European Medicines Agency

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EUROPEAN MEDICINES AGENCY DECISION

of 13 April 2009

on the review of a class waiver on condition(s) in accordance with Regulation (EC) No 1901/2006 of the European Parliament and of the Council as amended

(ONLY THE ENGLISH TEXT IS AUTHENTIC)

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THE EUROPEAN MEDICINES AGENCY,

Having regard to the Treaty establishing the European Community,

Having regard to Regulation (EC) No 1901/2006 of the European Parliament and of the Council of 12 December 2006 on medicinal products for paediatric use as amended and amending Regulation (EEC) No. 1768/92, Directive 2001/20/EC, Directive 2001/83/EC and Regulation (EC) No 726/2004[1],

Having regard to Regulation (EC) No 726/2004 of the European Parliament and of the Council of 31 March 2004 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency[2],

Having regard to the decisions of the European Medicines Agency, adopted on 3 December 2007, 21 April 2008, and 14 July 2008 (P/1/2007, P/17/2008, P/47/2008)

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued of its own motion on 3 April 2009 in accordance with Article 14 of Regulation (EC) No 1901/2006 as amended,

Having regard to Article 25 of Regulation (EC) No 1901/2006 as amended,

WHEREAS:

(1) The Paediatric Committee of the European Medicines Agency has given, a positive opinion of its own motion for a review of a class waiver on condition(s),

(2) It is therefore appropriate to adopt a Decision reviewing a class waiver on condition(s).

[1] OJ L 378, 27.12.2006, p.1
[2] OJ L 136, 30.4.2004, p. 1

HAS ADOPTED THIS DECISION:

Article 1

A review of a class waiver on condition(s), the details of which are set out in the Opinion of the Paediatric Committee of the European Medicines Agency annexed hereto, together with its appendices, is hereby agreed.

Article 2

This decision is applicable to all natural and legal persons intending to market a product falling within the scope of Article 1 of this Decision. .

Article 3

The decisions P/1/2007, P/17/2008, P/47/2008 of the European Medicines Agency respectively adopted on 3 December 2007, 21 April 2008, and 14 July 2008, are hereby repealed.

Done at London, 13 April 2009

For the European Medicines Agency
Thomas Lönngren
Executive Director

(Signature on file)

European Medicines Agency
Pre-authorisation Evaluation of Medicines for Human Use

Doc. Ref. EMEA/212945/2009

OPINION OF THE PAEDIATRIC COMMITTEE ON A CLASS WAIVER ON CONDITION(S) PURSUANT TO ARTICLE 12 AND ON THE REVIEW OF WAIVERS PURSUANT TO ARTICLE 14 OF REGULATION 1901/2006 AS AMENDED

Scope of the waiver

Condition(s): See Annex I

Opinion

1. The Paediatric Committee, having reviewed pursuant to Article 14 of Regulation (EC) No 1901/2006, as amended, the class waiver granted by the decision issued on 14 July 2008, and in particular the waiver granted in all subsets of the paediatric population for the medicinal products intended for the treatment of menopausal and other perimenopausal disorders, recommends as set out in Annex I:

- to revoke the waiver for medicinal products intended for the "Treatment of menopausal and other peri-menopausal disorders";
- to grant a waiver for medicinal products intended for the "Treatment of climacteric symptoms associated with decreased oestrogen levels, as occurring at menopause".

The Icelandic and the Norwegian Paediatric Committee members agree with the above-mentioned recommendation of the Paediatric Committee.

2. The grounds for the granting of a waiver are set out in the Annex II.

This opinion together with its revised Annex I and Annex II is forwarded to the Executive Director of the Agency.

London, 3 April 2009

On behalf of the PDCO
Dr Daniel Brasseur, Chairman

(Signature on file)

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ANNEX I

LIST OF CONDITIONS WAIVED AND WAIVERS REVOKED

LIST OF CONDITIONS WAIVED

- Treatment of oropharyngeal epithelial carcinoma (excluding nasopharyngeal carcinoma)
- Treatment of lung carcinoma (small cell and non-small cell carcinoma)
- Treatment of basal cell carcinoma
- Treatment of breast carcinoma
- Treatment of ovarian carcinoma (excluding rhabdomyosarcoma and germ cell tumours)
- Treatment of endometrial carcinoma
- Treatment of prostate carcinoma (excluding rhabdomyosarcoma)
- Treatment of hairy cell leukaemia
- Treatment of multiple myeloma
- Treatment of Alzheimer's Disease
- Treatment of vascular dementia and vascular cognitive disorder/impairment
- Treatment of organic amnesic syndrome (excluding amnesic syndrome caused by alcohol and other psychoactive substances)
- Treatment of amyotrophic lateral sclerosis
- Treatment of Parkinson's Disease (non-juvenile)
- Treatment of age-related macular degeneration
- Climacteric symptoms associated with decreased oestrogen levels, as occurring at menopause*
- Treatment of Chronic Obstructive Pulmonary Disease (COPD) (excluding chronic lung diseases associated with long-term airflow limitation, such as asthma, bronchopulmonary dysplasia, primary cilia dyskinesia, obstructive lung disease related to graft-versus-host disease after (bone-marrow) transplantation).
- Treatment of adenocarcinoma of the pancreas
- Treatment of gastric carcinoids
- Treatment of adenocarcinoma of the colon and rectum
- Treatment of bladder carcinoma
- Treatment of liver and intrahepatic bile duct carcinoma (excluding hepatoblastoma)

* See list of waivers revoked

- Treatment of kidney and renal pelvis carcinoma (excluding nephroblastoma, nephroblastomatosis, clear cell sarcoma, mesoblastic nephroma, renal medullary carcinoma and rhabdoid tumour of the kidney)
- Treatment of melanoma (from 0 to less than 12 years)[*]
- Treatment of gastric adenocarcinoma
- Treatment of chronic lymphocytic leukaemia
- Treatment of cervix and corpus uteri carcinoma
- Treatment of follicular lymphoma
- Treatment of primary osteoarthrosis (excluding secondary osteoarthrosis)
- Treatment of coronary atherosclerosis
- Treatment of peripheral atherosclerosis
- Treatment of Huntington Chorea
- Treatment of benign prostatic hyperplasia
- Treatment of erectile dysfunction
- Treatment of primary gout (excluding Lesch-Nyhan syndrome and other secondary forms of gout)

[*] See list of waivers revoked

LIST OF WAIVERS REVOKED

- Treatment of melanoma in all subsets of the paediatric population

Revoked on 14 July 2008

Therefore in accordance with Article 14(3) of Regulation (EC) No 1901/2006, as amended, the requirements set out in Articles 7 and 8 shall not apply to this condition for the subsets of the paediatric population from 12 to less 18 years until 15 July 2011.

- Treatment of menopausal and other peri-menopausal disorders in all subsets of the paediatric population

Revoked on 13 April 2009

Therefore, in accordance with Article 14(3) of Regulation (EC) No 1901/2006, as amended, the requirements set out in Articles 7 and 8 shall not apply to 'treatment of menopausal and other peri-menopausal disorders' for all subsets of the paediatric population until 15 April 2012.

ANNEX II

GROUNDS FOR THE GRANTING OF A WAIVER

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Scope

Whereas the conditions listed below occur only in adult populations, the Paediatric Committee (PDCO) recommends that for a medicinal product intended to treat one or more of these conditions, the production of the data in all subsets of the paediatric population in compliance with an agreed paediatric investigation plan shall be waived.

This list of waivers refers to symptomatic conditions only, as opposed to indications or diseases. In addition, the class waiver refers to the treatment of these conditions but not to the prevention or diagnosis of these conditions.

A medicinal product also developed for another condition not listed in Annex 1 will not be waived from the requirements of Regulation (EC) No 1901/2006, as amended.

The conditions listed in Annex 1 should not prevent an applicant from considering the development of a medicinal product in different or related conditions/indications for use in the paediatric population.

The PDCO may adopt further opinions recommending the granting of waivers in other conditions.
In addition the PDCO may adopt an opinion advocating the review of granted waivers as per Article 14 of Regulation (EC) No 1901/2006, as amended.

Voluntary submission of a paediatric investigation plan for a waived condition is still possible.

Grounds for granting or revoking a waiver

The references provided were identified through systematic search and may not be exhaustive nor necessarily available for the EU population.

The PDCO acknowledges that there may be anecdotal cases of occurrence of such conditions in the paediatric population.

- **Oropharyngeal epithelial carcinoma (excluding nasopharyngeal carcinoma)**

Oropharyngeal carcinoma usually occurs after the age of 45 and the average age of diagnosis is around the age of 60 years (1). The incidence reported in children aged 10-14 and 15-19 years in the US is 0.3 and 0.4 per 100,000 respectively (2).

- **Lung carcinoma (small cell and non-small cell)**

The mean age of diagnosis is above the age of 60, though rare cases occur in the 3rd decade of life. The incidence is less than 25 cases reported in children in the interval between 1997-2001 (2).

- **Basal cell carcinoma**

Basal cell carcinoma median age of diagnosis is around the age of 67, although 5-15 % of cases occur in patients aged 20-40 years. Basal cell carcinoma occasionally occurs in children with increased risk, e.g. following radiotherapy.

- **Breast carcinoma**

Age of diagnosis depends on the tumour type and can be as early as in the 3rd decade of life. The incidence is less than 25 cases reported in children in the interval between 1997-2001 (2).

- **Ovarian carcinoma (excluding rhabdomyosarcoma and germ cell tumours)**

The median age of patients with ovarian carcinoma is 60 years (3). Ovarian carcinoma is usually diagnosed after the age of 40. The incidence reported in children aged 10-14 and 15-19 years in the US is 0.7 and 1.4 respectively per 100,000 (2).

- **Endometrial carcinoma**

Endometrial carcinoma is usually diagnosed after the age of 50 years. Rare cases are reported under the age of 35 years.

- **Prostate carcinoma (excluding rhabdomyosarcoma)**

The incidence of prostate carcinoma increases with age and is rarely diagnosed before the age of 50 years (4,5). The incidence is less than 25 cases reported in children in the interval between 1997-2001 (2).

- **Hairy cell leukaemia**

Hairy cell leukaemia is diagnosed on average around the age of 50.

- **Mutliple myeloma**

Multiple myeloma median age of diagnosis is 71 years and only 1% of cases occur before the age of 40 (6). The incidence is less than 25 cases reported in children in the interval between 1997-2001 (2).

- **Alzheimer's Disease**

Alzheimer's disease rarely occurs before the age of 50 years and average age of onset is around the age of 65 (7). Familial Alzheimer's Disease occurs earlier in life and has been reported to occur as early as the age of 30.

- **Vascular dementia and vascular cognitive disorder/impairment**

Vascular dementia is an age-related condition based on cardiovascular or cerebrovascular conditions and the average age of diagnosis is usually above the age of 60 years.

- **Organic amnesic syndrome (excluding amnesic syndrome caused by alcohol and other psychoactive substances)**

Organic amnesic syndrome does not normally occur in the paediatric population.

- **Amyotrophic lateral sclerosis**

Amyotrophic lateral sclerosis is an adult onset disease with the earliest age of onset in the 3rd decade of life. The average age of diagnosis is 55 years.

- **Parkinson's Disease (non-juvenile)**

Parkinson's disease is usually diagnosed after the age of 50, although rare cases occur before the age of 40 years.

- **Age-related macular degeneration**

The average age of onset is after the age of 50. The estimated prevalence for the European population 65 years and older is 3.3 % and increases with age (8).

- **Climacteric symptoms associated with decreased oestrogen levels as occurring at menopause**

Menopause starts 12 months after the last menstrual period, while perimenopause refers to the time before menopause when vasomotor symptoms and irregular menses often commence. Climacteric is the general term for the time from the period of this transition to the early postmenopausal phase. Symptoms of menopause are considered to be secondary to the endocrine modifications that occur in perimenopause; these include fluctuation in ovarian steroid production, with an initially increased but subsequently permanently reduced estrogenic secretion. Typical climacteric symptoms include hot flashes or flushes, insomnia, weight gain and bloating, mood changes, irregular menses, mastodynia, and headache. These symptoms do not occur in paediatric age groups, except in very rare occasions of surgical or chemical castration when full ovarian activity was previously present, i.e. they do not occur in endocrine conditions associated with primary amenorrhoea.
The waiver does not cover conditions that may include reduced oestrogen levels as a risk factor, including (but not limited to) osteoporosis.

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- **Chronic Obstructive Pulmonary Disease (COPD)**

The condition should only be considered in an individual over the age of 40 with characteristic symptoms, according to the Global Initiative for Chronic Obstructive Lung Disease (9).
Granting a waiver for the condition COPD will not prevent consideration of paediatric development of medicinal products that might benefit paediatric patients with chronic lung diseases associated with long-term airflow limitation, such as asthma, bronchopulmonary dysplasia, primary cilia dyskinesia, obstructive lung disease related to graft-versus-host disease after bone-marrow transplantation, etc.

- **Adenocarcinoma of the pancreas**

Adenocarcinoma of the pancreas does not normally occur in the paediatric population and is usually diagnosed after the age of 45. The incidence reported in children below 20 years is 0.1 per 100,000 (10).

- **Gastric carcinoids**

Gastric carcinoids do not normally occur in the paediatric population. Gastric carcinoids usually occur after the age 30 years and the average age of diagnosis is around the age of 60 years (10, 11, 12, 13)

- **Adenocarcinoma of the colon and rectum**

SEED cancer statistics.

- **Bladder carcinoma**

Malignant bladder neoplasms of urothelial origin in children are rare. Most cases in adults are reported over the age of 40 years. Cases of bladder cancer in children under the age of 18 years that have been reported include exposure to cyclophosphamide and post treatment of neuropathic bladder by augmentation cystoplasty (10, 14-23).

- **Liver and intrahepatic bile duct carcinoma (excluding hepatoblastoma)**

The condition does not normally occur in the paediatric population.

- **Kidney and renal pelvis carcinoma (excluding nephroblastoma, nephroblastomatosis, clear cell sarcoma, mesoblastic nephroma, renal medullary carcinoma and rhabdoid tumour of the kidney)**

The condition does not normally occur in the paediatric population.

- **Melanoma**

Melanoma does not normally occur in the paediatric population from 0 to less than 12 years. The incidence reported in the US population for the age groups of 1-5 years, 5-9 years and 10-14 years is 0.10, 0.16 and 0.37 per 100,000 respectively (26). The incidence of melanoma in adolescents, however, is reported at 1.72/100,000 (15 – 19 years)(26) which enables this population to be included in clinical trials.

- **Gastric adenocarcinoma**

Gastric adenocarcinomas do not normally occur in the paediatric population. The incidence reported in children aged 0-14 years in Europe in 2002 was 0.002 per 100,000 (24).

- **Chronic lymphocytic leukaemia**

Chronic lymphocytic leukaemia does not normally occur in the paediatric population and is usually diagnosed above the age of 60 years.

- **Cervix and corpus uteri carcinoma**

Cervix and corpus uteri cancer do not normally occur in the paediatric population.

- **Follicular lymphoma**

The condition does not normally occur in the paediatric population.

- **Primary osteoarthrosis (excluding secondary osteoarthrosis)**

The condition does not normally occur in the paediatric population.

- **Coronary atherosclerosis**

The condition does not normally occur in the paediatric population.

- **Peripheral atherosclerosis**

The condition does not normally occur in the paediatric population.

- **Huntington Chorea**

The condition does not normally occur in the paediatric population.

- **Benign prostatic hyperplasia**

Benign prostatic hyperplasia does not normally occur in the paediatric population. It is usually diagnosed in males above the age of 50 years, rare cases occur already in the 3rd decade of life (25).

- **Erectile dysfunction**

The condition does not normally occur in the paediatric population.

- **Primary gout (excluding Lesch-Nyhan syndrome and other secondary forms of gout)**

The condition does not normally occur in the paediatric population.

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