

Product Information Bulletin



Safety and toxicology of PRONOVA™ UP alginate

PRONOVA™ sodium alginates are manufactured in accordance with cGMP guidelines (Code of Federal Regulations, Title 21, Part 210 and 211), NS-EN ISO 9001:2000 (Quality Management System) and ISO 13485:2003 (Medical Device Directive) standards. Ultrapure – UP- implies that the products contain low levels of residual endotoxin. The current specification is <100 EU/g. PRONOVA™ sodium alginate products are ideal for a wide variety of pharmaceutical, biomedical, biotechnology and tissue engineering applications. The safety and toxicology profile of ultrapure PRONOVA™ sodium alginate products is described in a Drug Master File submitted to the US FDA. The table below is meant to serve as a summary over some of the studies performed and the conclusions drawn from them.

Report number	Title	Animal species	Alginate products (apparent viscosity)	Concentration	Conclusion
ALG-95-001	Effect of sodium alginate on cell survival of V-79 and 3T3 cells cultured in vitro	In vitro cell culture 3T3 mouse fibroblasts V79 Chinese hamster	PRONOVA UP LVG (132 mPas) PRONOVA UP MVG (230 mPas)	0-1 mg/ml	Little or no effect on cell survival and colony-forming ability.
658/521	Single dose toxicity study by the intraperitoneal route	Mouse	PRONOVA UP MVG (230 mPas)	100, 250, 500 mg/kg	No mortality. No abnormal clinical signs, normal weight increase.
658/522	Single dose toxicity study by the intraperitoneal route	Rat	PRONOVA UP MVG (230 mPas)	100, 250, 500 mg/kg	No mortality. No abnormal clinical signs, normal weight increase.
658/523	Single dose toxicity study by the intraperitoneal route	Mouse	PRONOVA UP LVG (132 mPas)	100, 250, 500 mg/kg	No mortality. No abnormal clinical signs, normal weight increase.
658/524	Single dose toxicity study by the intraperitoneal route	Rat	PRONOVA UP LVG (132 mPas)	100, 250, 500 mg/kg	No mortality. No abnormal clinical signs, normal weight increase.
658/529	Single dose toxicity study by the intraperitoneal route	Rat	PRONOVA UP LVG (30 mPas)	100, 250, 500 mg/kg	No mortality. No abnormal clinical signs, normal weight increase.
658/530	Single dose toxicity study by the intraperitoneal route	Rat	PRONOVA UP LVG (3.5 mPas)	100, 250, 500 mg/kg	No mortality. No abnormal clinical signs, normal weight increase.
658/534	Single dose toxicity study by the intravenous route	Rat	Poly mannuronic acid – high molecular weight, intrinsic viscosity 16 dl/g	1, 10, 100 mg/kg	No mortality in 1 and 10 mg/kg groups, 50% mortality in 100 mg/kg group. No abnormal clinical signs in 1 of 10 mg/kg groups.
658/535	Single dose toxicity study by the intravenous route	Rat	Poly mannuronic acid – low molecular weight, intrinsic viscosity 6.8 dl/g	1, 10, 100 mg/kg	No mortality. No abnormal clinical signs, normal weight increase.
Poly-M-94-1	Pharmacokinetics of poly-M	Mouse	Poly mannuronic acid (¹⁴ C-labelled)	5 mg/kg	Oral: No absorption IV: half-life approx. 4 hr IP: half-life approx. 12.5 hr Elimination via urine.

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Technical Service

The information contained in this bulletin is intended to be general in nature. Techniques and data pertaining to specific uses for NovaMatrix/FMC products and new developments will be published periodically in the form of supplemental application bulletins. Our technical staff is ready to offer assistance in the use of NovaMatrix/FMC products.

Regulatory Status

PRONOVA™ sodium alginate meets the standards set forth in the current editions of the United States Pharmacopeia/National Formulary and European Pharmacopoeia. PRONOVA™ sodium alginate satisfies ASTM F 2064 for use in tissue engineered medical products (TEMPs). PRONOVA™ sodium alginate is manufactured in compliance with current Good Manufacturing Practice and described in a DMF submitted to the US FDA.

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