



Risk minimisation material

concerning the use of
Tracydal® (tranylcypromine) in
patients

Dietary advice

More information?

If you have any questions after reading this booklet, please contact your dietician/physician. For additional questions, you can also call or email the following address:

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Introduction

The risk minimisation materials for Tracydal[®] (tranylcypromine) have been assessed by the Dutch Medicines Evaluation Board (MEB). The risk minimisation materials describe how to reduce or prevent important risks of this medicine.

The administration of Tracydal[®] (tranylcypromine) increases the risk of hypertensive crisis (so-called “cheese reaction”).

- The patient must adhere to a low-tyramine diet (and regularly check their blood pressure), as described in this dietary advice.

The dietary advice for Tracydal[®] is also available on the website of Daleco Pharma B.V (www.dalecopharma.nl) and can also be installed as an “app” on your phone (Dutch only).

MAO-Inhibitors and tyramine

Your physician has prescribed you Tracydal[®]; a MAO-inhibitor. This medication can be used by patients to treat severe depression (multi-resistant depression, where treatment with two standard anti-depressants and the use of additional therapeutics (e.g. lithium) were not effective).

A MAO-inhibitor inhibits the enzyme Mono-Amine Oxidase (MAO). This enzyme plays an important role in the breakdown of neurotransmitters, such as serotonin, dopamine and noradrenaline. A shortage of these neurotransmitters could lead to a mood disorder, and the development of depression.

By inhibiting the enzyme MAO, the dopamine, serotonin and noradrenaline levels within the brain will no longer be reduced, preventing their shortage. The enzyme MAO also affects the breakdown of tyramine, (a protein-like substance) found within the human body. Therefore, when you are using a MAO-inhibitor the amount of tyramine present in your blood can increase.

Tyramine is a naturally occurring substance that is present in some foods. Fresh protein rich products contain relatively low levels of tyramine. However, when protein rich foods and beverages are kept over a prolonged period, the amount of tyramine will be increased. The tyramine content of food products will also increase if they undergo additional processing (e.g. drying or smoking). Therefore, it is important to consume fresh products and to pay close attention to how they are stored.

When you are using a MAO-inhibitor, you need to be aware of what you are eating and drinking. If the concentration of tyramine is too high in your blood, you may develop an extremely high blood pressure, with a rapid onset. In very rare cases, this may lead to organ damage or cerebral haemorrhage.

You can prevent this, by strictly adhering to a low-tyramine diet, which is further described in this booklet.

The diet with the use of a MAO-inhibitor

On the first day of treatment with Tracydal[®], you will start with a low-tyramine diet. You can still consume most products. This booklet will further explain what you should and should not eat.

It is advised to not consume more than one product from the second column in each product group per day.

Cheese

Dutch cheeses are made from pasteurised milk. Pasteurisation involves the heating of milk to 72 °C, which eliminates bacteria. Cheese from unpasteurised milk contains higher levels of tyramine, with packaging stating that “raw milk” or “lait cru” was used during its production. If these terms are found on the product label the cheese was made from unpasteurised milk.

Red crust cheeses (“Roodkorstkazen”) can only be consumed if they are made from pasteurized milk.

It is recommended to only purchase cheese that has been commercially packaged and to carefully look at the expiry date (EXP). After opening a block of cheese, it should not be stored in the fridge for longer than two weeks, even if the expiry date was not reached.

You are allowed to eat young cheese when it is melted (for example on a grilled sandwich or in a casserole).

What you can eat	What you can eat in moderation	What you cannot eat
Young cheese <ul style="list-style-type: none"> - Young Edammer - Young Gouda - Young Leidse (cumin) - Young Maaslander - Young Leerdammer; - Maasdammer 	Maximal two slices = 40 grams of young matured, matured or extra matured Dutch cheese <ul style="list-style-type: none"> - Goudse - Edammer - Maasdammer, Leerdammer - Leidse cheese(cumin) 	Melted-or cheese spread, smoked cheese, Farmers cheese <ul style="list-style-type: none"> - Old, aged Dutch cheese - Goat's milk cheese - Sheep's milk cheese
Packed soft cheese <ul style="list-style-type: none"> - Fresh cheese or quark - Hüttenkäse/Cottage cheese - Ricotta - Mozzarella - Feta made from cow's milk - Mascarpone - Red crust cheese made from pasteurised milk; e.g. Kernhem or Port Salut 	You can consume a max of 10 grams (1 tablespoon) of: <ul style="list-style-type: none"> - Parmesan cheese, pesto based on parmesan cheese - Swiss grated cheese 	Unpasteurised cheese Foreign cheese, such as: <ul style="list-style-type: none"> - Brie - Camembert - Emmenthaler - Cheddar - Gorgonzola, Roquefort and other blue cheese - Gruyère - Feta, made of sheep-or goat milk
Cream cheese <ul style="list-style-type: none"> - Mon Chou - Boursin - Paturain 		Cheese products <ul style="list-style-type: none"> - Cheese crisps - Salty cheese bits - Cheese biscuits - Cheese burgers - Cheese soufflés - Cheese sauce from packages

Meat, meat replacements, fish, chicken and eggs

The protein content in protein rich products, such as meat, meat replacement, meat products, chicken and eggs can be converted (when stored for longer time) by bacteria to tyramine. Therefore, it is important that these products are prepared and consumed shortly after purchase. Raw protein products can spoil more easily at temperatures higher than 4°C.

Steaming and/or smoking fish or meat products occurs at temperatures between 30 and 70°C. At these temperatures bacteria can multiply quickly, which increases the tyramine content in the product. Therefore, if the product label indicates that the product has been ‘smoked’ this product is not allowed to be consumed. This also includes products that have been prepared in a smoker.

Products that only contain “smoke flavouring” are allowed to be consumed.

What you can eat	What you can eat in moderation	What you cannot eat
<ul style="list-style-type: none"> - All kinds of meat, fish and chicken, except those mentioned in columns to the right. - All varieties of chicken and smoked chicken (with smoked aroma flavour) - Eggs - Beef (medium or rare), steak tartare, roast beef - Prawn crackers - Pickled herring (only from a jar) - Canned fish - Deep fried snacks without cheese 	<ul style="list-style-type: none"> - Peanut sauce marinated in soy sauce/sweet soya sauce (ketjap) - Salami (max 1 slice, 15 grams) <i>or</i> - Cervelas (max 1 slice, 15 grams) <i>or</i> - Smoked meat, raw ham, bacon, smoked bacon (max 15 grams) <i>or</i> - Toppings, that resembles these (maximal 1 slice, 15 grams) <i>or</i> - 1 Portion pâté of 15 grams - (Chicken)liver max 50 grams 	<ul style="list-style-type: none"> - Raw meat (e.g. carpaccio), raw fish (e.g. sushi), raw egg and raw chicken - Meat with cheese (e.g. cordon bleu, grilled sausage with cheese) and hamburgers with cheese. - Smoked chicken (with ingredient smoke) - Salt-cured meat - Steamed fish - Smoked fish and/or wood smoked fish like mackerel or salmon steaks - Dried fish, stockfish (unsalted dried fish), cod - Gravad Lax (cured salmon with salt, sugar and dill) Note: above especially with a fish buffet
<p>Only in factory packaging:</p> <ul style="list-style-type: none"> - Filet American - Ox sausage - Smoked sausage - Blood sausage 	<ul style="list-style-type: none"> - Anchovies (15 grams) - 1 fresh herring (Hollandse nieuwe) from the fishmonger 	<ul style="list-style-type: none"> - Smoked sausage which was not commercially produced - Handmade smoked sausage - HEMA smoked sausage

– Fresh fish that has been cooled and purchased from a fishmonger, baked, stewed or grilled (e.g. salmon or tuna)		Trassi (shrimp paste)
<i>Meat replacements, based on nuts, cereal, soy, egg as well as Quorn and Valess products without cheese are allowed</i>		

Soy products and fermented sauces

The process of fermentation causes certain chemical changes in a product, and this process is by caused micro-organisms (bacteria, yeast or fungus). Micro-organisms convert the protein from products into tyramine, and such fermented products should only be consumed in moderation. The way that a product has been fermented, determines how much of the product can be consumed. When you are eating in a restaurant specialising in Eastern/Oriental cuisine, you should ask if soy sauce or other Eastern-based sauces are used to prepare the dish.

What you can eat	What you can eat in moderation	What you cannot eat
<ul style="list-style-type: none"> – Bean curd – Tofu – Clear, yellow and red wok sauce 	<p>Tempeh (Fermented soy product). Maximum 100 grams each day provided that it is fresh and has been commercially packaged!</p>	<ul style="list-style-type: none"> – Worcestershire sauce – Tamari
All products which contains soy	<p>Sweet soy sauce (ketjap) and other similar products (1 table spoon). Opened bottles should be stored in the fridge, and used for a maximum of three months.</p>	<ul style="list-style-type: none"> – Other fermented eastern (fish) sauces, brown wok sauces – Miso
	<p>Peanut sauce Prepared with soy sauce/sweet soy sauce (1 portion =30 grams)</p>	

Fruits and Vegetables

Fresh fruits and vegetables have a low tyramine content. You can eat a diverse range of fruits and vegetables, except fermented cabbage (sauerkraut) and broad bean pods.

You may not eat sauerkraut, as this involves the fermentation of white cabbage. As the fermentation process takes six weeks, sauerkraut will contain tyramine.

The broad bean pod (primarily used in Mediterranean cuisine) is not allowed to be consumed.

What you can eat	What you can eat in moderation	What you cannot eat
<ul style="list-style-type: none"> - All sorts of vegetables and fruit - Legumes, such as kidney beans, brown beans, lentils, (chick)peas, husked broad beans - Dried fruit - Preserved vegetables, e.g. atjar tjampoer, pickles, pickled onion, etc. 		<ul style="list-style-type: none"> - (pasteurised) sauerkraut - Broad bean pod

Drinks and (after consultation with physician) alcoholic drinks

There are certain tea varieties available on the market, which have various "health claims" such as their beneficial use for blood pressure, metabolism, bowel movement, and for weight loss. As it is unknown what additives have been included in these 'healthy tea varieties', it is advised to not consume these products.

The creation of home-made Dutch liqueurs such as advocaat (also sold in country shops) and tokkelroom (kind of liqueur) are not allowed, as they contain raw eggs.

Heavy beers and sparkling wine (e.g. champagne/prosecco) contain higher levels of yeast and in turn, tyramine.

Drink no alcohol or at least no more than one glass each day*.

What you can drink	What you can drink in moderation	What you cannot drink
<ul style="list-style-type: none"> - (Soy) milk and buttermilk - (Fruit) tea and herbal tea, such as chamomile, cinnamon, mint, rooibos tea and green tea. - Winter blend tea - Water - Soft drinks - Sport drinks - Fruit juices - Coffee (with coffee milk) 	<ul style="list-style-type: none"> - Liquorice tea (maximal 0.5 L due to influence on blood pressure (glycyrrhizin acid)) - Good Night herb tea (Zonnatura). Max 1-2 cups 	<ul style="list-style-type: none"> - Unpasteurised milk - Other herbal teas such as; St John's Wort or tea varieties with health claims such as good for blood pressure, metabolism, bowel movement, etc.
<ul style="list-style-type: none"> - Alcohol free beer, alcohol free white beer and alcohol-free rosé beers 	<ul style="list-style-type: none"> - One glass of wine, port, sherry, advocaat <i>or</i> - One glass of a strong alcoholic drink <i>or</i> - One bottle of beer or radler - One glass of sparkling wine with a normal cork or screw cap (Frizzante) 	<ul style="list-style-type: none"> - Homemade advocaat or tokkelroom - Chianti wine - Champagne - Sparkling wine with a champagne cork iron wire (Spumante) - White or heavy beer - Belgium beer - Abbey beer - Beer with extra yeast - Draught beer

* Guidelines Goede Voeding Gezondheidsraad 2015

Desserts

If dairy products are made from pasteurised milk, are fresh and have been stored in a cool place, they will contain no tyramine.

Home-made tiramisu is a protein rich product. Compared to commercially produced tiramisu that has been manufactured in a chilled production facility, home-made tiramisu is made at room temperature.

What you can eat	What you can eat in moderation	What you cannot eat
(Soy) custard, (soy) yogurt, Skyr yogurt, biogarde, ice-cream, tiramisu ready-made, whipped cream	Commercially produced kefir (made with cow's milk); max. 150 ml	Home-made tiramisu Home-made kefir and kefir made with milk from either sheep or goats.

Yeast products

Yeast naturally contains a high content of tyramine. Therefore, any product that has additional yeast will also have high tyramine content. As the yeast content found in bread is transformed, you are allowed to consume bread.

“Reformproducten”(containing natural ingredients) may contain yeast, and it is advisable to read the packaging of these products. Yeast extract enhances the natural taste of food, and it allowed to be added in small quantities to soups and sauces.

What you can eat	What you can eat in moderation	What you cannot eat
Yeast for the preparation of: <ul style="list-style-type: none"> – Bread – Pie – Biscuits – Oliebollen (Dutch doughnuts) – Beschuiten – Pizza base 		Products which contain pure yeasts: <ul style="list-style-type: none"> – Marmite – Vegemite yeast extract paste – Vitamin R yeast extract Reform products which contain yeast: <ul style="list-style-type: none"> – Beer yeast – Bread drink
<ul style="list-style-type: none"> – Aromat flavourings – Yeast extract in soups and sauces in bags, tin or jar since they are containing a small amount of yeast extract 		Maggi flavouring

Single pan dishes, cooled dishes and going out for dinner

Pre-cooked meals from the fridge/freezer of the supermarkets are allowed (e.g. stews, nasi). During transport from the supermarket to your house, ensure that the pre-cooked meal remains below 10°C (it is recommended using a cooling bag during summer time). When you get home, place these meals directly into the fridge and consume each meal before the expiry date.

What you can eat	What you can in moderation	What you cannot eat
Single-pan dishes which contain no products from the column “ what you cannot eat ” and “ what you can eat in moderation ”, see above.		Single-pan dishes, pizza and cooled dishes which contain a lot of cheese (> 20 grams) or old or foreign cheeses or salami
		– Cheese fondue
		– Hamburgers and chicken/fish recipes and salad dishes which contains cheese

Other

Sports food such as protein shakes, generally contain a high concentration of amino acids (also the amino acids tryptophan and tyrosine). Tyramine can be formed through the conversion of tyrosine, and such protein shakes are not recommended.

What you can eat	What you can eat in moderation	What you cannot eat
Sandwich spread: <ul style="list-style-type: none"> – Peanut butter – Jam – Sprinkles (“hagelslag”) – Sandwich spread – Syrup 	<ul style="list-style-type: none"> – Sweet/salty liquorice; max. 50 grams. Due to its effects on blood pressure (glycyrrhizin acid) 	<ul style="list-style-type: none"> – Marmite – Vegemite yeast extract paste – Tartex
<ul style="list-style-type: none"> – Products with probiotics 		<ul style="list-style-type: none"> – Herbal preparations such as ginseng and St John’s Wort – Sour dough bread – Vitamin preparations with dosages higher than the accepted limits L-tryptophan* – Sport food products containing whey powder/ amino acids

		<ul style="list-style-type: none"> - Products containing turmeric, saffron
<ul style="list-style-type: none"> - Nuts and peanuts - Instant noodles in a cup or sachet (with herbs/vegetables/chicken) - Sport nutrition bars - Nougat - Marzipan - Bouillon tablets - Boemboe - Butter 		<ul style="list-style-type: none"> - Dampo bij droge hoest - Otrivin and comparable nose sprays which contain xylometazoline

*If you have a deficiency in certain vitamin(s), your physician or psychiatrist can prescribe a higher dosage. After any bariatric surgery or if you suffer from a resorption disorder, additional vitamins can be prescribed. If Vitamin D supplementation is required, depending on the dosage, it can be prescribed once per day, weekly or quarterly.

General advice

Regularly check the temperature of your refrigerator, by using a refrigerator thermometer. The measured temperature should not be above 7°C (preferred temperature is between 4 and 7°C).

By buying fresh products, keeping these in a cool place and consuming them quickly, the tyramine content in these products remains low.

An expiry date can be found on the bottle or container of all milk-containing products. It is important that you do not keep these products beyond this date. After opening any milk-based product, you may only use this product for a maximum of three days, even if the expiry date has not been reached. This advice also extends to coffee milk.

When you buy protein-based products from a shop that is constantly being replenished/re-stocked, the fresh protein-rich products will have a lower tyramine content.

Frozen meat, fish and chicken have to be thawed in a refrigerator or microwave and then directly prepared.

Eggs need to be stored in a cooled place (4-12 °C) and consumed before the printed expiry date.

Purchased pre-cooked meals that need to be stored, must be cooled down as soon as possible and placed in the refrigerator.

Prepared meat, fish, chicken and soup can be stored for up to 24 hours in the refrigerator.

After opening meat products, they can be stored in a refrigerator for a maximum of four days. Please take the expiry date into account.

Chocolate, shellfish, calamari and alcohol may cause a hypersensitivity reaction (e.g. a headache), which is not associated with the use of Tracydal[®]. If you notice any symptoms, then avoid these products.

If you are planning on going out for dinner, or if you have holiday plans to an exotic destination and wish to receive any additional food explanations and/or advice, you can contact the department Dietetics from the Parnassia group, via Daleco Pharma

If you notice severe or strange symptoms such as vomiting/nausea, severe headaches, a stiff neck or suffer from severe restlessness, please contact your treating physician immediately. These symptoms may be caused by an increased blood pressure.

When you visit a different physician or dentist, always inform them that you are taking Tracydal®.

Medications that were previously safe to take alone may have serious consequences when used in combination with MAO-inhibitors. Therefore, do not use any other medications than those that have been prescribed by your physician.

Some over-the-counter medications are dangerous to use in combination with MAO-inhibitors. Discuss the use of any over-the-counter medications with your physician.

If you stop using Tracydal®, you should continue to follow this dietary advice for another 14 days. This is because the (MAO) enzymatic activity only gradually returns to normal levels after treatment discontinuation. Therefore, the diet should be adhered to for an additional 14 days after stopping Tracydal use.

How do I keep the information up to date?

This dietary advice booklet will be updated on a regular basis.

To ensure that you always have the most up-to-date information, Daleco Pharma can inform you of any changes made to this booklet. If you would like to receive this information, please fill in the form below and post it to Daleco Pharma B.V., using an unstamped envelope.

Your details will be treated with the utmost confidentiality and will not be used for any commercial purposes!

.....Reply strip.....

Please keep me informed of any changes.

Name:.....Gender M/F

Address:

Postal code:.....

City:.....

Email:.....

The reply slip can be sent in an unstamped envelope to;

Daleco Pharma b.v.

Antwoordnummer: 13700

4157 ZX Enspijk

Regarding Tracydal® support

Blood pressure measurements

It is important to adhere to the dietary advice in this booklet while using Tracydal[®], as tyramine can increase in the body leading to an increase in your blood pressure.

Therefore, it is important to measure your blood pressure, especially during the start up phase of your treatment. You can use the results table inside this booklet to record your blood pressure measurements. You can also find these tables on www.dalecopharma.nl.

While taking Tracydal[®], you should measure your blood pressure twice per day, at and o' clock. Record your blood pressure measurement in the provided tables in this booklet every day. When visiting your physician, take this booklet with you, which contains your measured blood pressure results, so your physician can get an insight into your treatment.

A sudden rise in blood pressure can give the following symptoms: Headache, tinnitus, nausea and vision problems (seeing spots). You may also develop slight palpitations or a nosebleed.

If you develop these symptoms you need to check your blood pressure:

- If your blood pressure has not increased, or is only slightly higher than normal (systolic blood pressure to 140 mmHg and/or diastolic blood pressure to 95 mmHg), the symptoms are probably not blood pressure related. Measure your blood pressure again after an hour.
- If your blood pressure is increased more than normal (systolic blood pressure to 160 mmHg and diastolic blood pressure to 110 mmHg), but you have no other complaints, it is recommended to measure your blood pressure again after an hour.
- If your blood pressure remains elevated or if you develop other symptoms such as vomiting, chest pain/pressure, a stiff neck, pain between the shoulder blades, profuse sweating, shortness of breath, sudden restlessness and/or drowsiness, immediately go to the hospital's emergency room (ER).
- If your systolic blood pressure is above 180 mmHg and/or diastolic blood pressure above 100 mmHg, you are experiencing hypertensive crisis and immediate intervention is necessary. You will need to go the ER of a hospital, in order to lower your blood pressure. Do not drive to the hospital by

yourself. If there is nobody available to drive you to the hospital, call an ambulance (112) immediately.

You can get an infusion of phentolamine in the ER.

If you have no additional symptoms and your diastolic blood pressure has reduced to 120 - 140 mmHg, you will receive a 200mg capsule of labetalol (if you do not have asthma). An additional capsule may be administered after one hour if your blood pressure has not sufficiently reduced. You may also be provided with Nifedipine (Adalat).

If you have an accident which requires hospitalization, or if you have a planned surgery, it's important that the medical professionals who are treating you (paramedics, surgeons, physicians, etc.) know that you are using Tracydal®. This may affect the medications that can be prescribed by these medical professionals. This is also applicable for medication prescribed by dentists.

Therefore, always carry the patient card with you. On the patient card you can fill out your own personal details as well as the contact information of your regular physician. The hospital will be able to see that you are using Tracydal® and when necessary, they can contact your physician for more information.

As well as monitoring your blood pressure, it is important that you keep track of any side effects that may occur. You can do this with the help of the tables in this booklet. If you experience any side effects, discuss these with your physician. He/she will be able to determine if the side effects you have experienced stand alone or may be caused by other factors (e.g. other medication that you may be taking).

Additional information regarding Tracydal® (tranylcypromine) is available in the Summary of Product Characteristics (SmPC) and its associated package insert at www.cbg-meb.nl. The risk minimization materials are also available at www.dalecopharma.nl. This booklet and the patient card can be requested free of charge via Daleco Pharma BV: pvd@dada.nl, Tel +31(0)243030804.

Spontaneous reports remain important for the detection of side effects. In the Netherlands, you can report suspected side effects to the Netherlands Pharmacovigilance Centre Lareb, using the reporting form on their website (www.lareb.nl). Side effects can also be reported at any time to the marketing authorisation holder of this product; Daleco Pharma BV (pvd@dada.nl, Tel +31(0)243030804.

Dietary advice when using Tracydal® (tranylcypromine)
Daleco Pharma in cooperation with Parnassia group "The Hague"