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Questions and answers on the review of medicines containing methylphenidate

The European Medicines Agency (EMA) has completed a review of the safety of medicines containing methylphenidate. The Agency's Committee for Medicinal Products for Human Use (CHMP) has concluded that the benefits of these medicines continue to outweigh their risks when used to treat children aged six years and above and adolescents with attention deficit/hyperactivity disorder (ADHD). However, the Committee has concluded that the prescribing information for these medicines should be made consistent, in order to maximise their safe use across the European Union (EU). The review was carried out under an 'Article 31' referral¹.

What is methylphenidate?

Methylphenidate is a medicine that is used to treat children aged six years and over and adolescents who have ADHD. It belongs to a group of medicines called 'psychostimulants'. Methylphenidate has been available since the 1950s, and has become widely used for ADHD since the 1990s. It is available in all EU Member States as various trade names including Ritalin, Concerta, Equasym, Medikinet and Rubifen. It is available as 'immediate-release' tablets and capsules that release methylphenidate straight away, and as 'modified-release' tablets that work over a few hours.

What is ADHD?

ADHD is a condition in which children show a persistent inability to concentrate, hyperactivity and impulsive behaviour, and which can lead to psychological, emotional, social and educational problems.

Methylphenidate-containing medicines can be used to treat ADHD as part of a comprehensive treatment programme that includes psychological, educational and social interventions. These interventions may be focussed on the child, parents or teachers, and range from giving information and advice, to formal psychotherapy. Methylphenidate should only be prescribed under the supervision of a specialist in childhood behavioural disorders when other methods have not been successful in changing behaviour.

In ADHD, methylphenidate is thought to increase the levels of the neurotransmitters noradrenaline and dopamine in the spaces between nerve cells in some areas of the brain, enhancing activity in areas of the brain that control attention, the ability to focus, concentration and impulsive behaviours.

Why were methylphenidate-containing medicines reviewed?

Over the past few years, concerns have been raised over the safety of methylphenidate, particularly over the possible risk of cardiovascular disorders (problems affecting the heart and blood vessels) and cerebrovascular disorders (problems affecting the blood vessels in the brain). Consequently, the European Commission asked the CHMP to carry out a full assessment of the benefit-risk balance of methylphenidate-containing medicines and to issue an opinion on whether the marketing authorisations for medicines containing methylphenidate should be maintained, varied, suspended or withdrawn across the EU.

¹ Article 31 of Directive 2001/83/EC as amended, referral under Community interest.

Which data has the CHMP reviewed?

The CHMP has reviewed all of the available information on the safety of methylphenidate-containing medicines. This information came from studies carried out in experimental models and in humans, as well as information on side effects reported by doctors and patients since the medicines have been available on the market. The Committee also considered guidelines on the treatment of ADHD and on the screening and monitoring of patients before and during treatment.

The review focussed on cardiovascular safety (including increased blood pressure and heart rate, and disruption of the heart rhythm) and cerebrovascular safety (including stroke and migraine). In addition, the review looked at whether there is any evidence for a link between methylphenidate and psychiatric (mental) problems, reduced growth and sexual maturation. It also looked at information on the long-term effects of treatment.

What are the conclusions of the CHMP?

The Committee concluded that there was no need for an urgent restriction to the use of methylphenidate-containing medicines and that the benefits of methylphenidate-containing medicines continue to outweigh their risks, when they are used in their approved indication for children aged six years or over and adolescents with ADHD, as part of comprehensive treatment programmes. However, it concluded that new recommendations on prescribing the medicines and on pre-treatment screening and ongoing monitoring of patients are needed to maximise the safe use of these medicines.

Because the information provided to doctors on the safety of methylphenidate is not consistent across the EU, the Committee concluded that the product information of all methylphenidate-containing medicines authorised in the Member States should contain the following information:

- before treatment, all patients should be screened to see if they have any problems with their blood pressure or heart rate. The family history of cardiovascular problems should also be checked. Any patients with these problems should not be treated without specialist evaluation;
- during treatment, blood pressure and heart rate should be monitored regularly. Any problems that develop should be investigated promptly;
- there is a lack of information on the long-term effects of methylphenidate. For patients who take methylphenidate for more than a year, doctors should interrupt treatment at least once a year to determine whether continued treatment with methylphenidate is necessary;
- the use of methylphenidate could cause or worsen some psychiatric disorders such as depression, suicidal thoughts, hostility, psychosis and mania. All patients should be carefully screened for these disorders before treatment and monitored regularly for psychiatric symptoms during treatment;
- the height and weight of patients treated with methylphenidate should be monitored during treatment.

The CHMP also recommended that ‘risk management plans’ be put in place to monitor the safety of methylphenidate-containing medicines and minimise any possible long-term risks of their use. The plans should include educational materials for doctors who will prescribe methylphenidate. The Committee also recommended that information from ongoing studies into the medicine’s safety should be evaluated as soon as it becomes available, and that further studies should be carried out on the long-term effects of methylphenidate.

The full changes to be made to the prescribing information are given [here](#).

What are the recommendations for patients and prescribers?

- Methylphenidate-containing medicines remain suitable for the treatment of children aged six years or over and adolescents with ADHD as part of comprehensive treatment programmes.
- These medicines should only be prescribed and used in accordance with the updated prescribing information.
- Patients, parents or guardians who have any questions should speak to their doctor or pharmacist.

ANEXO I
RELACIÓN DE LOS NOMBRES DEL MEDICAMENTO, FORMA FARMACÉUTICA, DOSIS,
VÍA DE ADMINISTRACIÓN Y TITULAR DE LA AUTORIZACIÓN DE
COMERCIALIZACIÓN EN LOS ESTADOS MIEMBROS

Autorización de comercialización para los medicamentos que contienen METILFENIDATO

Estado miembro (UE/EEE)	Titular de la autorización de comercialización	Denominación de fantasía	Dosis	Forma farmacéutica	Vía de administración
AT - Austria	Janssen-Cilag Pharma GmbH Pfarrgasse 75 A-1232 Wien	Concerta 18 mg Retardtabletten	18 mg	Comprimido de liberación prolongada	Vía oral
AT - Austria	Janssen-Cilag Pharma GmbH Pfarrgasse 75 A-1232 Wien	Concerta 36 mg Retardtabletten	36 mg	Comprimido de liberación prolongada	Vía oral
AT - Austria	Janssen-Cilag Pharma GmbH Pfarrgasse 75 A-1232 Wien	Concerta 54 mg Retardtabletten	54 mg	Comprimido de liberación prolongada	Vía oral
AT - Austria	Janssen-Cilag Pharma GmbH Pfarrgasse 75 A-1232 Wien	Concerta 27 mg Retardtabletten	27 mg	Comprimido de liberación prolongada	Vía oral
BE - Bélgica	JANSSEN CILAG N.V. Roderveldlaan, 1 B-2600 BERCHEM	CONCERTA 18 MG	18 mg	Comprimido de liberación prolongada	Vía oral
BE - Bélgica	JANSSEN CILAG N.V. Roderveldlaan, 1 B-2600 BERCHEM	CONCERTA 36 MG	36 mg	Comprimido de liberación prolongada	Vía oral
BE - Bélgica	JANSSEN CILAG N.V. Roderveldlaan, 1 B-2600 BERCHEM	CONCERTA 54 MG	54 mg	Comprimido de liberación prolongada	Vía oral
BE - Bélgica	JANSSEN CILAG N.V. Roderveldlaan, 1 B-2600 BERCHEM	CONCERTA 27 MG	27 mg	Comprimido de liberación prolongada	Vía oral
BG Bulgaria:	Johnson & Johnson D.O.O. Smartinska 53, 1000 Ljubljana, Slovenia	Concerta	36 mg	Comprimido de liberación prolongada	Vía oral
BG Bulgaria:	Johnson & Johnson D.O.O. Smartinska 53, 1000 Ljubljana, Slovenia	Concerta	18 mg	Comprimido de liberación prolongada	Vía oral
BG Bulgaria:	Johnson & Johnson D.O.O. Smartinska 53, 1000 Ljubljana, Slovenia	Concerta	54 mg	Comprimido de liberación prolongada	Vía oral

CY – Chipre	Janssen-Cilag International N.V. Turnhoutseweg 30 B-2340 Beerse Belgium	Concerta	18 mg	Comprimido de liberación prolongada	Vía oral
CY – Chipre	Janssen-Cilag International N.V. Turnhoutseweg 30 B-2340 Beerse Belgium	Concerta	36 mg	Comprimido de liberación prolongada	Vía oral
CY – Chipre	Janssen-Cilag International N.V. Turnhoutseweg 30 B-2340 Beerse Belgium	Concerta	54 mg	Comprimido de liberación prolongada	Vía oral
CS – República Checa	Janssen-Cilag s.r.o., Karla Engliš 3201/6, 150 00 Praha 5 – Smíchov, Czech Republic	CONCERTA 18 mg	18 mg	Comprimido de liberación prolongada	Vía oral
CS – República Checa	Janssen-Cilag s.r.o., Karla Engliš 3201/6, 150 00 Praha 5 – Smíchov, Czech Republic	CONCERTA 36 mg	36 mg	Comprimido de liberación prolongada	Vía oral
CS – República Checa	Janssen-Cilag s.r.o., Karla Engliš 3201/6, 150 00 Praha 5 – Smíchov, Czech Republic	CONCERTA 54 mg	54 mg	Comprimido de liberación prolongada	Vía oral
DK - Dinamarca	Janssen-Cilag A/S Hammerbakken 19 DK-3460 Birkerød Denmark	CONCERTA	18 mg	Comprimido de liberación prolongada	Vía oral
DK - Dinamarca	Janssen-Cilag A/S Hammerbakken 19 DK-3460 Birkerød Denmark	CONCERTA	36 mg	Comprimido de liberación prolongada	Vía oral
DK - Dinamarca	Janssen-Cilag A/S Hammerbakken 19 DK-3460 Birkerød Denmark	CONCERTA	54 mg	Comprimido de liberación prolongada	Vía oral
ES - España	JANSSEN CILAG, SA Paseo de las doce estrellas, 5-7 Madrid 28042	CONCERTA 27 mg comprimidos de liberación prolongada	27 mg	Comprimido de liberación prolongada	Vía oral

ES - España	JANSSEN CILAG, SA Paseo de las doce estrellas, 5-7 Madrid 28042	CONCERTA 36 mg comprimidos de liberación prolongada	36 mg	Comprimido de liberación prolongada	Vía oral
ES - España	JANSSEN CILAG, SA Paseo de las doce estrellas, 5-7 Madrid 28042	CONCERTA 54 mg comprimidos de liberación prolongada	54 mg	Comprimido de liberación prolongada	Vía oral
ES - España	JANSSEN CILAG, SA Paseo de las doce estrellas, 5-7 Madrid 28042	CONCERTA 18 mg comprimidos de liberación prolongada	18 mg	Comprimido de liberación prolongada	Vía oral
ET – Estonia	Johnson & Johnson UAB, Geležinio Vilko g. 18A, LT-08104 Vilnius, Lithuania.	CONCERTA	18 mg	Comprimido de liberación prolongada	Vía oral
ET – Estonia	Johnson & Johnson UAB, Geležinio Vilko g. 18A, LT-08104 Vilnius, Lithuania.	CONCERTA	36 mg	Comprimido de liberación prolongada	Vía oral
ET – Estonia	Johnson & Johnson UAB, Geležinio Vilko g. 18A, LT-08104 Vilnius, Lithuania.	CONCERTA	54 mg	Comprimido de liberación prolongada	Vía oral
FI - Finlandia	Janssen-Cilag Oy Metsänneidonkuja 8 02130 Espoo FINLAND	Concerta	18 mg	Comprimido de liberación prolongada	Vía oral
FI - Finlandia	Janssen-Cilag Oy Metsänneidonkuja 8 02130 Espoo FINLAND	Concerta	27 mg	Comprimido de liberación prolongada	Vía oral
FI - Finlandia	Janssen-Cilag Oy Metsänneidonkuja 8 02130 Espoo FINLAND	Concerta	36 mg	Comprimido de liberación prolongada	Vía oral
FI - Finlandia	Janssen-Cilag Oy Metsänneidonkuja 8 02130 Espoo FINLAND	Concerta	54 mg	Comprimido de liberación prolongada	Vía oral
FR - Francia:	JANSSEN CILAG S.A. 1 rue Camille Desmoulins TSA 91003 92787 Issy-les-Moulineaux Cedex 9 France	CONCERTA LP	18mg	Comprimido de liberación prolongada	Vía oral

FR - Francia:	JANSSEN CILAG S.A. 1 rue Camille Desmoulins TSA 91003 92787 Issy-les-Moulineaux Cedex 9 France	CONCERTA LP	27mg	Comprimido de liberación prolongada	Vía oral
FR - Francia:	JANSSEN CILAG S.A. 1 rue Camille Desmoulins TSA 91003 92787 Issy-les-Moulineaux Cedex 9 France	CONCERTA LP	36mg	Comprimido de liberación prolongada	Vía oral
FR - Francia:	JANSSEN CILAG S.A. 1 rue Camille Desmoulins TSA 91003 92787 Issy-les-Moulineaux Cedex 9 France	CONCERTA LP	54mg	Comprimido de liberación prolongada	Vía oral
IE - Irlanda	Janssen-Cilag Ltd, Saunderton, High Wycombe HP14 4HJ, Buckinghamshire, England.	Concerta XL	18mg. 27mg 36mg, 54mg	Comprimido de liberación prolongada	Vía oral
LV – Letonia	UAB Johnson & Johnson, Geležinio Vilko g. 18A, LT-08104 Vilnius, Lithuania.	CONCERTA	18 mg	Comprimido de liberación prolongada	Vía oral
LV – Letonia	UAB Johnson & Johnson, Geležinio Vilko g. 18A, LT-08104 Vilnius, Lithuania.	CONCERTA	36 mg	Comprimido de liberación prolongada	Vía oral
LV – Letonia	UAB Johnson & Johnson, Geležinio Vilko g. 18A, LT-08104 Vilnius, Lithuania.	CONCERTA	54 mg	Comprimido de liberación prolongada	Vía oral
LT – Lituania	UAB „Johnson & Johnson“, Geležinio Vilko g. 18A, LT-08104 Vilnius, Lithuania.	CONCERTA	18 mg	Comprimido de liberación prolongada	Vía oral

LT – Lituania	UAB „Johnson & Johnson“, Geležinio Vilko g. 18A, LT-08104 Vilnius, Lithuania.	CONCERTA	36 mg	Comprimido de liberación prolongada	Vía oral
LT – Lituania	UAB „Johnson & Johnson“, Geležinio Vilko g. 18A, LT-08104 Vilnius, Lithuania.	CONCERTA	54 mg	Comprimido de liberación prolongada	Vía oral
PT - Portugal	Janssen-Cilag Farmacêutica, Lda. - Estrada Consiglieri Pedroso, 69 A - Queluz de Baixo - 2734-503 Barcarena	Concerta	18 mg	Comprimido de liberación prolongada	Vía oral
PT - Portugal	Janssen-Cilag Farmacêutica, Lda. - Estrada Consiglieri Pedroso, 69 A - Queluz de Baixo - 2734-503 Barcarena	Concerta	36 mg	Comprimido de liberación prolongada	Vía oral
PT - Portugal	Janssen-Cilag Farmacêutica, Lda. - Estrada Consiglieri Pedroso, 69 A - Queluz de Baixo - 2734-503 Barcarena	Concerta	54 mg	Comprimido de liberación prolongada	Vía oral
RO Rumanía	Janssen-Pharmaceutica N.V. Tumhoutseweg 30 2340 Beerse Belgium	Concerta 18 mg	18 mg	Comprimidos recubiertos con película de liberación prolongada	Vía oral
RO Rumanía	Janssen-Pharmaceutica N.V. Tumhoutseweg 30 2340 Beerse Belgium	Concerta 36 mg	36 mg	Comprimidos recubiertos con película de liberación prolongada	Vía oral
RO Rumanía	Janssen-Pharmaceutica N.V. Tumhoutseweg 30 2340 Beerse Belgium	Concerta 54 mg	54 mg	Comprimidos recubiertos con película de liberación prolongada	Vía oral
SE – Suecia	Janssen-Cilag AB Box 7073 SE-192 07 Sollentuna Sweden	Concerta	18, 27 36, 54 mg	Comprimido de liberación prolongada	Vía oral
UK – Reino Unido	JANSSEN-CILAG LIMITED, SAUNDERTON, HIGH WYCOMBE, BUCKINGHAMSHIRE, HP14 4HJ, UNITED KINGDOM	CONCERTA® XL	18MG	COMPRIMIDO DE LIBERACIÓN PROLONGADA	Vía oral

UK – Reino Unido	JANSSEN-CILAG LIMITED, SAUNDERTON, HIGH WYCOMBE, BUCKINGHAMSHIRE, HP14 4HJ, UNITED KINGDOM	CONCERTA® XL	36MG	COMPRIMIDO DE LIBERACIÓN PROLONGADA	Vía oral
UK – Reino Unido	JANSSEN-CILAG LIMITED, SAUNDERTON, HIGH WYCOMBE, BUCKINGHAMSHIRE, HP14 4HJ, UNITED KINGDOM	CONCERTA® XL	54MG	COMPRIMIDO DE LIBERACIÓN PROLONGADA	Vía oral
UK – Reino Unido	JANSSEN-CILAG LIMITED, SAUNDERTON, HIGH WYCOMBE, BUCKINGHAMSHIRE, HP14 4HJ, UNITED KINGDOM	CONCERTA® XL	27MG	COMPRIMIDO DE LIBERACIÓN PROLONGADA	Vía oral
IS	Janssen-Cilag AB c/o Vistor hf., Hörgatún 2, 212 Garðabær, Iceland.	Concerta	54 mg	Comprimido de liberación prolongada	Vía oral
IS	Janssen-Cilag AB c/o Vistor hf., Hörgatún 2, 212 Garðabær, Iceland.	Concerta	27 mg	Comprimido de liberación prolongada	Vía oral
IS	Janssen-Cilag AB c/o Vistor hf., Hörgatún 2, 212 Garðabær, Iceland.	Concerta	36 mg	Comprimido de liberación prolongada	Vía oral
IS	Janssen-Cilag AB c/o Vistor hf., Hörgatún 2, 212 Garðabær, Iceland.	Concerta	18 mg	Comprimido de liberación prolongada	Vía oral
DE - Alemania	Janssen-Cilag GmbH 41457 Neuss or Janssen Cilag GmbH Raiffeisenstr.8 41470 Neuss, Germany	CONCERTA 18 mg Retardtabletten	18. mg	Comprimido de liberación prolongada	Vía oral
DE - Alemania	Janssen-Cilag GmbH 41457 Neuss or Janssen Cilag GmbH Raiffeisenstr.8 41470 Neuss, Germany	CONCERTA 27 mg Retardtabletten	27. mg	Comprimido de liberación prolongada	Vía oral
DE - Alemania	Janssen-Cilag GmbH 41457 Neuss or Janssen Cilag GmbH Raiffeisenstr.8 41470 Neuss, Germany	CONCERTA 36 mg Retardtabletten	36. mg	Comprimido de liberación prolongada	Vía oral
DE - Alemania	Janssen-Cilag GmbH 41457 Neuss or Janssen Cilag GmbH Raiffeisenstr.8 41470 Neuss, Germany	CONCERTA 54 mg Retardtabletten	54. mg	Comprimido de liberación prolongada	Vía oral

EL - Grecia	JANSSEN-CILAG PHARMACEUTICAL S.A.C.I EIRINIS AVENUE 56, PEFKI, 15121 Tel: +30-210-6140061 Fax: +30-210-6140072	CONCERTA®	18 MG 36 MG 54 MG	COMPRIMIDO DE LIBERACIÓN PROLONGADA	Vía oral
MT - Malta	Janssen-Cilag International N.V. Turnhoutseweg 30 B-2340 Beerse Belgium	Concerta®	18 mg	Comprimido de liberación prolongada	Vía oral
MT - Malta	Janssen-Cilag International N.V. Turnhoutseweg 30 B-2340 Beerse Belgium	Concerta®	36 mg	Comprimido de liberación prolongada	Vía oral
MT - Malta	Janssen-Cilag International N.V. Turnhoutseweg 30 B-2340 Beerse Belgium	Concerta®	54 mg	Comprimido de liberación prolongada	Vía oral
NL – Países Bajos	Janssen-Cilag B.V.; Dr. Paul Janssenweg 150 ; 5026 RH TILBURG/NL	Concerta 18 mg	18 mg	Comprimidos de liberación prolongada	Vía oral
NL – Países Bajos	Janssen-Cilag B.V.; Dr. Paul Janssenweg 150 ; 5026 RH TILBURG/NL	Concerta 27 mg	27 mg	Comprimidos de liberación prolongada	Vía oral
NL – Países Bajos	Janssen-Cilag B.V.; Dr. Paul Janssenweg 150 ; 5026 RH TILBURG/NL	Concerta 36 mg	36 mg	Comprimidos de liberación prolongada	Vía oral
NL – Países Bajos	Janssen-Cilag B.V.; Dr. Paul Janssenweg 150 ; 5026 RH TILBURG/NL	Concerta 54 mg	54 mg	Comprimidos de liberación prolongada	Vía oral
NO - Noruega	Janssen-Cilag AS Hoffsveien 1D 0275 Oslo, Norway	Concerta	18mg 27mg 36 mg 54 mg	Comprimido de liberación prolongada	Vía oral

PL - Polonia	Janssen-Cilag International N.V. Turnhoutseweg 30 B-2340 Beerse Belgium	Concerta®	18 mg	Comprimido de liberación prolongada	Vía oral
PL - Polonia	Janssen-Cilag International N.V. Turnhoutseweg 30 B-2340 Beerse Belgium	Concerta®	36 mg	Comprimido de liberación prolongada	Vía oral
PL - Polonia	Janssen-Cilag International N.V. Turnhoutseweg 30 B-2340 Beerse Belgium	Concerta®	54 mg	Comprimido de liberación prolongada	Vía oral
LU - Luxemburgo	Janssen Cilag N.V./S.A Roderveldlaan 1, B- 2600 Berchem	Concerta	18 mg	Comprimidos de liberación prolongada	Vía oral
LU - Luxemburgo	Janssen Cilag N.V./S.A Roderveldlaan 1, B- 2600 Berchem	Concerta	27 mg	Comprimidos de liberación prolongada	Vía oral
LU - Luxemburgo	Janssen Cilag N.V./S.A Roderveldlaan 1, B- 2600 Berchem	Concerta	36 mg	Comprimidos de liberación prolongada	Vía oral
LU - Luxemburgo	Janssen Cilag N.V./S.A Roderveldlaan 1, B- 2600 Berchem	Concerta	54 mg	Comprimidos de liberación prolongada	Vía oral
SI	Johnson & Johnson d.o.o. Smartinska 53, 1000 Ljubljana, Slovenia	Concerta 18 mg tablete s podaljšanim sproščanjem	18 mg	Comprimidos de liberación prolongada	Vía oral
SI	Johnson & Johnson d.o.o. Smartinska 53, 1000 Ljubljana, Slovenia	Concerta 36 mg tablete s podaljšanim sproščanjem	36 mg	Comprimidos de liberación prolongada	Vía oral
SI	Johnson & Johnson d.o.o. Smartinska 53, 1000 Ljubljana, Slovenia	Concerta 54 mg tablete s podaljšanim sproščanjem	54 mg	Comprimidos de liberación prolongada	Vía oral