

Instruction for BUPROPION TAPERINGSTRIP™

Please ensure you have the correct prescription and order form in front of you. There are several different order forms for Antidepressants (24), Anti-psychotics (23), Sedatives (19), Anti-epileptics (7), Hormones (1) & Analgetics (4).

PLEASE READ CAREFULLY BEFORE FILLING IN THE PRESCRIPTION AND ORDER FORM

1. A sudden termination of treatment with bupropion or a sudden reduction in dosage can lead to significant withdrawal symptoms. To avoid this, the daily dose should be reduced in small steps gradually over a period of time. This can be done using tapering strips™.
2. One or more tapering strips™ can be used to gradually reduce the dose of bupropion to a desired lower dose or to zero. If more than one strip is needed the final dose of the previous strip is always equal to the starting dose of the following strip.
3. The treating physician should plan the tapering schedule together with the patient. It is not possible to predict the perfect schedule for each patient. Some patients are far more sensitive to withdrawal symptoms than others, and some patients cope with symptoms better than others. The risk of withdrawal symptoms and their intensity can be reduced by choosing a more gradual tapering schedule. There are two options when choosing a tapering schedule:
 - 1) **Variable** - Choose a tapering schedule for the first 28 days only, then use the patient's experiences and feedback to inform the remainder of the tapering trajectory. To do this only the **black** part of table 4 on page 4 has to be filled in. The experiences of the patient during the first weeks (withdrawal symptoms or not) can then be used to choose the tapering trajectories for the following strip(s) by filling in in the **red** part of the table 5 on page 5.
 - 2) **Fixed** - Choose a tapering schedule for the entire period of the dosage reduction. To do this, fill in both the **black** and (if applicable) the **red** part of table 4 on page 4.
4. Bupropion tapering strips™ are only available on prescription. The signed prescription and order form is seen as a valid prescription. After filling in the form, the treating physician should terminate any current prescription for bupropion at the local pharmacy.
5. In most countries, the costs of the medication in the tapering strips™ are covered by health insurance. Tapering and stabilisation strips contain medication for a fixed period of 28 days, all strips have the same price. Tapering strip™: € 77.-; Stabilization strip € 38.50 for a period of 28 days; Prices are subject to change, so please check before ordering.
6. Once the prescription and order form has been received by the Regenboog Apotheek, the tapering strip™ will be shipped to the patient's home address (Europe, North America and Australia) within a week.
7. A tapering strip™ contains 28 numbered pouches, with each pouch containing several tablets. The number of pills may vary per day. The total dose of the medication reduces over time as the patient takes the pills in each daily pouch.
8. The patient starts their tapering schedule on a Sunday by taking the pills in the first pouch, numbered 028. **By counting down**, the patient finishes four weeks later on a Saturday, by taking the pills in the last pouch, numbered 001. By doing this, the patient can easily keep track of how many doses and days are left.
9. Each pouch of the strip is printed with the sequence number, the colour and strength of each tablet, the total number of tablets and the name of the pharmacy.
10. **STABILIZATION**: A stabilization strip can keep the patient on a fixed dose for a desired period of time. Such stabilization may be necessary if tapering appears to be going too fast for the patient, or the patient does not wish to reduce the dose to zero, but remain at an optimal lower dose. The stabilization strip can be produced at almost any desired dose rounded off to 5 mg bupropion.
11. In some cases, the patient is currently using a dose that is higher or different from the starting dose of the standard available tapering strips (see table 4 on page 4). These patients can also reduce their dose gradually by using **customized** tapering strips™ for the first part of the taper (see table 4 on page 4).

12. For bupropion, the following tapering strips™ are standard available:

Startdose bupropion	Enddose bupropion	Tapering period	Name of the strip	step dose reduction	average dose reduction	average dose reduction
300 mg/day	150 mg/day	28 days	BPRP 300-150/28days	5 / 10 mg	5,4 mg/day	12,5%/week
150 mg/day	75 mg/day	28 days	BPRP 150-75/28days	5 mg	2,7 mg/day	12,5%/week
150 mg/day	zero	28 days	BPRP 150-0/28days	5 / 10 mg	5,4 mg/day	25%/week
75 mg/day	25 mg/day	28 days	BPRP 75-25/28days	5 mg	1,8 mg/day	16,7%/week
75 mg/day	zero	28 days	BPRP 75-0/28days	5 mg	2,7 mg/day	25%/week
25 mg/day	zero	28 days	BPRP 25-0/28days	5 mg	0,9 mg/day	25%/week
stable	. . . mg/day	28 days	BPRP stable	0 mg	no reduction	0%/week

The table below shows how many mg of bupropion each daily pouch contains.

Schedule: bupropion		300 - 150	150 - 75	150 - 0	75 - 25	75 - 0	25 - 0
Sachet No	Intake day	mg	mg	mg	mg	mg	mg
sachet 28	sunday	300	150	150	75	75	25
sachet 27	monday	295	145	145	75	70	25
sachet 26	tuesday	290	145	140	70	70	25
sachet 25	wednesday	285	140	135	70	65	20
sachet 24	thursday	280	140	130	70	65	20
sachet 23	friday	270	135	125	65	60	20
sachet 22	saturday	265	135	120	65	60	20
sachet 21	sunday	260	130	115	60	55	20
sachet 20	monday	255	130	105	60	55	20
sachet 19	tuesday	250	125	100	60	50	15
sachet 18	wednesday	245	120	95	55	50	15
sachet 17	thursday	240	120	90	55	45	15
sachet 16	friday	235	115	85	55	45	15
sachet 15	saturday	230	115	80	50	40	15
sachet 14	sunday	220	110	75	50	40	15
sachet 13	monday	215	110	70	45	35	10
sachet 12	tuesday	210	105	65	45	30	10
sachet 11	wednesday	205	105	60	45	30	10
sachet 10	thursday	200	100	55	40	25	10
sachet 9	friday	195	95	50	40	25	10
sachet 8	saturday	190	95	45	40	20	5
sachet 7	sunday	185	90	40	35	20	5
sachet 6	monday	180	90	30	35	15	5
sachet 5	tuesday	170	85	25	30	15	5
sachet 4	wednesday	165	85	20	30	10	5
sachet 3	thursday	160	80	15	30	10	5
sachet 2	friday	155	80	10	25	5	5
sachet 1	saturday	150	75	5	25	5	5

IMPORTANT NOTICE: Tapering strips™ are not intended to replace medical care provided by a physician. Careful counselling and monitoring of the patient remains essential during and after treatment with tapering strips.

Please note: Treatment with the tapering strip™ supports the tapering of medication, reducing withdrawal effects to a minimum. If withdrawal effects do occur, they will be not as intensive or prolonged as during a traditional tapering approach. This will make it easier for the treating physician to recognize a relapse (**such as a** return of depression or anxiety) and to distinguish between relapse or withdrawal effects in good time.

There is a noticeable difference in timing between the occurrence of withdrawal symptoms and relapse. Withdrawal symptoms usually occur shortly or immediately after the start of tapering. Relapse usually occurs at a later stage, often after tapering with bupropion has been completed. While withdrawal symptoms become less severe and disappear over time, symptoms as a result of relapse tend to remain and may even get worse.

Should you have any questions or if you require more information, please contact Paul Harder, pharmacist at the Regenboog Apotheek at pharder@regenboogapotheek.nl or + 31-(0)6-25072020.

Instructions for the prescription and order form for tapering strips™

1. MEDICAL INDICATION: please, mark all the indications applicable to the patient:
 - i. **preventive** reducing the risk of withdrawal symptoms or relapse effects caused by diminishing the dose too quickly.
 - ii. **reduction anxiety** patient is excessively anxious about tapering, for example as a result of comorbid anxiety disorder.
 - iii. **failed attempt** previous attempts to stop or reduce the dose have failed.
 - iv. **distinction** distinguishing between withdrawal symptoms and possible relapse.
 - v. **slow metabolizer** the lowest dose causes a high plasma concentration, increasing the risk of withdrawal effects.
 - vi. **high dose** the patient has used the medication for a period of 6 months at a dose at least 150% of the defined daily dose.
2. Fill in the patient's details.
3. Fill in the details of the treating physician.
4. Fill in the table. Below you can see four examples showing the different ways of filling in the table:

- a. **Total reduction**, using **3** tapering strips™: mark **3** boxes
(schedule 3 x 28 days = 84 days)

starting dose EXAMPLE	taper duration	STRIP 1 28 days	STRIP 2 28 days	STRIP 3 28 days	STRIP 4 28 days
30 mg/day	112 days	<input type="checkbox"/> EXMPL 30-10	<input type="checkbox"/> EXMPL 10-5	<input type="checkbox"/> EXMPL 5-2	<input type="checkbox"/> EXMPL 2-0
	84 days	<input checked="" type="checkbox"/> EXMPL 30-10	<input checked="" type="checkbox"/> EXMPL 10-5	<input checked="" type="checkbox"/> EXMPL 5-0	
	56 days	<input type="checkbox"/> EXMPL 30-10	<input type="checkbox"/> EXMPL 10-0		

- b. **Dose reduction** using **2** tapering strips™: mark **2** boxes
(schedule 2 x 28 days = 56 days)

starting dose EXAMPLE	taper duration	STRIP 1 28 days	STRIP 2 28 days	STRIP 3 28 days	STRIP 4 28 days
30 mg/day	112 days	<input type="checkbox"/> EXMPL 30-10	<input type="checkbox"/> EXMPL 10-5	<input type="checkbox"/> EXMPL 5-2	<input type="checkbox"/> EXMPL 2-0
	84 days	<input checked="" type="checkbox"/> EXMPL 30-10	<input checked="" type="checkbox"/> EXMPL 10-5	<input type="checkbox"/> EXMPL 5-0	
	56 days	<input type="checkbox"/> EXMPL 30-10	<input type="checkbox"/> EXMPL 10-0		

- c. **Customized schedule** please mark each box, and fill in the desired start and end dose for each strip.
Total duration = number of strips x 28 days.

CUSTOMIZED	2 x 28 days	<input checked="" type="checkbox"/> EXMPL	from 60 - 30 mg	<input checked="" type="checkbox"/> EXMPL	from 30 - 10 mg
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- d. **Stabilization** to a steady dose: mark the box, and fill in daily dose and number of repeats
(in this example: 17 mg/day and 2x repeats=> schedule (1 + 2) x 28 days = 84 days)

STABILIZATION	28 days	<input checked="" type="checkbox"/> EXMPL stab.	17 mg/day	2 repeats
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5. Sign the prescription.
6. Fax the prescription to the Regenboog Apotheek: **+31-(0)85-2736129**

NOTE: Please only fax the order and prescription form.

Do not fax the instruction sheets.

Order and prescription form

R/ Prescription = order form for BUPROPION tapering strips™ ZI-number: 16413822

- 1a.** Medical indication: preventive reduction anxiety failed attempt distinction slow metabolizer high dose
1b. Duration of bupropion use: <1 year 1-2 years 2-5 years 5-10 years >10 years

2. Full name of patient:

Date of birth: . . . - . . . - gender: M / F

Address:

.....

City, postal code and country:

E-mail address: Telephone no:

3. Name of treating physician:

Medical registration number:

Address:

Postal code and country:

E-mail address:

Telephone no:

4. Please, fill in the table, following the instructions above.

Startdose BUPROPION	Tapering period	STRIP 1 28 days	STRIP 2 28 days	STRIP 3 28 days	STRIP 4 28 days	STRIP 5 28 days
450 mg/day	140 days	<input type="checkbox"/> BPRP 450-300	<input type="checkbox"/> BPRP 300-150	<input type="checkbox"/> BPRP 150-100	<input type="checkbox"/> BPRP 100-50	<input type="checkbox"/> BPRP50-0
	112 days	<input type="checkbox"/> BPRP 450-300	<input type="checkbox"/> BPRP 300-150	<input type="checkbox"/> BPRP 150-50	<input type="checkbox"/> BPRP 50-0	
	84 days	<input type="checkbox"/> BPRP 450-300	<input type="checkbox"/> BPRP 300-150	<input type="checkbox"/> BPRP 150-0		
300 mg/day	112 days	<input type="checkbox"/> BPRP 300-150	<input type="checkbox"/> BPRP 150-100	<input type="checkbox"/> BPRP 100-50	<input type="checkbox"/> BPRP 50-0	
	84 days	<input type="checkbox"/> BPRP 300-150	<input type="checkbox"/> BPRP 150-50	<input type="checkbox"/> BPRP 50-0		
	56 days	<input type="checkbox"/> BPRP 300-150	<input type="checkbox"/> BPRP 150-0			
150 mg/day	84 days	<input type="checkbox"/> BPRP 150-100	<input type="checkbox"/> BPRP 100-50	<input type="checkbox"/> BPRP 50-0		
	56 days	<input type="checkbox"/> BPRP 150-50	<input type="checkbox"/> BPRP 50-0			
	28 days	<input type="checkbox"/> BPRP 150-0				
100 mg/day	56 days	<input type="checkbox"/> BPRP 100-50	<input type="checkbox"/> BPRP 50-0			
	28 days	<input type="checkbox"/> BPRP 100-0				
50 mg/day	28 days	<input type="checkbox"/> BPRP 50-0				
customized	. X 28 days	<input type="checkbox"/> BPRP	<input type="checkbox"/> BPRP	<input type="checkbox"/> BPRP	<input type="checkbox"/> BPRP	<input type="checkbox"/> BPRP
set-up	1 X . . days	<input type="checkbox"/> BPRP				
stable	28 days	<input type="checkbox"/> BPRP stable	. . . mg/day	. . repeats	dose round off to 10 mg	please send immediately

COSTS Tapering and stabilisation strips contain medication for a fixed period of 28 days, all strips have the same price. Tapering strip™: € 77.-; Stabilization strip € 38.50 for a period of 28 days; Prices are subject to change.

5. Date: Stamp of treating physician

Signature of treating physician:

Shipping address: Regenboog Apotheek, Antwoordnummer 16500, 4840 WJ BAVEL, The Netherlands

Order and prescription form

R/ Prescription = order form for BUPROPION tapering strips™ ZI-number: 16413822

1. Continuation Tapering

2. Full name of patient:

Date of birth: . . . - . . . - gender: M / F

Address:

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City, postal code and country:

E-mail address: Telephone no:

3. Name of treating physician:

Medical registration number:

Address:

Postal code and country:

E-mail address:

Telephone no:

5. Please, fill in the table, following the instructions above.

Startdose BUPROPION	Tapering period	STRIP 1 28 days	STRIP 2 28 days	STRIP 3 28 days	STRIP 4 28 days	STRIP 5 28 days
450 mg/day	140 days	<input type="checkbox"/> BPRP 450-300	<input type="checkbox"/> BPRP 300-150	<input type="checkbox"/> BPRP 150-100	<input type="checkbox"/> BPRP 100-50	<input type="checkbox"/> BPRP 50-0
	112 days	<input type="checkbox"/> BPRP 450-300	<input type="checkbox"/> BPRP 300-150	<input type="checkbox"/> BPRP 150-50	<input type="checkbox"/> BPRP 50-0	
	84 days	<input type="checkbox"/> BPRP 450-300	<input type="checkbox"/> BPRP 300-150	<input type="checkbox"/> BPRP 150-0		
300 mg/day	112 days	<input type="checkbox"/> BPRP 300-150	<input type="checkbox"/> BPRP 150-100	<input type="checkbox"/> BPRP 100-50	<input type="checkbox"/> BPRP 50-0	
	84 days	<input type="checkbox"/> BPRP 300-150	<input type="checkbox"/> BPRP 150-50	<input type="checkbox"/> BPRP 50-0		
	56 days	<input type="checkbox"/> BPRP 300-150	<input type="checkbox"/> BPRP 150-0			
150 mg/day	84 days	<input type="checkbox"/> BPRP 150-100	<input type="checkbox"/> BPRP 100-50	<input type="checkbox"/> BPRP 50-0		
	56 days	<input type="checkbox"/> BPRP 150-50	<input type="checkbox"/> BPRP 50-0			
	28 days	<input type="checkbox"/> BPRP 150-0				
100 mg/day	56 days	<input type="checkbox"/> BPRP 100-50	<input type="checkbox"/> BPRP 50-0			
	28 days	<input type="checkbox"/> BPRP 100-0				
50 mg/day	28 days	<input type="checkbox"/> BPRP 50-0				
customized	. X 28 days	<input type="checkbox"/> BPRP	<input type="checkbox"/> BPRP	<input type="checkbox"/> BPRP	<input type="checkbox"/> BPRP	<input type="checkbox"/> BPRP
set-up	1 X . . days	<input type="checkbox"/> BPRP				
stable	28 days	<input type="checkbox"/> BPRP stable	. . . mg/day	. . repeats	dose round off to 10 mg	please send immediately

COSTS Tapering and stabilisation strips contain medication for a fixed period of 28 days, all strips have the same price.
Tapering strip™: € 77.-; Stabilization strip € 38.50 for a period of 28 days; Prices are subject to change.

6. Date: Stamp of treating physician

Signature of treating physician:

Shipping address: Regenboog Apotheek, Antwoordnummer 16500, 4840 WJ BAVEL, The Netherlands

SUMMARY, 24 May 2018

Antidepressant tapering strips to help people come off medication more safely

Peter Groot and Jim van Os

Antidepressant users who have come to the end of treatment and wish to stop can suffer withdrawal symptoms, even when following their doctor's advice. In some cases, these withdrawal symptoms can be so severe that they prevent the user from stopping their medication. This can often be problematic for the patient and can result in unnecessary prescriptions, additional cost for health services and potential long-term health issues.

An observational study published in the journal *Psychosis* shows that antidepressant withdrawal symptoms can be minimised or avoided by using prepackaged medication in tapering strips. Tapering medication makes safe withdrawal possible by utilising pills of small dosages to make much smaller dosage reductions than can be achieved using standard registered dosages. This approach makes tapering easy for the antidepressant user and the doctor. The study shows that more patients are successful using tapering strips when compared to those who had tried to reduce using other methods and allows patients who have previously tried and failed to withdraw the opportunity to succeed in coming off their antidepressant medication.

What is tapering medication?

Tapering medication is prepackaged in tapering strips which make it easy for the patient to reduce without needing to follow complicated instructions. Furthermore the strips make it easy for doctors to prescribe personalised tapering schedules for their patients. A tapering strip consists of 28 sachets on a roll, with each sachet providing the medication for a single day. The daily dosage in each sachet is a little less or equal to that of the previous day. A doctor, psychiatrist or therapist can prescribe tapering schedules tailored to and in consultation with the patient in a shared decision-making approach. Using currently available standard registered dosages, gradual tapering is often difficult and, in some cases, impossible to achieve. Due to these limitations, current tapering guidelines are also difficult to follow for both the prescriber and the patient.

About the study

The study reviewed 1121 questionnaires completed by patients who wanted to withdraw from their antidepressant medications. The majority (75%, $n = 895$) wanted to taper off completely. Of these, 62% ($n = 692$) had previously made one or more tapering attempts. Almost everyone (97%) had suffered withdrawal symptoms during these earlier attempts, which were rated as very severe by 49% (7 on a scale of 1-7). The duration of antidepressant use varied from less than a year to more than 30 years (median: 2-5 years).

A comparison of withdrawal with or without tapering medication

All patients were asked about their tapering experience, using a scale from 1-7, where 1 = very good and 7 = very bad. In addition, they were asked if they had experienced withdrawal symptoms on a 1-7 scale, where 1 = not at all and 7 = very much. Patients were also asked to rate their previous attempts to withdraw, therefore making a comparison possible between tapering medication and other methods.

Study findings

The main results of the study are that, of the 895 people who used tapering strips to taper the antidepressant they used:

- 71% ($n = 636$) succeeded in a median time of 56 days (2 tapering strips).

- 21% (n = 192) did not complete the taper, 8% (n = 67) because they were still tapering, 4% (n = 39) due to withdrawal symptoms and 6% (n = 53) due to relapse (defined as the recurrence of complaints such as anxiety or depression).

The results of this study show that, for patients who had previously tried and failed to withdraw, the use of tapering medication in tapering strips could enable them to withdraw successfully.

Tapering medication enables shared decision making

For patients who wish to withdraw, attempting to taper using standard registered doses increases the risk of withdrawal symptoms, leading to an increased risk of withdrawal failure and unnecessary long-term antidepressant use. Allowing patients and doctors to work together to define personalised tapering schedules has been shown to reduce withdrawal symptoms and increase the chances of success. By doing this, doctors can focus on patient recovery and more easily distinguish between withdrawal symptoms and relapse, which is important in avoiding the unnecessary prescribing of antidepressant medications.

Applying tapering principles to other medications

The results of this study are relevant for people using other psychotropic medications such as antipsychotics or benzodiazepines. This is important for people with psychosis who will often be taking multiple medications. The use of tapering medication in tapering strips offers the opportunity to make safe, gradual dosage adjustments while minimising unpleasant withdrawal symptoms even in those patients who are taking multiple medications. The use of tapering strips enables a level of flexibility and personalisation that is simply not achievable using conventional standard registered dosages.

Information about taperingstrips can be found on the User Research Center of Maastricht University website www.taperingstrip.org

Dr. Peter C. Groot is a researcher and expert by experience at the User Research Center of Maastricht University and volunteer at the Cinderella Therapeutics Foundation. Prof. Jim van Os is Chairman of the Brain Division at the Utrecht University Medical Center.

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