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Merck Research Laboratories
Worldwide Product Safety & Epidemiology

PERIODIC SAFETY UPDATE REPORT FOR:
Measles, Mumps, and Rubella Virus Vaccine Live, MSD

01-Jan-1999 to 31-Dec-2003

International Birth Date: 15-Sep-1978 (United States)

Date of this Report: **22-Jan-2004**

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The term 'Misuse' is herein interpreted in the context of *use that deviates from what is recommended*, i.e., what is described in the CCDS or the package circular (Prescribing Information). Misuse is applied broadly to conditions of shipping, storage and administration, including doses given when contraindicated, at an inappropriate age, too soon or too late, by an incorrect route, etc. In MedDRA, 'Misuse' maps to the preferred terms of 'Medication Error', which includes such lower level terms as *expired drug, wrong drug administered, wrong patient, inappropriate schedule, expired drug, vaccine not stored properly*, etc.

Conclusion

The Company will continue to monitor reports of product misuse as part of the ongoing safety evaluation of measles, mumps, and rubella virus vaccine live.

9.6 Use During Pregnancy

9.6.1 New Reports of Pregnancy Exposures Between 01-Jan-1999 and 31-Dec-2003

During the reporting period of this PSUR, the Company received a total of 292 spontaneous reports of maternal exposure to measles, mumps, and rubella virus vaccine live during pregnancy. Two-hundred fifty-three (253) of the reports were prospective and the remaining 39 were retrospective reports.

A prospective report of exposure during pregnancy is defined as a report for which the Company first learned of the exposure during the pregnancy and the outcome of the pregnancy may be subsequently reported.

A retrospective report of exposure during pregnancy is defined as a report for which the Company first learned of the exposure after the outcome of the pregnancy was known. The pregnancy outcomes of these 292 reports are presented in Table 9.6.1.

Table 9.6.1
New Reports Received
Summary of Pregnancy Exposures
01-Jan-1999 to 31-Dec-2003

	Total Reports of Pregnancy Exposure	Live Births	Elective Abortions	Spontaneous Abortions	Abortion (Not specified)	Fetal Death	Outcome Unknown
Prospective Reports	253	33	3	6	1		210
Retrospective Reports	39	24 [a,b]	2	11		2	

[a] One report of limb hypoplasia congenital

[b] One report of microcephaly and mental retardation

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9.6.1.1 Prospective Reports

The pregnancy outcomes of the 253 prospective reports of exposure to measles, mumps, and rubella virus vaccine live during pregnancy were: 33 live births, 3 elective abortions, 6 spontaneous abortions, and 1 abortion (not specified). The pregnancy outcomes of the remaining 210 reports are unknown.

9.6.1.2 Retrospective Reports

The pregnancy outcomes of the 39 retrospective reports of exposure to measles, mumps, and rubella virus vaccine live during pregnancy were: 24 live births, 2 elective abortions, 11 spontaneous abortions, and 2 fetal (intra-uterine) deaths.

9.6.2 Congenital Anomalies

During the reporting period of the PSUR, in all of the new reports of exposure to measles, mumps, and rubella virus vaccine live during pregnancy, there were no prospective reports of congenital anomalies and 2 retrospective reports of congenital anomalies. In the first retrospective report (WAES [redacted], information was received concerning a 22-year-old female who was vaccinated with the first dose of dose of measles virus vaccine live (+) mumps virus vaccine live (+) rubella virus vaccine live (second generation) one month before the beginning of her pregnancy. At 29 weeks gestation, an echography was performed and a congenital anomaly (i.e., a pathology of the fetus' lower limbs) was observed. At 40 weeks gestation, the patient gave birth by Cesarean to a male with an "ectromelia consisting of hypoplasia of the fibula." The male infant was evaluated: Apgar score test = 9/10, weight = 4,270 g, height = 50 cm, and cranial perimeter = 37 cm. The second retrospective report (WAES [redacted] concerned a 23-year-old female who was vaccinated with one dose of measles virus vaccine live (+) mumps virus vaccine live (+) rubella virus vaccine live (second generation). Subsequently the patient learned that she became pregnant at approximately the time of vaccination. The patient gave birth to a female who was diagnosed with microcephaly as an infant and with mental retardation. The infant sought unspecified medical treatment. The microcephaly and mental retardation were considered disabling adverse events.

Comment

In the pregnancy reports with known outcomes, 2 retrospective reports of congenital anomalies have been received during the reporting period. It is not known whether measles, mumps, and rubella virus vaccine live can cause fetal harm when administered to a pregnant woman or can affect reproductive capacity. Therefore, the vaccine should not be administered to pregnant females; furthermore, pregnancy should be avoided for three months following vaccination. During the reporting period of this PSUR, the CCDS has been updated to include text stating that exposure to mumps infection during the first trimester of pregnancy may increase the rate of spontaneous abortion.

9.6.3 Previously Identified Reports

During the reporting period of this PSUR, follow-up information was received concerning the outcomes of 24 previously identified reports in which women were exposed to measles, mumps,

and rubella virus vaccine live during pregnancy and in which the pregnancy outcomes were unknown at the time of previous PSURs (prospective reports). In the 24 reports with follow-up information, 20 pregnancies resulted in normal healthy newborns, 2 reports involved patients who were lost to follow-up, 1 report involved a patient who underwent an elective abortion, and 1 report involved a congenital anomaly. This report (WAES [redacted]) involving a congenital anomaly concerned a patient who gave birth to a female with Down's syndrome (Trisomy 21). The physician felt that Down's syndrome was not associated with the vaccine.

Table 9.6.3

Summary of Pregnancy Exposures from Previously Identified Reports
(Follow-up Information Received)
01-Jan-1999 to 31-Dec-2003

	Total Reports of Pregnancy Exposure	Live Births	Elective Abortions	Lost to Follow-Up
Prospective Reports	24	21 [a]	1	2

[a] One report of Down's syndrome (Trisomy 21)

Comment

Merck & Co., Inc. will continue efforts to obtain outcome information for all reports of exposure to measles, mumps, and rubella virus vaccine live during pregnancy.

9.6.4 Use During Lactation

During the reporting period of this PSUR, 3 reports of exposure during lactation involving measles, mumps, and rubella virus vaccine were identified. In 1 report (WAES [redacted]), a mother was vaccinated with measles virus vaccine live (+) mumps virus vaccine live (+) rubella virus vaccine live (second generation). Her 11-month-old baby was breastfeeding when the mother was vaccinated. Approximately 14 days post-vaccination, her child broke out in a fine rash along with a high fever. Subsequently, the patient recovered from fine rash and fever. The reporting nurse felt that fine rash and fever were related to therapy with measles-mumps-rubella vaccine. The second report (WAES [redacted]) concerned a 30-year-old female who was vaccinated with measles virus vaccine live (+) mumps virus vaccine live (+) rubella virus vaccine live (second generation). The physician reported that the patient had been breastfeeding her 4 month old son. No adverse events were reported. In the third report (WAES [redacted]), the male infant "broke out with a measles like rash" after breast feeding.

Comment

The Company will continue to monitor all reports of exposure during pregnancy and lactation as part of its ongoing evaluation of the safety of measles, mumps, and rubella virus vaccine.