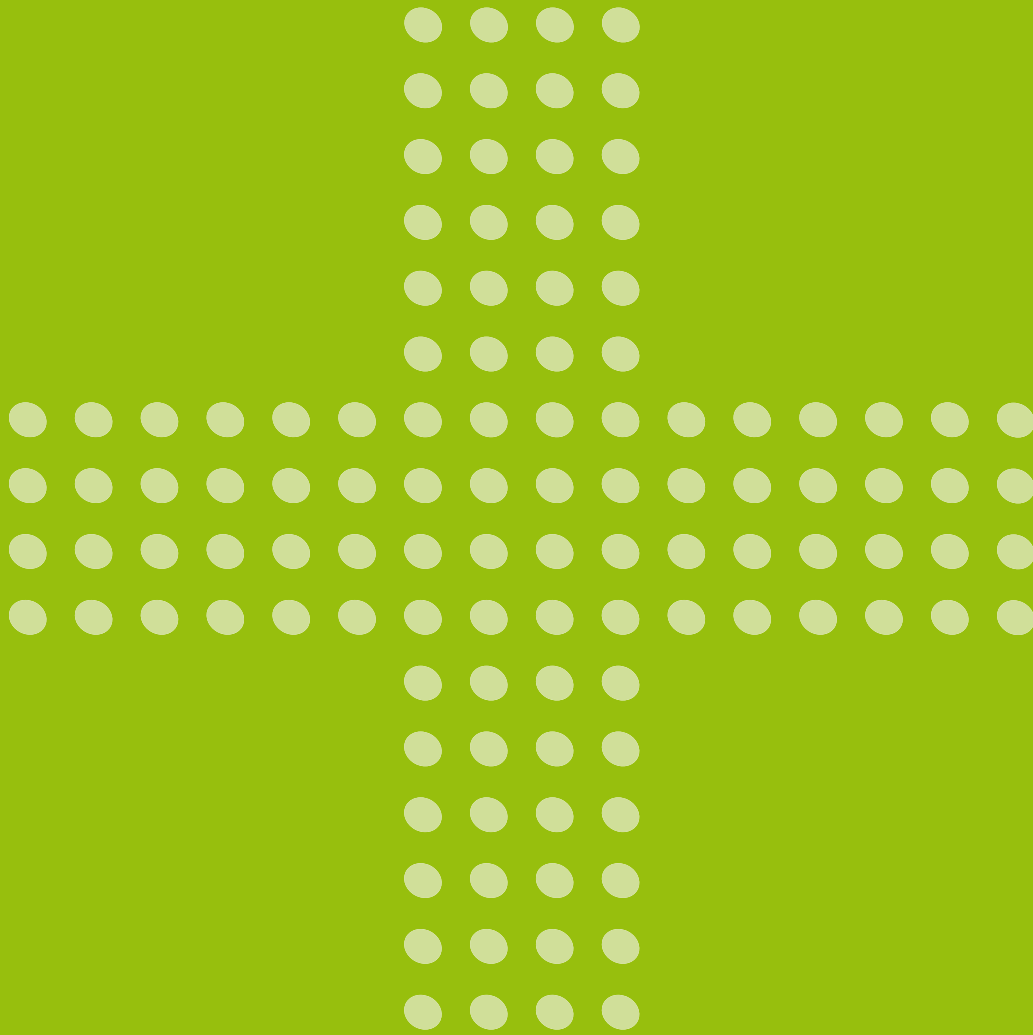


mediprene®



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ELASTO
A HEXPOL COMPANY

MEDICAL APPLICATIONS



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Introduction

Mediprene® thermoplastic elastomers are suitable for a wide variety of uses in the medical and pharmaceutical market and new applications are being developed all the time. Mediprene® compounds combine the performance of vulcanised rubbers with the processing properties of thermoplastics, delivering sophisticated design opportunities through a wide and flexible range of products.

Thermal and mechanical properties can be designed into the formulations and Mediprene® compounds are fully recyclable and thus fulfil environmental requirements. Mediprene® thermoplastic elastomers have proven to be strong alternatives as replacement for PVC. They are completely synthetic and latex free thereby minimizing allergy risks.

The right TPE formulation is the key to a safe and successful medical product. When a standard formulation does not meet the needs of a unique application, we will apply our expertise in formulating a custom solution.

Raw material selection

In order to be called Mediprene®, the raw material constituents of the compound must not only comply with food contact norms like FDA 21CFR and 2002/72/EC, but also have medical approvals, assuring their biocompatibility. We have introduced a clear policy for the selection of raw materials for Mediprene® compounds, typically consisting of; SEBS rubber, paraffinic oil and polypropylene:

- The rubber should be selected from a series of rubbers where representative grades have passed USP Class VI
- The paraffinic oil should be a medicinal white oil, complying with the European Pharmacopoeia for light liquid paraffin
- The polypropylene should be a medical grade that has passed USP Class VI

Originating from medical raw materials with high biocompatibility status and compounded under clean conditions, Mediprene® thermoplastic elastomers are the material of choice for medical customers who want to maximize the probability that their devices will pass relevant medical tests.

Regulatory compliance

The basis for a successful outcome in medical tests is a strict raw material selection strategy, only allowing raw materials that, from a medical point of view, are highly qualified. The raw materials are then compounded together under clean conditions with high consistency.

To further assure the customer, representative grades from the Mediprene® standard series (500200M and 500900M, respectively) have been tested by the Scantox Laboratory in Denmark for cytotoxicity according to USP <87>/ISO 10993-5 and for biocompatibility according to USP Class VI. All materials that were tested successfully passed (copies of the certificates are available on request.). The other compounds in the Mediprene® standard series with hardness values between 20 ShA (500200M) and 90 ShA (500900M) consist of the same raw materials and would therefore probably pass if tested. Note that there is an overlap between some tests in USP Class VI and tests described in parts of ISO 10993, meaning that the material is highly likely to pass parts of ISO 10993 when having passed USP Class VI. However, be aware that it is always the responsibility of the supplier of the finished product to perform relevant tests to ensure that the complete device fulfils the compliance criteria that have been set up for the product.

The external test institute Normpack supervises that raw materials used for Mediprene® compounds comply with food contact norms. Certificates from Normpack, stating which norms and directives are fulfilled, are available on request.



Regulatory information

The purpose of this section is to briefly describe the tests in the United States Pharmacopoeia (USP) and ISO 10993 that have been done on representative grades from the Mediprene® standard series. This section also contains comments on compliance with European Pharmacopoeia (EP) monographs.

Cytotoxicity tests – USP <87> and ISO 10993-5

The elution test, as described both in monograph 87 of the United States Pharmacopoeia and in part 5 of ISO 10993, includes the following steps:

- The sample material is extracted with sodium chloride solution or serum-free mammalian cell culture medium under well-defined conditions
- A cell culture (L-929 mammalian fibroblast cells) is exposed to the sample extract as well as a positive and a negative control under well-defined conditions
- The cells are checked (appearance, cell lysis etc) after 48 hours and the response to the sample extract is judged with help of the guidelines in USP <87> as none, slight, mild, moderate or severe (grades 0-4).

The requirements of the test according to USP <87> are met if the response to the sample extract is not greater than 2 (mildly reactive). ISO 10993-5 does not contain a pass/fail criterium for this test.

Biocompatibility tests according to USP (USP Class VI)

Biological reactivity tests, in vivo, are described in USP <88>. Six plastic classes are defined – USP Class I-VI, among which USP Class VI requires the most exhaustive testing. USP Class VI contains the following main tests:

- **Systemic injection test**
- **Intracutaneous test**
- **Implantation test**

Except for the implantation test, tests are carried out using extracts of the material to be tested. These extracts are prepared with differed solvents under well-specified conditions (surface area, temperature, time etc). For the implantation test small sample strips (minimum 10x1 mm) are used. Below is a brief description of each test and its purpose.

Systemic injection test

Purpose:

To determine the biological response of mice to the material by injection of specific extracts prepared from samples of the material.

Test:

Extracts of the sample material in sodium chloride solution, 1 in 20 solution of alcohol in sodium chloride solution, polyethylene glycol 400 and vegetable oil, respectively, as well as blanks are injected into albino mice. The mice are then observed at different time intervals up to 72 hours after injection. If none of the animals treated with the extract of the material shows a significantly greater biological reactivity than the animals treated with the blank, the material has passed the test.

Intracutaneous test

Purpose:

To determine the local biological response of rabbits to the material by injection of specific extracts prepared from samples of the material.

Test:

Extracts of the sample material in sodium chloride solution, 1 in 20 solution of alcohol in sodium chloride solution, polyethylene glycol 400 and vegetable oil, respectively, as well as blanks are injected into albino rabbits intracutaneously. Each extract is injected into two animals on one side of the spinal column and the blank on the opposite side. The injection sites are examined for evidence of tissue reactions such as erythema, edema and necroses at different time intervals up to 72 hours after injection. The observations for both extract and blank sites are rated on a numerical scale based on guidelines given in USP <88> every time the sites are inspected. After 72 hours the overall mean score for each sample and each corresponding blank



is calculated. If the difference in mean score between sample and blank is 1.0 or less the material extracted has passed the test.

Implantation test

Purpose:

To evaluate the reaction of living tissue to the material by the implantation of a sample into the tissue of a rabbit.

Test:

The paravertebral muscle of two rabbits is implanted – each by four strips of the sample material and two strips of USP High-Density Polyethylene RS. The animals are kept minimum 120 hours and are then sacrificed by an overdose of anaesthetic agent or other suitable agent. The tissue is cut and the tissue portion surrounding each strip is examined for hemorrhage, necrosis, discolorations, infections and encapsulation. Encapsulation is determined by measuring the width of the capsule and rated on a numerical scale based on the guidelines given in USP <88>. The difference between the average scores for the sample and the control are calculated. If the difference is 1.0 or less the material has passed the test, alternatively if the difference in sample and control mean scores for more than one of the implant sites is less than or equal to 1 for any implanted animal.

Note that, even though representative Mediprene® grades have passed these implantation tests, the We do not supply thermoplastic elastomers for implants.

European Pharmacopoeia (EP)

The European Pharmacopoeia contains monographs and other texts that are designed to be appropriate to the needs of regulatory authorities, people engaged in quality control and manufacturers of starting materials and medicinal products.

We have successfully tailor-made Mediprene® grades that have passed selected monographs in chapter 3.1 of the European Pharmacopoeia, dealing with materials used for the manufacture of containers. Please consult our medical team for advice if compliance with a special EP monograph is needed.

Formulation stability, change, notification and availability

We are well aware of the severe consequences that most medical customers face when a formulation is changed. Therefore, Mediprene® formulations are never changed unless one or more of its constituents cease to exist.

In case a Mediprene® formulation has to be changed due to the termination of one or more raw materials, we will inform customers in due time to qualify a replacement compound.

Clean line production and quality

Mediprene® thermoplastic elastomers are produced with modern production equipment, designed for easy cleaning and with traceability and documentation based on the requirements of ISO 13485:2003 (Medical devices). To achieve the high cleanliness that every medical customer has the right to expect, special measures are taken, such as:

- Thorough and well documented cleandown of the compounding line before running Mediprene® compounds
- Closed systems from ribbon blender to packaging
- Special precautions in the ribbon blender and packaging areas
- Operators wearing clean clothes, gloves and hairnet

Mediprene® grades are all manufactured under strict quality control, ensuring product property consistency. Our site producing Mediprene® compounds is accredited to ISO 9001, ISO 14001 and ISO 13485.



Product performance

Special features

- Flexibility and elasticity
- Transparent grades available
- Can be easily coloured in any shade
- Soft touch
- Excellent resistance to many fluids used in the health care environment
- PVC, silicone and latex free
- Adhesion to PP or PE without modification in overmoulding and coextrusion
- Processable with ordinary methods for thermoplastics processing, such as injection moulding and extrusion.
- Short cycle times

Colouring recommendations

For Mediprene® compounds, polyolefin based masterbatch is recommended for colouring. Not to violate the high medical status of the Mediprene® compound, the colour masterbatch should have passed USP Class VI or comparable tests.

Processing recommendations

Mediprene® compounds can be processed using conventional thermoplastic equipment for injection moulding, extrusion etc. Processing temperatures normally range from 180°C to 210°C. The compounds in the standard series are not hygroscopic and thus do not need predrying.

Waste disposal

All Mediprene® grades are fully recyclable and, where possible, reprocessable during manufacturing. When burned, Mediprene® compounds do not emit toxic fumes.

Application examples

Mediprene® thermoplastic elastomers can be used in various applications such as face masks, incontinence care products, connectors, IV systems, intubation equipment, seals, resealable membranes, drip chambers, wound care products, tubing, medical packaging and soft touch grips on medical devices. We are continuously working with our customers to develop new applications for Mediprene® compounds.

Sterilization performance

Many medical devices are sterilized prior to use, sometimes several times during their lifetime. Therefore it is important that the materials used retain their properties after numerous sterilizations.

Representative Mediprene® grades have been sterilized with the following methods:

- Steam/Autoclave
- Ethylene oxide (EtO)
- Gamma irradiation (25 kGy and 50 kGy)

Their properties have been evaluated before and after sterilization. This investigation shows that ethylene oxide sterilization is the most gentle sterilization method for Mediprene® thermoplastic elastomers. A more detailed technical bulletin summarizing the sterilization test results is available on request.



A selection of available Mediprene® grades

Weather resistance: Good.

Chemical resistance: Good, excluding organic solvents and oils.

Service temperature: From -50°C to max +125°C, depending on hardness.

Mediprene grade	Hardness Shore A or D	Colour	Specific gravity g/cm ³	Tensile Strength MPa	Elongation at Break %	Tear Strength kN/m	Modulus 100% MPa	Modulus 300% MPa	MFR g/10min
Test method	ASTM D2240 (4mm)		ASTM D792	ASTM D638	ASTM D638	ASTM D624	ASTM D638	ASTM D638	ASTM D1238
500000M	0 A	Translucent	0.88	1	>1000	5	0.1	0.2	0.3 ⁽¹⁾
500050M	5 A	Translucent	0.88	2	>1000	12	0.1	0.2	3 ⁽¹⁾
500120M	12 A	Translucent	0.88	4	>800	23	0.2	0.5	25 ⁽²⁾
500200M	20 A	Translucent	0.89	4	>800	12	0.3	0.8	1 ⁽²⁾
500250M	25 A	Translucent	0.89	2	>500	15	0.4	0.9	5 ⁽³⁾
500300M	30 A	Translucent	0.89	5	>800	15	0.6	1	18 ⁽³⁾
500350M	35 A	Translucent	0.89	6	>700	16	0.8	2	0.5 ⁽²⁾
500400M	40 A	Translucent	0.89	5	>600	16	1	2	14 ⁽³⁾
500422M	42 A	Transparent	0.89	6	>600	40	0.7	2	12 ⁽²⁾
500450M	45 A	Translucent	0.89	7	>600	23	1	2	2 ⁽³⁾
500520M	52 A	Translucent	0.89	6	>600	24	1	3	0.5 ⁽³⁾
500600M	60 A	Translucent	0.89	11	>700	27	2	3	0.7 ⁽³⁾
500650M	65 A	Translucent	0.89	10	>600	37	2	4	2 ⁽³⁾
500700M	70 A	Translucent	0.89	13	>700	37	3	4	4 ⁽³⁾
500750M	75 A	Translucent	0.89	16	>700	43	3	4	3 ⁽³⁾
500800M	80 A	Translucent	0.89	18	>700	49	4	5	3 ⁽³⁾
500900M	90 A	Translucent	0.89	10	>500	53	6	8	1 ⁽²⁾
520621M	62 D	Translucent	0.89	37	>700	194	17	17	7 ⁽⁴⁾

⁽¹⁾ 190°C/0.325 kg, ⁽²⁾ 190°C/2.16 kg, ⁽³⁾ 190°C/5 kg, ⁽⁴⁾ 230°C/2.16 kg

All the above information about chemical and physical properties consists of values measured in tests on injection moulded test specimens. We provide written and illustrated advice in good faith. This should only be regarded as being advisory and does not absolve the customers from doing their own tests and trials, to determine the suitability of the material or the intended applications. We retain the right to make changes without prior notice.

Let's share expertise and gain synergies!

The customer provides the product requirements and we supply the expertise in thermoplastic elastomers in medical applications. By working together from the very beginning of a project we can create extraordinary products.

The Mediprene® standard series is the start-up point in most projects, but we often apply our expertise in formulating custom solutions for unique applications. Creating grades with enhanced characteristics, for example modified surface wetting or processing properties. All modifications and developments follow the Mediprene® raw material selection policy.

Sweden

t : 46 (0) 532 60 75 00

f : 46 (0) 532 60 75 99

info@elasto.se

United Kingdom

t : 44 (0)161 654 6616

f : 44 (0)161 654 2333

sales@elasto.co.uk

France

t : 33 (0) 160 43 17 17

f : 33 (0) 160 43 11 13

pascal.gruyer@elastotpe.com

For further information or to download this and other publications please visit

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