29 October 2018[1]
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Pharmacovigilance Risk Assessment Committee (PRAC)

New product information wording – Extracts from PRAC recommendations on signals

Adopted at the 1-4 October 2018 PRAC

The product information wording in this document is extracted from the document entitled 'PRAC recommendations on signals' which contains the whole text of the PRAC recommendations for product information update, as well as some general guidance on the handling of signals. It can be found ***here*** (in English only).

New text to be added to the product information is underlined. Current text to be deleted is ~~struck through~~.

1. Direct acting antivirals (DAAV) indicated for the treatment of hepatitis C[2] – Dysglycaemia (EPITT no 19234)

Summary of product characteristics

4.4. Special warnings and precautions for use

Use in diabetic patients

Diabetics may experience improved glucose control, potentially resulting in symptomatic hypoglycaemia, after initiating HCV {direct acting antiviral / DAA} treatment. Glucose levels of diabetic patients initiating {direct acting antiviral / DAA} therapy should be closely monitored, particularly within the first 3 months, and their diabetic medication modified when necessary. The physician in charge of the diabetic care of the patient should be informed when {direct acting antiviral / DAA} therapy is initiated.

Package leaflet

2. What you need to know before you take {product name}

[1] Intended publication date. The actual publication date can be checked on the webpage dedicated to PRAC recommendations on safety signals.
[2] Daclatasvir; dasabuvir; elbasvir, grazoprevir; glecaprevir, pibrentasvir; ledipasvir, sofosbuvir; ombitasvir, paritеprevir, ritonavir; sofosbuvir; sofosbuvir, velpatasvir; sofosbuvir, velpatasvir, voxilaprevir

30 Churchill Place ● Canary Wharf ● London E14 5EU ● United Kingdom
Telephone +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5525
Send a question via our website www.ema.europa.eu/contact

Warnings and precautions

Talk to your doctor or pharmacist before taking this medicine if you:

- Have diabetes. You may need closer monitoring of your blood glucose levels and/or adjustment of your diabetes medication after starting {product name}. Some diabetic patients have experienced low sugar levels in the blood (hypoglycaemia) after starting treatment with medicines like {product name}.

2. Dolutegravir – Evaluation of preliminary data from an observational study on birth outcomes in human immunodeficiency virus (HIV)-infected women (EPITT no 19244)

Summary of product characteristics

4.6. Fertility, pregnancy and lactation

Women of childbearing potential

Women of childbearing potential (WOCBP) should undergo pregnancy testing before initiation of dolutegravir. WOCBP who are taking dolutegravir should use effective contraception throughout treatment.

Pregnancy

Preliminary data from a surveillance study has suggested an increased incidence of neural tube defects (0.9%) in mothers exposed to dolutegravir at the time of conception compared with mothers exposed to non-dolutegravir containing regimens (0.1%).

The incidence of neural tube defects in the general population ranges from 0.5-1 case per 1,000 live births (0.05-0.1%). As neural tube defects occur within the first 4 weeks of foetal development (at which time the neural tubes are sealed) this potential risk would concern women exposed to dolutegravir at the time of conception and in early pregnancy. Due to the potential risk of neural tube defects, dolutegravir should not be used during the first trimester unless there is no alternative.

More than 1000 outcomes from second and third trimester exposure in pregnant women indicate no evidence of increased risk of malformative and foeto/neonatal negative effects. However, as the mechanism by which dolutegravir may interfere in human pregnancy is unknown, the safety in use during the second and third trimester cannot be confirmed. Dolutegravir should only be used during the second and third trimester of pregnancy when the expected benefit justifies the potential risk to the foetus.

In animal reproductive toxicology studies, no adverse development outcomes, including neural tube defects, were identified (see section 5.3). Dolutegravir was shown to cross the placenta in animals.

Package leaflet

2. What you need to know before you take {product name}

Pregnancy

If you are pregnant, if you become pregnant, or if you are planning to have a baby:

-> Talk to your doctor about the risks and benefits of taking {product name}.

Taking {product name} at the time of becoming pregnant or during the first twelve weeks of pregnancy, may increase the risk of a type of birth defect, called neural tube defect, such as spina bifida (malformed spinal cord).

If you could get pregnant while receiving {product name}, you need to use a reliable method of barrier contraception (for example, a condom) with other methods of contraception including oral (pill) or other hormonal contraceptives (for example, implants, injection), to prevent pregnancy.

Tell your doctor immediately if you become pregnant or are planning to become pregnant. Your doctor will review your treatment. Do not discontinue {product name} without consulting your doctor, as this may harm you and your unborn child.

3. Hormonal contraceptives[3] – Suicidality with hormonal contraceptives following a recent publication (EPITT no 19144)

Summary of product characteristics

4.4. Special warnings and precautions for use

Depressed mood and depression are well-known undesirable effects of hormonal contraceptive use (see section 4.8). Depression can be serious and is a well-known risk factor for suicidal behaviour and suicide. Women should be advised to contact their physician in case of mood changes and depressive symptoms, including shortly after initiating the treatment.

Package leaflet

2. What you need to know before you take {product name}

Warnings and precautions

Psychiatric disorders:

Some women using hormonal contraceptives including {product name} have reported depression or depressed mood. Depression can be serious and may sometimes lead to suicidal thoughts. If you experience mood changes and depressive symptoms contact your doctor for further medical advice as soon as possible.

[3] Chlormadinone, estradiol; chlormadinone acetate, ethinylestradiol ; conjugated estrogens, medrogestone ; conjugated estrogens, medroxyprogesterone acetate; conjugated estrogens, norgestrel; cyproterone, ethinylestradiol; cyproterone acetate, estradiol valerate; desogestrel; desogestrel ,ethinylestradiol; dienogest, estradiol; dienogest, ethinylestradiol; drospirenone, estradiol; drospirenone, ethinylestradiol; estradiol, estriol, levonorgestrel; estradiol, gestodene; estradiol, levonorgestrel; estradiol, medroxyprogesterone acetate; estradiol, nomegestrol acetate; estradiol, norethisterone; estradiol, norgestimate; estradiol (17-beta), progesterone; estradiol (17-beta), trimegestone; estradiol valerate, norgestrel; ethinylestradiol, etonogestrel; ethinylestradiol, etynodiol; ethinylestradiol, gestodene; ethinylestradiol, gestodene; ethinylestradiol, levonorgestrel; ethinylestradiol, lynestrenol; ethinylestradiol, norethisterone; ethinylestradiol, norgestimate; ethinylestradiol, norgestrel; levonorgestrel, ethinylestradiol; ethinylestradiol; levonorgestrel; medroxyprogesterone; mestranol, norethisterone; nomegestrol; nomegestrol acetate, estradiol; norelgestromin, ethinyl estradiol; norethisterone

4. Teriflunomide – Dyslipidaemia (EPITT no 19227)

Summary of product characteristics

4.8. Undesirable effects

Tabulated list of adverse reactions

Metabolism and nutrition disorders
Frequency 'Not known'': Dyslipidaemia

Package leaflet

4. Possible side effects

Not known (frequency cannot be estimated from the available data)

- abnormal levels of fats (lipids) in the blood