepristone (RU 486) for Treatment of Endometriosis -- Summary -- UTERINE LEIOMYOMAS (FIBROIDS) -- Utility of Mifepristone for Treatment of Uterine Leiomyomas -- BREAST CANCER -- Mechanism of Action -- Clinical Issues -- Adjuvant Therapy and Chemoprevention -- Resistance -- Dose Issues -- Conclusions -- MENINGIOMAS -- Conclusions -- REFERENCES -- 5 Antiglucocorticoid Effects of Antiprogesterins -- GLUCOCORTICOID FUNCTION -- THERAPEUTIC USE OF MIFEPRISTONE (RU 486) AS ANANTIGLUCOCORTICOID -- ADVERSE ANTIGLUCOCORTICOID EFFECTS OF ANTIPROGESTINS -- REFERENCES. 6 Animals as Models for Studying Antiprogesterins -- REFERENCES -- APPENDIXES -- A Agenda for the IOM Workshop "Antiprogesterins: Assessing the Science," April 13-14, 1993 -- B Background Papers and Presentations (In Order of Presentation at IOM Workshop) -- B1 1993: RU 486-A DECADE ON TODAY AND TOMORROW -- ANTIHORMONES: THE 20 YEARS BEFORE RU 486 -- CHEMISTRY: NOVEL MOLECULES -- CELLULAR AND MOLECULAR MECHANISMS OF ACTION OF ANTIPROGESTINS: THE RECEPTOR AT THE CENTER -- Ligand Binding -- Receptor Transconformation -- Heat Shock Protein Binding -- Receptor Dimerization -- Binding to DNA -- Studies of Chromatin -- Gene Transcription -- PHYSIOPHARMACOLOGICAL REPRODUCTIVE EFFECTS -- REPRODUCTIVE MEDICINE (TABLE B1.4) -- Voluntary Early Pregnancy Interruption -- Pregnancy Interruption After Nine Weeks of Amenorrhea -- Initiation of Labor -- Contragestive and Contraceptive Methods Using RU 486 -- Emergency Post-Coital Contraception (Contraceptive or Contragestive According to When it is Applied) -- Late Luteal Phase Administration (Occasional Use) (Contragestive) -- Monthly Premenstrual, Late Luteal Phase Administration (Repeated Use) (Contragestive) -- Early Luteal Phase Administration (Once a Month) (Anti-Implantation) -- Endometrial Contraception" (Daily Delivery of Very Low Dose) (Contraceptive and Contragestive) -- Ovulation Suppression (Daily Delivery of a Low Dose) (Contraceptive) -- Male Contraception -- MEDICAL APPLICATIONS (TABLE B1.4) -- Uterine Diseases -- Endometriosis -- Fibroids -- Breast Cancer -- Meningioma -- ANTIGLUCOCORTICOSTEROID EFFECTS -- CONCLUSIONS -- Use for Voluntary Pregnancy Interruption -- Contraception -- Cancer -- Novel Antiprogesterins: Biology and Chemistry -- ACKNOWLEDGMENTS -- REFERENCES -- B2 OVERVIEW AND BACKGROUND: MECHANISM OF ACTION OF ANTIPROGESTINS -- INTRODUCTION -- STRUCTURE AND FUNCTION OF THE PROGESTERONE RECEPTOR. The Hormone Binding Domain -- The DNA Binding Domain -- Transactivation Function -- Association with Other Proteins -- Phosphorylation of the Progesterone Receptor -- Progesterone-Receptor Function -- MECHANISMS OF ACTION OF PROGESTERONE ANTAGONISTS -- Binding of Antagonists to Progesterone Receptors -- Formation of Dimers and DNA Binding Complexes -- Effects of Antagonists on Transcriptional Activation -- Other Effects of

Antagonists on Receptors -- SUMMARY AND FUTURE AREAS OF STUDY -- REFERENCES -- B3 THE USE OF ANTIPROGESTINS IN THE REPRODUCTIVE CYCLE -- USE OF ANTIPROGESTINS IN THE REPRODUCTIVE CYCLE -- Basic Concepts and Assumptions -- Assessment Issues in Evaluating Antiprogestins -- Potential Uses of Antiprogestins -- Follicular Phase Administration of RU 486 -- Other Strategies for Administration of RU 486 During the Menstrual Cycle -- TOXICITY -- QUESTIONS FOR FUTURE RESEARCH -- SUMMARY -- REFERENCES -- B4 POTENTIAL CONTRACEPTIVE EFFECTS OF ANTIGESTOGENS -- ABSTRACT -- INTRODUCTION -- PHYSIOLOGICAL STUDIES IN THE MENSTRUAL CYCLE -- POSSIBLE CONTRACEPTIVE USES OF MIFEPRISTONE -- Inhibition of Ovulation -- Post-Coital Contraception -- Endometrial Contraception -- Late Post-Coital Contraception -- FUTURE DEVELOPMENTS -- Basic Research -- Mode of Action -- Clinical Studies -- REFERENCES -- B5 USE OF ANTIPROGESTINS BEFORE 63 DAYS OF AMENORRHEA -- INTRODUCTION -- EFFECT OF MIFEPRISTONE DURING EARLY PREGNANCY -- TERMINATION OF EARLY PREGNANCY -- Mifepristone Alone -- Mifepristone in Combination with Prostaglandin -- Practical Guidelines for Clinical Use of Mifepristone in Combination with Prostaglandin -- FURTHER DEVELOPMENTS IN MEDICAL TERMINATION OF EARLY PREGNANCY -- CONCLUSIONS -- REFERENCES -- B6 USES OF ANTIPROGESTINS AFTER 63 DAYS OF AMENORRHEA -- RU 486 FOR SECOND-TERM PREGNANCY TERMINATION -- RU 486 FOR INTRAUTERINE FETAL DEATH (IUD).
CERVICAL RIPENING WITH RU 486 PRIOR TO SURGICAL ABORTION -- RU 486 FOR LABOR INDUCTION -- REFERENCES -- B7 COMMENTS ON SESSION II -- USE OF MIFEPRISTONE AND PROSTAGLANDIN FOR FIRST-TRIMESTER ABORTION -- Need for Medical Supervision -- Acceptability of Medical Versus Surgical Abortion -- Number of Visits Required -- Appropriate Dose of Mifepristone -- Side Effects -- SECOND-TRIMESTER ABORTIONS -- CONTRACEPTION -- POST-COITAL CONTRACEPTION -- CERVICAL RIPENING -- SUMMARY -- B8 USE OF ANTIPROGESTINS IN THE MANAGEMENT OF ENDOMETRIOSIS AND LEIOMYOMA -- ABSTRACT -- INTRODUCTION -- ENDOMETRIOSIS -- Antiprogestin in the Treatment of Endometriosis -- Pilot Study -- Long-Term, Low-Dose Studies -- LEIOMYOMA (FIBROID TUMOR) -- Antiprogestin in the Management of Leiomyoma- Dose-Response Studies -- 50-mg Dose -- 25- and 5-mg Doses -- Outcome -- ACKNOWLEDGMENTS -- REFERENCES -- B9 ANTIPROGESTINS AND THE TREATMENT OF BREAST CANCER -- INTRODUCTION -- PROGESTERONE AND THE NORMAL BREAST -- PROGESTERONE AND BREAST CANCER -- Progestin Agonists and Tumor Induction -- Progestin Agonists and Growth of Established Tumors -- PROGESTERONE ANTAGONISTS AND THE TREATMENT OF BREAST CANCER -- Human Breast Cancer Cell Lines -- Animal Models of Mammary Cancer -- Human Clinical Trials -- PROGESTIN RESISTANCE -- SUMMARY AND FUTURE PROSPECTS -- REFERENCES -- B10 USES OF RU 486 AS AN ANTIGLUCOCORTICOID -- HOW DO GLUCOCORTICOIDS ACT? -- PHYSIOLOGIC ROLE OF GLUCOCORTICOIDS -- RU 486 AS AN ANTIGLUCOCORTICOID -- RESEARCH DIRECTIONS FOR ANTIGLUCOCORTICOIDS -- REFERENCES -- B11 PRIMATE MODELS FOR THE STUDY OF ANTIPROGESTINS IN REPRODUCTIVE MEDICINE -- PART I: ACTIVITY EXPRESSIONS OF ANTIPROGESTINS -- Progesterone Antagonists -- Antiglucocorticoid Activity -- Noncompetitive Antiestrogenic (Antiproliferative) Activity -- Sources of Antiprogestins.
PART II: NONCOMPETITIVE ANTIESTROGENIC ACTIVITY OF PROGESTERONE ANTAGONISTS -- Initial Evidence of Noncompetitive

Antiestrogenic Activity of Mifepristone -- Dose-Dependent Blockade of the Proliferative Action of Estradiol Endometrium by Mifepristone -- Mifepristone-Induced Elevations of Estrogen Receptor in Primate Endometrium -- REFERENCES -- B12 ANTIPROGESTOGENS: PERSPECTIVES FROM A GLOBAL RESEARCH PROGRAM -- ABSTRACT -- INTRODUCTION -- COMPOUNDS -- Progesterone Synthesis Inhibitors -- Progesterone-Receptor Blockers -- ANIMAL MODELS -- Receptor Binding -- Plasma Protein Binding -- Pregnant Guinea Pig Model -- MECHANISMS OF ACTION -- Prostaglandin Metabolism -- Myometrial Gap Junctions -- Estrogen and Progesterone Receptors -- POSSIBLE USES -- PROSPECTS -- ACKNOWLEDGMENT -- REFERENCES -- C Observers at the Workshop on Antiprogestins: Assessing the Science April 13-14, 1993 -- Index.

Sommario/riassunto

Mifepristone (RU486), the first clinically available antiprogestin, has generated great interest since its discovery in the early 1980s. Today, it is recognized that mifepristone, along with other antiprogestins, has a potentially significant therapeutic role in human health and disease, with likely applicability to a variety of pregnancy-related conditions (e. g., management of labor) and to contraception, endometriosis, and cancer, among others. But because mifepristone has been studied and used most widely as a means of nonsurgical abortion, political issues have thus far limited research on the drug and prevented its introduction into the U.S. market. This book provides an unbiased evaluation of current knowledge about both the fundamental nature of antiprogestins as well as their possible use in treating numerous diseases and conditions, and it contains recommendations for future research.
