SUMMARY OF PRODUCT CHARACTERISTICS FOR LEVODOPA-CONTAINING PRODUCTS (INCL. COMBINATION PRODUCTS):

Impulse control disorders

Patients should be regularly monitored for the development of impulse control disorders. Patients and carers should be made aware that behavioural symptoms of impulse control disorders including pathological gambling, increased libido, hypersexuality, compulsive spending or buying, binge eating and compulsive eating have been reported can occur in patients treated with dopamine agonists and/or other dopaminergic treatments containing levodopa including [insert brand name] for Parkinson’s disease. Review of treatment is recommended if such symptoms develop.

Section 4.8

Impulse control disorders

Patients treated with dopamine agonists and/or levodopa for treatment of Parkinson’s disease, especially at high doses, have been reported as exhibiting signs of pathological gambling, increased libido, hypersexuality, compulsive spending or buying, binge eating and compulsive eating can occur in patients treated with dopamine agonists and/or other dopaminergic treatments containing levodopa including [insert brand name], generally reversible upon reduction of the dose or treatment discontinuation (see section 4.4. ‘Special warnings and precautions for use’)

SUMMARY OF PRODUCT CHARACTERISTICS FOR DOPAMINE AGONIST PRODUCTS

Section 4.4

Impulse control disorders

Patients should be regularly monitored for the development of impulse control disorders. Patients and carers should be made aware that behavioural symptoms of impulse control disorders including pathological gambling, increased libido, hypersexuality, compulsive spending or buying, binge eating and compulsive eating have been reported can occur in patients treated with dopamine agonists including [insert brand name] for Parkinson’s disease. Dose reduction/tapered discontinuation should be considered if such symptoms develop.
Section 4.8
Impulse control disorders
Patients treated with dopamine agonists and/or levodopa for treatment of Parkinson’s disease, especially at high doses, have been reported as exhibiting signs of Pathological gambling, increased libido, hypersexuality, compulsive spending or buying, binge eating and compulsive eating can occur in patients treated with dopamine agonists including [insert brand name], generally reversible upon reduction of the dose or treatment discontinuation (see section 4.4. ‘Special warnings and precautions for use’).

SUMMARY OF PRODUCT CHARACTERISTICS FOR SINGLE CONSTITUENT COMT INHIBITOR PRODUCTS – TOLCAPONE / ENTACAPONE

There is currently no consistent class wording in the SPCs for these products, so just the proposed wording is shown.

Section 4.4
Impulse control disorders
Patients should be regularly monitored for the development of impulse control disorders. Patients and carers should be made aware that behavioural symptoms of impulse control disorders including pathological gambling, increased libido, hypersexuality, compulsive spending or buying, binge eating and compulsive eating can occur in patients treated with dopamine agonists and/or other dopaminergic treatments such as [insert brand name of COMT inhibitor] in association with levodopa. Review of treatment is recommended if such symptoms develop.

Section 4.8
Impulse control disorders
Pathological gambling, increased libido, hypersexuality, compulsive spending or buying, binge eating and compulsive eating can occur in patients treated with dopamine agonists and/or other dopaminergic treatments such as [insert COMT inhibitor brand name] in association with levodopa. (see section 4.4 ‘Special warnings and precautions for use’).

PACKAGE LEAFLET FOR LEVODOPA-CONTAINING PRODUCTS

There is currently no consistent or class wording in the SPCs for levodopa product PILs, so just the proposed wording is shown below. These are identical to that proposed for dopamine agonists, except for the decision over treatment, in line with the proposed SPC changes.

Section 2 BEFORE YOU TAKE ….

Take special care with…

Tell your doctor if you or your family/carer notices you are developing urges or cravings to behave in ways that are unusual for you or you cannot resist the impulse, drive or temptation to carry out certain activities that could harm yourself or others. These behaviours are called
impulse control disorders and can include addictive gambling, excessive eating or spending, an abnormally high sex drive or an increase in sexual thoughts or feelings. Your doctor may need to review your treatments.

4. POSSIBLE SIDE EFFECTS

You may experience the following side effects:

- inability to resist the impulse to perform an action that could be harmful, which may include:
  - Strong impulse to gamble excessively despite serious personal or family consequences.
  - Altered or increased sexual interest and behaviour of significant concern to you or to others, for example, an increased sexual drive.
  - Uncontrollable excessive shopping or spending
  - Binge eating (eating large amounts of food in a short time period) or compulsive eating (eating more food than normal and more than is needed to satisfy your hunger)

Tell your doctor if you experience any of these behaviors; they will discuss ways of managing or reducing the symptoms.

PACKAGE LEAFLET FOR DOPAMINE AGONIST PRODUCTS

There is currently no consistent or class wording in the SPCs for dopamine agonist product PILs, so just the proposed wording is shown below.

Section 2 BEFORE YOU TAKE ….

Take special care with…
Tell your doctor if you or your family/carer notices that you are developing urges or cravings to behave in ways that are unusual for you and you cannot resist the impulse, drive or temptation to carry out certain activities that could harm yourself or others. These are called impulse control disorders and can include behaviours such as addictive gambling, excessive eating or spending, an abnormally high sex drive or an increase in sexual thoughts or feelings. Your doctor may need to adjust or stop your dose.

4. POSSIBLE SIDE EFFECTS

You may experience the following side effects:

- inability to resist the impulse, drive or temptation to perform an action that could be harmful to you or others, which may include:
  - Strong impulse to gamble excessively despite serious personal or family consequences.
Altered or increased sexual interest and behaviour of significant concern to you or to others, for example, an increased sexual drive.

Uncontrollable excessive shopping or spending

Binge eating (eating large amounts of food in a short time period) or compulsive eating (eating more food than normal and more than is needed to satisfy your hunger)

Tell your doctor if you experience any of these behaviors; they will discuss ways of managing or reducing the symptoms

PACKAGE LEAFLET FOR SINGLE CONSTITUENT COMT INHIBITOR PRODUCTS

There is currently no consistent or class wording in the SPCs for single constituent COMT inhibitor products, just the proposed wording is shown below.

Section 2 BEFORE YOU TAKE ….

Take special care with…
Tell your doctor if you or your family/carer notices you are developing urges or cravings to behave in ways that are unusual for you or you cannot resist the impulse, drive or temptation to carry out certain activities that could harm yourself or others. These behaviours are called impulse control disorders and can include addictive gambling, excessive eating or spending, an abnormally high sex drive or an increase in sexual thoughts or feelings. Your doctor may need to review your treatments.

4. POSSIBLE SIDE EFFECTS

You may experience the following side effects:

- inability to resist the impulse to perform an action that could be harmful, which may include:
  - Strong impulse to gamble excessively despite serious personal or family consequences.
  - Altered or increased sexual interest and behaviour of significant concern to you or to others, for example, an increased sexual drive.
  - Uncontrollable excessive shopping or spending
  - Binge eating (eating large amounts of food in a short time period) or compulsive eating (eating more food than normal and more than is needed to satisfy your hunger)

Tell your doctor if you experience any of these behaviors; they will discuss ways of managing or reducing the symptoms
SUMMARY OF PRODUCT CHARACTERISTICS FOR LEVODOPA-CONTAINING PRODUCTS (INCL. COMBINATION PRODUCTS)

Rubriek 4.4 – Bijzondere waarschuwingen en voorzorgen bij gebruik

Stoornissen in de impulsbeheersing

Patiënten dienen regelmatig gecontroleerd te worden op het ontstaan van stoornissen in de impulsbeheersing. Patiënten en verzorgers dienen erop geattendeerd te worden dat in het gedrag van patiënten die behandeld worden met dopamine-agonisten en/of andere dopaminergie producten die levodopa bevatten, waaronder [productnaam], symptomen van een stoornis in de impulsbeheersing kunnen optreden, waaronder pathologisch gokken, verhoogd libido, hypersonsualiteit, compulsief geld uitgeven of koopgedrag, eetbuien en compulsief eetgedrag. Als dergelijke symptomen zich ontwikkelen wordt aanbevolen de behandeling te heroverwegen.

Rubriek 4.8 - Bijwerkingen

Stoornissen in de impulsbeheersing

Pathologisch gokken, verhoogd libido, hyperseksualiteit, compulsief geld uitgeven of koopgedrag, eetbuien en compulsief eetgedrag kan optreden bij patiënten die behandeld worden met dopamine-agonisten en/of andere dopaminergie producten die levodopa bevatten, waaronder [productnaam] (zie rubriek 4.4).

SUMMARY OF PRODUCT CHARACTERISTICS FOR DOPAMINE AGONIST PRODUCTS

Rubriek 4.4 – Bijzondere waarschuwingen en voorzorgen bij gebruik

Stoornissen in de impulsbeheersing

Patiënten dienen regelmatig gecontroleerd te worden op het ontstaan van stoornissen in de impulsbeheersing. Patiënten en verzorgers dienen erop geattendeerd te worden dat in het gedrag van patiënten die behandeld worden met dopamine-agonisten, waaronder [productnaam], symptomen van een stoornis in de impulsbeheersing kunnen optreden, waaronder pathologisch gokken, verhoogd libido, hypersonsualiteit, compulsief geld uitgeven of koopgedrag, eetbuien en compulsief eetgedrag. Als dergelijke symptomen zich ontwikkelen dient dosisreductie/geleidelijk stoppen van de behandeling te worden overwogen.

Rubriek 4.8 - Bijwerkingen

Stoornissen in de impulsbeheersing

Pathologisch gokken, verhoogd libido, hyperseksualiteit, compulsief geld uitgeven of koopgedrag, eetbuien en compulsief eetgedrag kan optreden bij patiënten die behandeld worden met dopamine-agonisten, waaronder [productnaam] (zie rubriek 4.4).
SUMMARY OF PRODUCT CHARACTERISTICS FOR SINGLE CONSTITUENT COMT INHIBITOR PRODUCTS – TOLCAPONE / ENTACAPONE

Rubriek 4.4 – Bijzondere waarschuwingen en voorzorgen bij gebruik

Stoornissen in de impulsbeheersing
Patiënten dienen regelmatig gecontroleerd te worden op het ontstaan van stoornissen in de impulsbeheersing. Patiënten en verzorgers dienen erop geattendeerd te worden dat in het gedrag van patiënten die behandeld worden met dopamine-agonisten en/of andere dopaminerge behandelingen, zoals [productnaam] in combinatie met levodopa, symptomen van een stoornis in de impulsbeheersing kunnen optreden, waaronder pathologisch gokken, verhoogd libido, hyperseksualiteit, compulsief geld uitgeven of kooipgedrag, eetbuien en compulsief eetgedrag. Als dergelijke symptomen zich ontwikkelen wordt aanbevolen de behandeling te heroverwegen.

Rubriek 4.8 - Bijwerkingen

Stoornissen in de impulsbeheersing
Pathologisch gokken, verhoogd libido, hyperseksualiteit, compulsief geld uitgeven of kooipgedrag, eetbuien en compulsief eetgedrag kan optreden bij patiënten die behandeld worden met dopamine-agonisten en/of andere dopaminerge behandelingen, zoals [productnaam] in combinatie met levodopa (zie rubriek 4.4).

PACKAGE LEAFLET FOR LEVODOPA-CONTAINING PRODUCTS

Rubriek 2 - Wanneer mag u dit middel niet gebruiken of moet u er extra voorzichtig mee zijn?

Wanneer moet u extra voorzichtig zijn met dit middel?
Vertel het uw arts wanneer u of uw familie/verzorger merkt dat u de neiging of het verlangen ontwikkelt om gedrag te vertonen dat niet bij u past of wanneer u de impuls, aandrang of verleiding niet kunt weerstaan om dingen te doen die uzelf of anderen schade kunnen berokkenen. Dergelijk gedrag wordt een stoornis in de impulsbeheersing genoemd en kan bestaan uit onder andere gokverslaving, overmatig eten of geld uitgeven, een abnormaal grote behoefte aan seks of een toename van seksuele gedachten of gevoelens. Het kan nodig zijn dat uw arts uw behandeling opnieuw beoordeelt.

Rubriek 4 - Mogelijke bijwerkingen

U kunt last krijgen van de volgende bijwerkingen:

- Niet instaat zijn om de impuls te onderdrukken om iets te doen wat schadelijk kan zijn, bijvoorbeeld:
  - een sterke impuls om veel te gokken, ondanks de ernstige gevolgen die dit voor u of uw familie heeft
  - een veranderde of toegenomen seksuele interesse of gedrag waar u of anderen zich erg bezorgd om maken, bijvoorbeeld een toegenomen behoefte aan seks
  - een onbedwingbare behoefte om veel te kopen of uit te geven
  - eetbuien (het eten van grote hoeveelheden voedsel in korte tijd) of dwangmatig eten (meer dan normaal eten en meer dan nodig is om uw honger te stillen).
Vertel het uw arts als u merkt dat u dergelijk gedrag vertoont. Hij/zij zal met u overleggen hoe deze verschijnselen behandeld of verminderd kunnen worden.

PACKAGE LEAFLET FOR DOPAMINE AGONIST PRODUCTS

Rubriek 2 - Wanneer mag u dit middel niet gebruiken of moet u er extra voorzichtig mee zijn?

Wanneer moet u extra voorzichtig zijn met dit middel?

Vertel het uw arts wanneer u of uw familie/verzorger merkt dat u de neiging of het verlangen ontwikkelt om gedrag te vertonen dat niet bij u past of wanneer u de impuls, aandrang of verleiding niet kunt weerstaan om dingen te doen die uzelf of anderen schade kunnen berokkenen. Dergelijk gedrag wordt een stoornis in de impulsbeheersing genoemd en kan bestaan uit onder andere gokverslaving, overmatig eten of geld uitgeven, een abnormaal grote behoefte aan seks of een toename van seksuele gedachten of gevoelens. Het kan nodig zijn dat uw arts uw dosering aanpast of de behandeling stopt.

Rubriek 4 - Mogelijke bijwerkingen

U kunt last krijgen van de volgende bijwerkingen:

- Niet instaat zijn om de impuls te onderdrukken om iets te doen wat schadelijk kan zijn, bijvoorbeeld:
  - een sterke impuls om veel te gokken, ondanks de ernstige gevolgen die dit voor u of uw familie heeft
  - een veranderde of toegenomen seksuele interesse of gedrag waar u of anderen zich erg bezorgd om maken, bijvoorbeeld een toegenomen behoefte aan seks
  - een onbedwingbare behoefte om veel te kopen of uit te geven
  - eetbuien (het eten van grote hoeveelheden voedsel in korte tijd) of dwangmatig eten (meer dan normaal eten en meer dan nodig is om uw honger te stillen).

Vertel het uw arts als u merkt dat u dergelijk gedrag vertoont. Hij/zij zal met u overleggen hoe deze verschijnselen behandeld of verminderd kunnen worden.

PACKAGE LEAFLET FOR SINGLE CONSTITUENT COMT INHIBITOR PRODUCTS

Rubriek 2 - Wanneer mag u dit middel niet gebruiken of moet u er extra voorzichtig mee zijn?

Wanneer moet u extra voorzichtig zijn met dit middel?

Vertel het uw arts wanneer u of uw familie/verzorger merkt dat u de neiging of het verlangen ontwikkelt om gedrag te vertonen dat niet bij u past of wanneer u de impuls, aandrang of verleiding niet kunt weerstaan om dingen te doen die uzelf of anderen schade kunnen berokkenen. Dergelijk gedrag wordt een stoornis in de impulsbeheersing genoemd en kan bestaan uit onder andere gokverslaving, overmatig eten of geld uitgeven, een abnormaal grote behoefte aan seks of een toename van seksuele gedachten of gevoelens. Het kan nodig zijn dat uw arts uw behandeling opnieuw beoordeelt.
Rubriek 4 - Mogelijke bijwerkingen

U kunt last krijgen van de volgende bijwerkingen:

- Niet instaat zijn om de impuls te onderdrukken om iets te doen wat schadelijk kan zijn, bijvoorbeeld:
  - een sterke impuls om veel te gokken, ondanks de ernstige gevolgen die dit voor u of uw familie heeft
  - een veranderde of toegenomen seksuele interesse of gedrag waar u of anderen zich erg bezorgd om maken, bijvoorbeeld een toegenomen behoefte aan seks
  - een onbedwingbare behoefte om veel te kopen of uit te geven
  - eetbuien (het eten van grote hoeveelheden voedsel in korte tijd) of dwangmatig eten (meer dan normaal eten en meer dan nodig is om uw honger te stillen).

Vertel het uw arts als u merkt dat u dergelijk gedrag vertoont. Hij/zij zal met u overleggen hoe deze verschijnselen behandeld of verminderd kunnen worden.
Annex 2

Summary Assessment Report of the PhVWP July 2012

Levodopa, dopamine agonists and COMT inhibitors – Risk of impulse control disorders

Key message

Behavioural symptoms of impulse control disorders (ICDs) may occur in patients taking levodopa and/or dopamine agonists at normal doses, irrespective of the indication. Patients should be regularly monitored for ICD symptoms, which include pathological gambling, hypersexuality, increased libido, compulsive buying or spending and compulsive or binge eating.

Safety concern and reason for current safety review

Accumulating data on the risk of impulse control disorders (ICDs) in association with levodopa- and/or dopamine agonist-containing medicinal products have become available. Some of the ICDs described are not currently included in the product information for these products, and also the data suggest that ICDs may occur in indications for these products other than Parkinson’s disease. The PhVWP therefore agreed to review these data to ensure the product information reflects the latest available evidence.

Clinical setting

Levodopa and dopamine agonists have been available since the 1970s as forms of dopamine replacement therapy in Parkinson’s disease (PD), a disease which is caused by loss of nerve cells in certain part of the brain leading to a reduction in the amount of the neurotransmitter dopamine in the brain. Some medicinal products containing levodopa or a dopamine agonist are authorised for indications other than PD.

Levodopa is used alone or in combination with various metabolic inhibitors, including catechol-O-methyltransferase (COMT) inhibitors. COMT is an enzyme degrading dopamine in the body.

The active substances included in the review were levodopa, the dopamine agonists apomorphine, bromocriptine, cabergoline, lisuride, pergolide, piribedil, pramipexole, quinagolide, ropinirole and rotigotine and the COMT inhibitors benserazide, carbidopa, entacapone and tolcapone.

Information on the data assessed

Data from spontaneous reporting schemes, published case reports and studies on the risk of ICDs with levodopa and dopamine agonists, especially data on ICDs currently not included in the product information and on the risk of ICDs in non-PD indications, were assessed [1-41].

Outcome of the assessment

The PhVWP considered that the updated review of the more recent spontaneous reporting data, published case reports and studies [1-41] showed that a range of behavioural symptoms of ICDs may occur in patients taking levodopa and/or dopamine agonists, at normal doses, irrespective of the indication. Reported symptoms included pathological gambling, hypersexuality and increased libido, which are already included in the product information for most products containing levodopa or a
dopamine agonist. The symptoms also included compulsive buying or spending and compulsive or binge eating, which are currently not included in the product information for most products.

The PhVWP concluded to recommend that the summaries of product characteristics (SmPCs) and package leaflets (PLs) should be updated as follows:

for levodopa-containing medicinal products authorised in the EU (single substance and combination products including those containing COMT inhibitors) to include:

in SmPC section 4.4, that:
- patients should be regularly monitored for the development of impulse control disorders; patients and carers should be made aware that behavioural symptoms of impulse control disorders including pathological gambling, increased libido, hypersexuality, compulsive spending or buying, binge eating and compulsive eating can occur in patients treated with dopamine agonists and/or other dopaminergic treatments containing levodopa; review of treatment is recommended if such symptoms develop;

in SmPC section 4.8:
- impulse control disorders: pathological gambling, increased libido, hypersexuality, compulsive spending or buying, binge eating and compulsive eating can occur in patients treated with dopamine agonists and/or other dopaminergic treatments containing levodopa (see SmPC section 4.4);

in PL section 2, that:
- one should tell the physician if the patient, family member or the carer notices that the patient is developing urges or cravings to behave in ways that are unusual for the patient or the patient cannot resist the impulse, drive or temptation to carry out certain activities that could harm the person or others; these behaviours are called impulse control disorders and can include addictive gambling, excessive eating or spending, an abnormally high sex drive or an increase in sexual thoughts or feelings; the physician may need to review the treatments;

in PL section 4, that:
- the patient may experience the following side effects: inability to resist the impulse to perform an action that could be harmful, which may include: strong impulse to gamble excessively despite serious personal or family consequences, altered or increased sexual interest and behaviour of significant concern to you or to others, for example, an increased sexual drive, uncontrollable excessive shopping or spending, binge eating (eating large amounts of food in a short time period) or compulsive eating (eating more food than normal and more than is needed to satisfy your hunger), and to tell the physician if any of these behaviors are experienced; the physician will discuss ways of managing or reducing the symptoms;

for apomorphine, bromocriptine, cabergoline, lisuride, pergolide, piribedil, pramipexole, quinagolide, ropinirole or rotigotine-containing medicinal products authorised in the EU to include:

in SmPC section 4.4, that:
- patients should be regularly monitored for the development of impulse control disorders; patients and carers should be made aware that behavioural symptoms of impulse control disorders including pathological gambling, increased libido, hypersexuality, compulsive spending or buying, binge eating and compulsive eating can occur in patients treated with dopamine agonists; dose reduction/tapered discontinuation should be considered if such symptoms develop;

in SmPC section 4.8:
- impulse control disorders: pathological gambling, increased libido, hypersexuality, compulsive spending or buying, binge eating and compulsive eating can occur in patients treated with dopamine agonists (see SmPC section 4.4);
in PL section 2, that:
- one should tell the physician if the patient, family member or the carer notices that the patient is developing urges or cravings to behave in ways that are unusual for the patient or the patient cannot resist the impulse, drive or temptation to carry out certain activities that could harm the person or others; these behaviours are called impulse control disorders and can include addictive gambling, excessive eating or spending, an abnormally high sex drive or an increase in sexual thoughts or feelings; the physician may need to adjust or stop the dose;

in PL section 4, that:
- the patient may experience the following side effects: inability to resist the impulse to perform an action that could be harmful, which may include: strong impulse to gamble excessively despite serious personal or family consequences, altered or increased sexual interest and behaviour of significant concern to you or to others, for example, an increased sexual drive, uncontrollable excessive shopping or spending, binge eating (eating large amounts of food in a short time period) or compulsive eating (eating more food than normal and more than is needed to satisfy your hunger), and to tell the physician if any of these behaviors are experienced; the physician will discuss ways of managing or reducing the symptoms;

for entacapone or tolcapone-containing medicinal products authorised in the EU (COMT inhibitor single substance products, but use only recommended together with levodopa) to include:

in SmPC section 4.4, that:
- patients should be regularly monitored for the development of impulse control disorders; patients and carers should be made aware that behavioural symptoms of impulse control disorders including pathological gambling, increased libido, hypersexuality, compulsive spending or buying, binge eating and compulsive eating can occur in patients treated with dopamine agonists and/or other dopaminergic treatments in association with levodopa; review of treatment is recommended if such symptoms develop;

in SmPC section 4.8:
- impulse control disorders: pathological gambling, increased libido, hypersexuality, compulsive spending or buying, binge eating and compulsive eating can occur in patients treated with dopamine agonists and/or other dopaminergic treatments in association with levodopa (see SmPC section 4.4);

in PL section 2, that:
- one should tell the physician if the patient, family member or the carer notices that the patient is developing urges or cravings to behave in ways that are unusual for the patient or the patient cannot resist the impulse, drive or temptation to carry out certain activities that could harm the person or others; these behaviours are called impulse control disorders and can include addictive gambling, excessive eating or spending, an abnormally high sex drive or an increase in sexual thoughts or feelings; the physician may need to review the treatments;

in PL section 4, that:
- the patient may experience the following side effects: inability to resist the impulse to perform an action that could be harmful, which may include: strong impulse to gamble excessively despite serious personal or family consequences, altered or increased sexual interest and behaviour of significant concern to you or to others, for example, an increased sexual drive, uncontrollable excessive shopping or spending, binge eating (eating large amounts of food in a short time period) or compulsive eating (eating more food than normal and more than is needed to satisfy your hunger), and to tell the physician if any of these behaviors are experienced; the physician will discuss ways of managing or reducing the symptoms.

References


Registratiehouder
(t.a.v. registratieafdeling)

Your letter Your reference Utrecht,-- --.. Case number Our reference ../.. Case manager Telephone number

Subject
Request for change in the product information following the PhVWP/CMDh decision

Levodopa, dopamine agonist and COMT inhibitors – Risk of impulse control disorders

Following assessment of the available data assessed by the PhVWP on Levodopa, dopamine agonist and COMT inhibitor products and the risk of impulse control disorders (ICDs), all Marketing Authorisation (MA) holders for products with Apomorphine, Bromocriptine, Cabergoline, Entacapone, Levodopa, Lisuride, Pergolide, Piribedil, Pramipexole, Quinagolide, Ropinirole, Rotigotine, or Tolcapone as active ingredient are being requested to submit type IB variations (variation number C1.3.a) (or equivalent national procedures – see below) for their relevant products to implement the PhVWP/CMD(h) decision.

Link to the website with the published decision: http://www.hma.eu/222.html

You are requested to change the SmPC and Package Leaflet (PL) of

\(<product> \quad <RVC>\)

The agreed texts, together with the translation in Dutch, are attached to this letter.

These texts should be included literally in the SmPC and PL. However, you are requested to check the SmPC and PL carefully to make sure that there is no overlap with the current texts. If there is such overlap, you should replace the current text with wording from the agreed texts.

With regard to PL wording, further user testing by individual MA holders will not be expected on this occasion.

For products registered via an MRP or DCP procedure, the RMS takes responsibility on behalf of the CMSs to request the variation from the MA holder and initiate the procedure.

The applications do not require supporting information or expert statements and will be accepted by Member States Competent Authorities without further assessment or amendment.

If there is no reason to update your product information via a type IB variation, you are requested to reply to this letter with a statement that the product information does not need to be changed.

How to submit this variation in the Netherlands
The MEB has pre-assigned you the following case number for this variation: <XXXXX>. You are requested to send your application data package and future correspondence to the case@cbg-meb.nl e-mail address.

Please mention the following information.

‘Subject’ field of the e-mail:
  - Case <XXXXX>
  - Name of the medicinal product and RVG number or Procedure number (if NL=RMS)

Message body:
  - Case <XXXXX>
  - Implementation of the PhVWP/CMD(h) decision by request of the MEB.

Attachments:
  - Completed application form
  - Checked guideline regarding the variation
  - Product information (SmPC, PL and/or labeling, if applicable) affected with this variation (tracked and clean in a Word format).

If the product was registered via MRP/DCP with NL = RMS, you are also asked to include a dispatch list with the submission dates in the CMSs. Please, be informed that you have to submit in such case, both the English texts and the national translations.

**Timetable for implementation**
You should submit variations no later than 14 November 2012.

On behalf of the Medicines Evaluation Board
in the Netherlands,

Drs. A.H.P. van Gompel

*This notification has been produced centrally in an automated process and consequently does not bear a signature.*

Attachments:
Annex 1: Agreed texts (UK and Dutch versions)
Annex 2: Summary assessment report