

From the Chief Medical Officer:
Dr Henrietta Campbell CB

URGENT COMMUNICATION

HSS(MD)39-2004

All General Practitioners (for cascade to Practice Nurses including those working in Well-woman and Family Planning Clinics, and Sessional GPs)

Community Pharmacists

Medical Directors of HSS Trusts for cascade to:

- Consultants in Obstetrics and Gynaecology
- Consultants in Genitourinary Medicine
- Family Planning Clinics

Directors of Public Health in HSS Boards

Directors of Pharmaceutical Services in HSS Boards & Trusts

Directors of Nursing in HSS Boards

Directors of Nursing in HSS Trusts for cascade to:

- Midwifery Services Managers

Prescribing Advisers in HSS Boards

GP Advisers in HSS Boards

Regional Medicines & Poisons Information Service

Castle Buildings

Upper Newtownards Road

STORMONT, BT4 3SQ

Tel: 02890520563

Fax: 02890520724

Email:

henrietta.campbell@dhsspsni.gov.uk

Your Ref:

Our Ref:

Date: 18 November 2004

Dear Colleague

UPDATED PRESCRIBING ADVICE ON THE EFFECT OF DEPO-PROVERA CONTRACEPTION ON BONES

Attached is updated information on prescribing advice on the effect of depo-provera contraception on bone mineral density. Included in this communication are:

1. advice from Professor Gordon Duff, Chairman, Committee on Safety of Medicines; and
2. an information sheet for women. This may also be found on the MHRA website (<http://www.mhra.gov.uk>).

We would be most grateful if this information could be brought to the attention of staff working in the area of women's health.

Yours sincerely

HENRIETTA CAMPBELL (DR)
CHIEF MEDICAL OFFICER

JUDITH HILL (MISS)
CHIEF NURSING OFFICER

NORMAN MORROW (DR)
CHIEF PHARMACEUTICAL OFFICER

UPDATED PRESCRIBING ADVICE ON THE EFFECT OF DEPO-PROVERA CONTRACEPTION ON BONES

Dear Colleague

I am sending you this updated advice in advance of its general release to enable you to prepare for any questions that you may receive.

The effect of Depo-Provera in reducing bone mineral density (BMD) has been recognised for many years and a warning is included in prescribing information. Several new studies, especially involving adolescents, have been completed. Following careful review of the available data the Committee on Safety of Medicines has today updated its advice.

NEW ADVICE FOR PRESCRIBERS

The CSM advises that:

- In adolescents, Depo-Provera may be used as first-line contraception but **only** after other methods have been discussed with the patient and considered to be unsuitable or unacceptable;
- In women of all ages, careful re-evaluation of the risks and benefits of treatment should be carried out in those who wish to continue use for more than 2 years;
- In women with significant lifestyle and/or medical risk factors for osteoporosis, other methods of contraception should be considered.

THE EFFECT OF DEPO-PROVERA ON BONE MINERAL DENSITY

The key points to note are that:

- It is well established that Depo-Provera reduces BMD in many women who use it.
- It is not yet known whether the effect on BMD increases the risk of osteoporosis and fractures in later life.
- The reduction in BMD is duration-dependent for the first few years of use after which the effect appears to plateau.
- There is some evidence that BMD starts to recover when Depo-Provera is stopped but the extent of recovery is currently unknown and may be related to duration of exposure.
- The effect of Depo-Provera may be more important in adolescents in whom the usual process of bone mineral accretion may be reversed. In this population, the effect of Depo-Provera on attainment on peak bone mass is not known.

Background

Depo-Provera is a long-acting, progestogen-only contraceptive that is administered intramuscularly every 12 weeks. Many of those who use Depo-Provera may do so because they are oestrogen-intolerant or because they are unable to comply with a daily contraceptive regimen.

Previous studies have shown that Depo-Provera causes a reduction in BMD in users^{1,2} and warnings have been included in product information for several years.

In adult women, BMD appears to start to recover when Depo-Provera is stopped^{3,4} and limited data suggest that, at menopause, the bone density of previous users may be no different from that of women who have never used Depo-Provera⁵⁻⁷. However, there are some data to suggest that the rate of recovery is dependent on the duration of use.

In adolescents it is recognised that attaining peak bone mass is an important factor in minimising the risk of future osteoporosis. There is now evidence that Depo-Provera causes a loss of BMD in adolescents, at a time when BMD is normally increasing^{8,9}. For this reason it is possible that the effect of Depo-Provera in adolescents may be more significant than in adults. As in adults, there is some evidence for reversibility of effect in adolescents, but it is not known whether BMD recovers to the level attainable if Depo-Provera had not been used. Whilst the reversal of BMD gain has been consistently observed, the clinical implications of these findings remain unknown.

There is currently no evidence to say whether use of Depo-Provera at any age is associated with an increased risk of osteoporosis and fracture in later life, but this possibility should be considered when prescribing Depo-Provera. Further research is being pursued.

Sources of Further Information

An information sheet for women is attached and may also be found on the MHRA website (<http://www.mhra.gov.uk>).

For telephone enquiries, please call the Medicines and Healthcare products Regulatory Agency 020 7084 2000.

Professor Gordon Duff
Chairman
Committee on Safety of Medicines

References

- 1) Cundy T et al., BMJ 1991;303:13-16
- 2) Cromer BA et al., J Paediatrics 1996;129:671-6
- 3) Pettiti DB et al., Obs & Gynaecol 2000;95:736-744
- 4) Scholes D et al., Epidemiology 2002;13:581-7
- 5) Cundy T et al., BMJ 1994;308:1567-8
- 6) Orr-Walker BJ et al., Clin Endocrinol. 1998;49:615-618
- 7) Cundy T et al., Am J Obs Gynae. 2002;186:978-983
- 8) Edwards CP et al., J Paediatr Adolesc Gynaecol 1998;11:201-210
- 9) Lara-Torre E et al., J Paediatr Adolesc Gynaecol 2004;17

Suspected ADRs should be reported via the Yellow Card scheme (www.yellowcard.gov.uk). For additional reporting advice refer to the MHRA website <http://medicines.mhra.gov.uk/>.

UPDATED ADVICE ABOUT DEPO-PROVERA CONTRACEPTIVE

Depo-Provera is a very effective and safe contraceptive injection. One potential side effect that has been studied for a long time is how Depo-Provera use affects bones. New research about this effect, particularly in young people, has resulted in updated information and guidance about using Depo-Provera. This is provided below. If you have any concerns or questions after reading this leaflet, you should talk to the person who usually provides your contraception at your next appointment.

What is Depo-Provera?

Depo-Provera is a progestogen-only contraceptive injection that is given every 12 weeks. It is particularly suitable for those who cannot use oestrogen or who find it difficult to remember a daily pill.

What is the effect of Depo-Provera on bones?

Depo-Provera works by lowering levels of the female hormone oestrogen and these low oestrogen levels can reduce bone mineral density (BMD), which is a slight thinning of the bones. Women who have used Depo-Provera tend to have lower BMD than women who have not used Depo-Provera. The effects of Depo-Provera on bone are greatest during the first 2-3 years of use. Following this, the levels of BMD tend to stabilise and there appears to be some recovery when Depo-Provera is stopped. Research is being carried out to show whether the bones recover completely after long-term use of Depo-Provera or whether this effect increases the risk of osteoporosis (weak bones) and fractures in later life. Pregnancy can also lead to temporary thinning of bones.

Why were young people (under 19 years old) included in the new research?

The bones of healthy teenagers are growing rapidly and the increases in BMD that occur in teenage years are important for maintaining healthy bones during adulthood and providing protection against the development of osteoporosis in later life. The use of Depo-Provera in teenagers is associated with a reduction in BMD at a time when it should be increasing. The bones start to recover when Depo-Provera is stopped, but it is not yet known whether the reduction in BMD recovers completely.

What is the updated advice?

New users

- Adults - Depo-Provera is an effective contraceptive injection but it may make your bones slightly thinner in the first few years of use. However, your bones gradually return to normal when you stop using it and may be no different from non-users after a few years.
- Teenagers - Treatment with Depo-Provera may reduce your BMD at a time when it should be increasing. It is not yet known if these effects are fully reversible. If you are thinking of using Depo-Provera, it is important that you also know about all the other choices of contraception first to see if another method might be more suitable for you. Talk about this with your health professional/doctor/nurse.

Current users

- Adults and teenagers - There is no need for you to stop using Depo-Provera injections based on this information. However, use of Depo-Provera may make your bones slightly thinner than non-users. If you wish to keep using Depo-Provera for more than 2 years the person who provides your contraception may wish to make sure that this is still the best option for you.

Keeping bones healthy

There are several things you can do to help your bones including regular weight-bearing exercise (e.g. walking or running), a healthy diet including adequate calcium (e.g. from dairy products) and vitamin D (e.g. from oily fish) and cutting down on smoking and drinking alcohol.

Certain medicines such as high dose glucocorticoids (steroids), anti-epileptics, and thyroid hormones can increase your risk of developing osteoporosis (weak bones). Tell your health professional/doctor/nurse if you are taking these or any other medicines - they may recommend a more suitable method of contraception.

Further information

Further information and advice may be found on the Medicines and Healthcare products Regulatory Agency's website (<http://www.mhra.gov.uk>)

