formoline L112 | formoline L112 EXTRA

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Information for professionals

Guideline-based use and efficacy of the lipid binders formoline L112 and formoline L112 EXTRA in the therapy of overweight and obesity

Active dietary fibre to correct malnourishment from a high-fat diet

- **The active dietary fibre L112 of natural origin reduces calorie absorption from dietary fats by up to 2/3**
- **Scientifically proven efficacy**
- **Very well tolerated**
- **Available in 2 strengths – as required**

1. Medical device

formoline L112 and formoline L112 EXTRA are medical devices certified throughout the EU. Quality, safety and efficacy meet the requirements of Regulation (EU) 2017/745. This has been tested and certified by professionals at an independent government-notified body.

2. Composition

The main ingredient of formoline L112 and formoline L112 EXTRA is the active dietary fibre polyglucosamine L112 (73 %): specification L112 of ß-1,4-polymer of D-glucosamine and N-acetyl-D-glucosamine from crustacean shells

The excipients used are: ascorbic acid, tartaric acid, tableting excipients (plant-based cellulose, croscarmellose sodium, plant-based magnesium stearate, povidone, silicon dioxide).

It does not contain flavour enhancers, preservatives or colourants and is free of gelatine, gluten, lactose and cholesterol. It is also suitable for people with diabetes as it contains no utilisable carbohydrates.

3. Indication and intended purpose

Indication:
For the treatment of overweight and obesity

formoline L112 or formoline L112 EXTRA is intended for adults with a body mass index (BMI) above 25 in conjunction with a reduced calorie diet.

Intended purpose:
Lipid binder
- for weight reduction
- for weight management

with LDL cholesterol-lowering accompanying effect

formoline L112 and formoline L112 EXTRA reduce the digestibility of lipids through physical binding, thus leading to reduced calorie absorption. As a result, they support weight reduction, maintenance of weight loss and the lowering of LDL cholesterol.

4. Mechanism of action of polyglucosamine L112

The active substance polyglucosamine L112 acts as a lipid adsorbent in the gastrointestinal tract. It has been shown that polyglucosamine fibres have the ability to adsorb and bind therapeutically relevant quantities of lipids.

The active dietary fibre polyglucosamine L112 cannot be digested. In the acid milieu of the stomach, polyglucosamine L112 is protonated at the free amino groups so that positively charged amino groups ($-NH_3^+$) are now present. The dietary fat absorbed is split to a minor extent by lipases already present in the stomach and to a greater extent by the pancreatic lipases into glyceride and free fatty acids. The free fatty acids are primarily bound through ionic bonds between the negatively charged carboxyl groups of the fatty acids ($-COO^-$) and the positive charges of polyglucosamine L112.

At the pH values in the upper digestive tract, a gel structure forms which, because of its lipophilic character, can bind other lipophilic substances such as cholesterol and neutral fats (Fig. 1). If formoline L112 and formoline L112 EXTRA are taken as recommended with a fat-containing meal, polyglucosamine L112 can form the gel with the dietary fats and achieve its optimal effect (Fig. 2).

Diagram of lipid adsorption

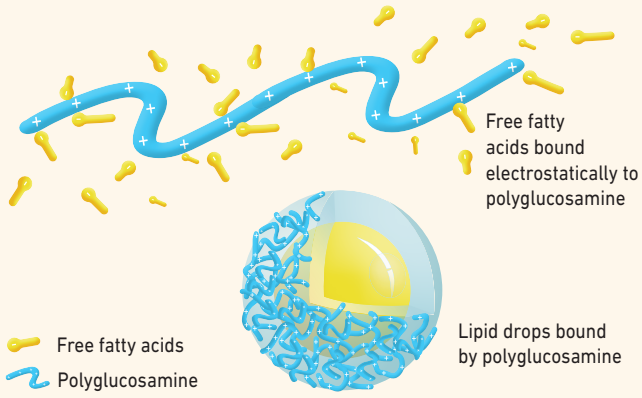

Figure 1: modified diagram of lipid adsorption as proposed by Hennen W. J., 1996 [1].

The optimal quality of the raw material is critical for the fat binding capacity of polyglucosamine L112. Every batch of raw material is tested and is only used in production if it has a fat binding capacity of at least 680 g fat per 1 g raw material (Fig. 2).

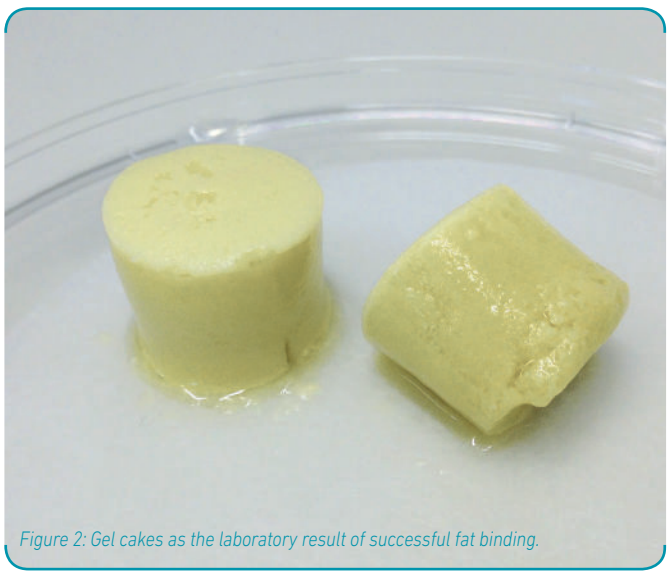

Figure 2: Gel cakes as the laboratory result of successful fat binding.

Lipid absorption, normally a highly effective process occurring through the wall of the small intestine, is significantly reduced in the presence of polyglucosamine L112. Mono-unsaturated fatty acids, nonpolar lipids and undigested fats are bound to polyglucosamine L112 and can no longer be absorbed.

It was demonstrated in a controlled study that polyglucosamine L112 reduces the absorption of lipids from food by up to 2/3 (Fig. 3), which demonstrates the enormous fat binding capacity of polyglucosamine L112 in vivo as well [2]. After binding, dietary fats cannot be absorbed in the small intestine. Calorie intake is substantially decreased. If this is less than calorie consumption, weight reduction occurs. No fatty stools are formed when formoline L112 and formoline L112 EXTRA are used.

Reduction in lipid absorption from dietary fats

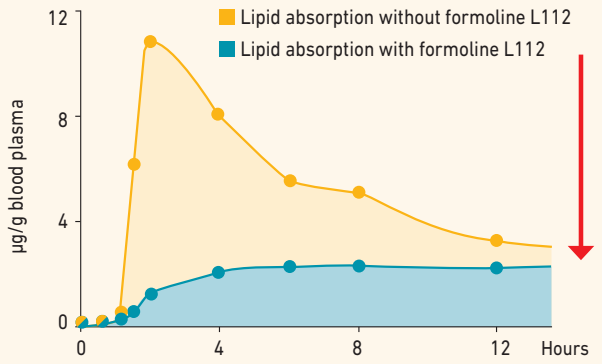

Figure 3: Lipid absorption in the blood plasma with and without polyglucosamine L112 according to Cnubben 2016 [2].

5. How to use formoline

5.1 Taking formoline

For weight loss: Take 2 tablets
formoline L112 or formoline L112 EXTRA twice daily at the two meals with the highest fat content.

For weight management, the dosage can be reduced to 2 tablets daily.

Swallow the tablets whole together with plenty of low-calorie fluid (at least 250 ml) to ensure that the tablets make their

way into the stomach. Since formoline L112 and formoline L112 EXTRA are preparations rich in dietary fibre, make sure that you consume enough fluids (at least 2 litres per day).

To ensure that the requirement for essential fatty acids and fat-soluble vitamins (A, D, E and K) is met, we recommend taking formoline L112 or formoline L112 EXTRA with 2 out of 3 main meals only. You should consume at least one meal per day containing high-quality oils that supply the body with fat-soluble vitamins and essential fatty acids. If required, a multivitamin preparation can also be taken as a supplement to ensure a sufficient supply of vitamins.

It is not recommended that formoline L112 or formoline L112 EXTRA are taken with high-vitamin meals (e.g. salad, vegetables), with high-quality oils or with omega-3 fatty acids (salmon etc.) as partial binding of the fat-soluble vitamins and essential fatty acids may occur.

5.2 Recommendations for use

Too high an energy intake, in the form of dietary fats in particular, is regarded as a cause of overweight and obesity. So the average daily fat intake is up to 136 g fat [3]. As one gram fat contains approximately double the energy of one gram carbohydrate or protein, a restriction on fat intake is regarded as an effective method of weight reduction [4]. Many people, however, find it difficult to reduce their daily fat intake in line with this. If this is the case, formoline L112 and formoline L112 EXTRA as effective lipid adsorbents can bind a majority of the dietary fats in the gastrointestinal tract [2] and avoid further energy generation.

The products are particularly suitable for people who are overweight who cannot or do not wish to follow a radical low-fat diet. So they support successful weight reduction in people already on a fat-conscious diet containing up to 80 g fat per day.

5.3 Contraindications

Do not take formoline L112/formoline L112 EXTRA if you:

- Have a known allergy to crustaceans or to any of the ingredients,
- Are underweight (BMI <18.5 kg/m^2),
- Are pregnant or breastfeeding,
- suffer from chronic constipation, intestinal obstruction etc.; or
- are on long-term medication that reduces intestinal activity.

Consult a doctor before taking formoline L112/formoline L112 EXTRA in the following cases:

- long-term medication use,
- serious gastrointestinal disease, or after surgery on the gastrointestinal tract,
- elderly people (older than 80 years)

5.4 Interactions

The fat binding capacity of formoline L112 and formoline L112 EXTRA means that they may also bind fat-soluble active pharmaceutical ingredients (such as anti-epileptic drugs, blood thinners, hormone preparations, contraceptive pill) or fat-soluble vitamins (A, D, E, K) as well as dietary fats. The availability of fat-soluble (lipophilic) active substances may be reduced. In this case, it is recommended to leave a gap of at least four hours before taking formoline L112 and formoline L112 EXTRA.

5.5 Side effects / Overdose

formoline L112/formoline L112 EXTRA is generally very well tolerated. In very rare cases (in less than 1/10,000 users), an adverse reaction in the form of constipation, flatulence or allergic reaction has been reported. These symptoms were temporary and disappeared rapidly without medical intervention. Constipation is generally caused by too little fluid intake while simultaneously increasing fibre intake. formoline L112/formoline L112 EXTRA can therefore be regarded as a very well tolerated product in the therapy of overweight.

6. Clinical studies

6.1 Efficacy of polyglucosamine for weight loss – confirmed in a randomised, double-blind, placebo-controlled clinical study (Pokhis et al. 2015)

A study involving 115 participants confirms that by taking formoline L112 a 30 % higher weight loss is achieved compared with guideline therapy with hypocaloric diet (-500 kcal) and light physical activity [5].

The subjects followed a standard treatment consisting of a reduced calorie diet and increased daily physical activity and took 2 x 2 tablets formoline L112 vs. placebo for at least 24 weeks.

- By taking formoline L112, the subjects achieved a 30 % higher weight loss compared with guideline therapy with a calorie-conscious diet and light physical activity.

- Weight loss of 5 % of baseline weight was achieved in 52 % of the participants in the formoline L112 group as early as 8 weeks. In the placebo group, this was achieved in just under 20 % of the participants (Fig. 4).

Significant advantage in weight loss

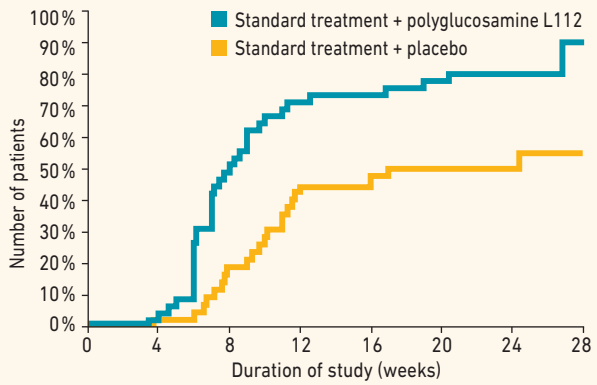

Figure 4: Number of patients who reduced their bodyweight by more than 5 %, based on Pokhis 2015 [5].

Thus weight loss in the formoline L112 group was 30 % more successful than in the placebo group. This advantage was also maintained after 3 and 6 months.

6.2 Randomised, double-blind, clinical comparative study of polyglucosamine in the treatment of overweight and obesity (Stoll et al. 2017)

This three-month study involving 64 participants shows that polyglucosamine L112 is more effective in weight reduction than orlistat (60 mg). In the formoline L112 group, participants lost significantly more weight on average (6.7 kg) than with orlistat (-4.8 kg, $p<0.01$, t-test) [6].

6.3 Randomised, double-blind, placebo-controlled, long-term clinical study in the treatment of obesity (Cornelli et al. 2017)

The study which involved 100 participants (BMI 30 – 35 kg/m^2) shows the efficacy of polyglucosamine L112 regarding weight reduction compared with placebo. In addition to taking tablets, both groups implemented a calorie reduction (-10 %) by an accompanying change in nutrition, e.g. a reduction in carbohydrates and simultaneous increase in the proportion of vegetables in meals to achieve a comparative volume of food with a reduced number of calories.

In addition, physical activity in daily life was increased. With these measures and additional intake of 2 x 2 tablets of polyglucosamine L112, the participants achieved, in 12 months, a 50 % higher weight loss than by taking a placebo.

- By taking polyglucosamine L112, a significantly greater reduction in bodyweight and waist circumference occurred (12.1 kg, -12.7 %; 13.3 cm, -11.6 %) than on placebo (8.0 kg, -7.8 %; 10.2 cm, -8.8 %; $p<0.001$, ANOVA). (Fig. 5)

Weight loss in 12 months

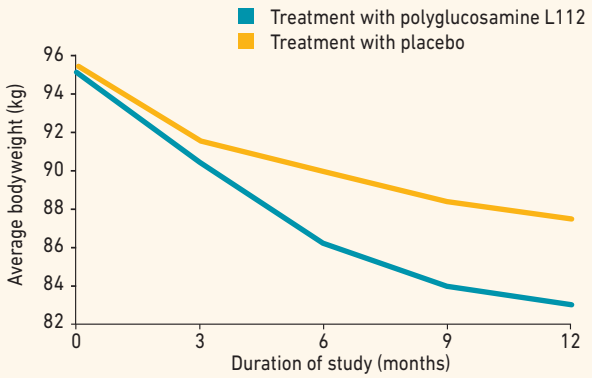

Figure 5: Change in bodyweight over one year [7].

- A significantly greater reduction in plasma lipids and hs-CRP were seen in the polyglucosamine L112 group than in the placebo group (Fig. 6).

Improvement in blood values

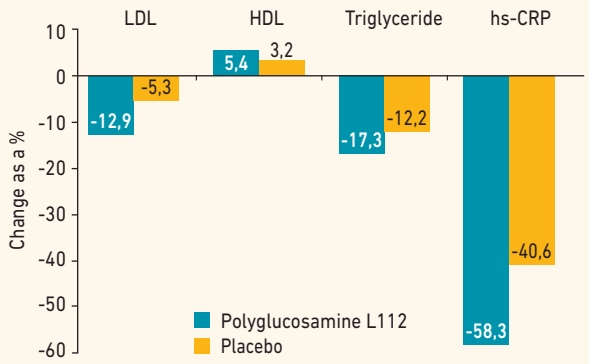

Figure 6: Change in blood values over 12 months [7].

- The treatment was very well tolerated. Only a few cases of constipation occurred. 97 subjects (49 (L112) and 48 (placebo)) completed the study, which indicates excellent adherence [7].

6.4 Randomised, placebo-controlled, clinical study of the effect of polyglucosamine on LDL cholesterol (Lütjohann et al. 2018)

The effect of polyglucosamine L112 on serum LDL cholesterol was also the focus of a twelve-week, randomised and placebo-controlled study. Serum samples from 116 overweight subjects were analysed at baseline and after twelve weeks of taking polyglucosamine or placebo.

The results show again a significant reduction in LDL cholesterol (-8.67 mg/dL) in the polyglucosamine group, whereas no significant decrease (-1.0 mg/dL) was seen in the placebo group. The authors suspect that this clinically relevant drop in LDL concentration in subjects in the polyglucosamine group is due to the binding of cholesterol from the food in the stomach and intestine [8].

6.5 Meta-analysis of the effect of polyglucosamine on weight loss and metabolic parameters in obesity (Perna et al. 2020)

A meta-analysis of 4 randomised and placebo-controlled clinical studies involving 399 participants in total conducted in 2020 shows that daily ingestion of polyglucosamine in combination with reduced calorie intake and more exercise has positive effects on bodyweight, BMI and waist circumference. Higher waist circumference is associated with increased risk of the development of diabetes, cardiovascular disease and the metabolic syndrome. A reduction in waist circumference with the help of polyglucosamine can minimise this risk [9].

7. Information on efficacy

formoline L112 and formoline L112 EXTRA can effectively support weight reduction in overweight and obesity. Healthy eating and moderate daily exercise have been shown to be other important factors for successful weight reduction therapy. They can work optimally as lipid adsorbent only if the food intake contains relevant amounts of fat. The products are not suitable for people on a low-fat diet. Other dietary components such as sugar, carbohydrate, protein or alcohol bind to a minimal extent only to polyglucosamine L112. They are either transformed into energy or stored in the form of fat if necessary.

8. Summary

In summary, it can be concluded that formoline L112 and formoline L112 EXTRA are effective and safe products for supporting the treatment of overweight and for weight management. They are very well tolerated and can be taken over the long term.

The reduced absorption of lipids on polyglucosamine L112 leads to a decreased energy intake and thus contributes to clinically relevant weight reduction [5-7, 9]. An improvement in overall health (e.g. in the metabolic syndrome) in overweight people is the result [9]. The effect of lipid absorption has been documented for polyglucosamine L112 [2].

If the products are used in accordance with the recommendations in the package leaflet, it is possible for overweight patients to achieve considerable success with formoline L112/formoline L112 EXTRA and a fat-conscious diet containing approximately 80 g fat per day. A lasting weight reduction requires a change in diet in terms of calorie- and fat-conscious nutrition combined with appropriate individual exercise therapy. The dietary recommendations on formoline L112 and formoline L112 EXTRA meet the nutritional guidelines for healthy eating formulated by nutritionists with the aim of establishing sensible and sustainable eating behaviour [4]. The products help people to acquire healthy and sensible eating behaviour gradually and to maintain it in the long term [5, 7].

This can also counter the yo-yo effect. Other forms of diet that radically undersupply the body over a long period lower the basal metabolic rate. The result is an unintended and particularly rapid weight gain after stopping a weight reduction diet of this kind [10]. When used as an aid to weight reduction, significant and long-term weight reduction can be achieved with formoline L112 and formoline L112 EXTRA and patient adherence can be significantly increased through a sense of achievement [5-7, 9].

List of references:

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State of the art: May 2022

The summary on safety and clinical performance can be found under www.certmedica.com/SSCP.

formoline L112 EXTRA is recommended for people weighing more than 75 kg. It contains 50 % more active substance.

Medical device with CE marking CE 0123

Basic UDI-DI: 426010333L112T4

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