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Abiraterone
risk of hypoglycaemia from interaction with pioglitazone and repaglinide

Quick Read
Concomitant administration of abiraterone (used in the treatment of prostate cancer) and oral antidiabetic agents can be associated with a risk of hypoglycaemia due to a pharmacokinetic interaction.

Abiraterone is a selective 17a-hydroxilase-C17, 20-liase (CYP17) inhibitor, an enzyme that is necessary for the biosynthesis of androgens in testicular, adrenal and prostate tumour tissues. In association with prednisone or prednisolone, it is indicated in the treatment of metastatic prostate cancer and of castration-resistant metastatic prostate cancer.

Abiraterone is a known inhibitor of CYP2D6 and CYP2C8, which are involved in the metabolism of various drugs. Caution should therefore be exerted when abiraterone is co-administered with medicines that are activated or metabolized by those enzymes. Interactions with **dextromethorphan** and **pioglitazone** are already known and are listed in the Summaries of the Product Characteristics (SPC), as are potential interactions with drugs metabolized by CYP2D6 (**metoprolol, propranolol, desipramine, venlafaxine, haloperidol, risperidone, propafenone, flecainide, codeine, oxycodone, tramadol**).

Following publication of an article by **Tucci et al** reporting on cases of severe hypoglycaemia in patients simultaneously on abiraterone and oral antidiabetic agents, the European Medicines Agency (EMA) Pharmacovigilance Risk Assessment Committee (PRAC) undertook a revision of all available cases from clinical trials, post-marketing and from the literature. In January 2020, the PRAC agreed that a **pharmacokinetic interaction** can plausibly cause hypoglycaemia. The SPC and Information Leaflet texts will be changed accordingly as a risk minimization measure:

4.4. Special warnings and precautions for use

[…]

Cases of hypoglycaemia have been reported when ZYTIGA was administered to patients with pre-existing diabetes receiving pioglitazone or repaglinide (see section 4.5); therefore, blood sugar should be measured frequently in patients with diabetes.

4.5. Interaction with other medicinal products and other forms of interaction

[…]

Patients should be monitored for signs of toxicity related to a CYP2C8 substrate with a narrow therapeutic index if used concomitantly. Examples of medicinal products metabolised by CYP2C8 include pioglitazone and repaglinide (see section 4.4).

Sílvia Duarte

INDEX CARD

Director: Fátima Canedo
Editor: Rui Pombal
Contributors: Adriana Gamboa, Ana Severiano, Ana Sofia Martins, Cristina Mousinho, Fátima Bragança, Fátima Hergy, Magda Pedro, Márcia Silva, Patrícia Catalão, Sílvia Duarte
Publishing Assistant: Inocência Pinto
Advisory Board: Conselho Diretivo do INFARMED, I.P.
INFARMED – Autoridade Nacional do Medicamento e Produtos de Saúde, I.P.
Parque de Saúde de Lisboa, Av. do Brasil, N.º 53, 1749-004 Lisboa
Phone: +351 217 987 100
E-mail: farmacovigilancia@infarmed.pt
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Mysimba® (Bupropion + Naltrexone)
safe use

Quick Read
Therapy with Mysimba® requires periodical benefit-risk assessments. In addition to mostly neuropsychiatric contraindications, cardiovascular factors need also be taken into account, including arterial hypertension and its control.

Mysimba® is an association of two active ingredients, naltrexone chlorhydrate and bupropion chlorhydrate. It is indicated as an adjuvant to a low-calorie diet and increased physical activity in weight treatment in adult patients (≥ 18 years) with a body mass index (BMI) ≥ 30 kg/m2 (obese) or from ≥ 27 kg/m2 to < 30 kg/m2 (excessive weight) in the presence of one or more weight-related comorbidities (e.g., type 2 diabetes, dyslipidaemia or hypertension).

In order to promote the safe use of Mysimba®, **Educational Materials** are available for physicians (see below) to remind them of:

- indications and the need to discontinue treatment should concerns arise regarding its safety or tolerability or if, after 16 weeks, patients have lost less than 5% of their initial body weight;
- contraindications, warnings and precautions, as well as patient characteristics putting them at increased risk of adverse reactions.

Mysimba® **should not be used** in patients with/on:

- **Non-controlled hypertensiona**
- Seizure disorder, history of seizures or known CNS tumour
- Current opioid or opioid agonist dependence
- Treatment of acute alcohol, benzodiazepine or opioid withdrawal syndrome
- Current or past diagnosis of bulimia or anorexia nervosa
- Tratamento concomitante com bupropiom ou naltrexona
- History of bipolar disorder
- MAO inhibitor therapy in the last 14 dayss
- Severe liver failure or end-stage kidney failure

Moreover, patients with **any of the following factors** are at **increased risk of adverse reactions**:

- **Controlled hypertension**
- Moderate liver failure
- Moderate or severe kidney failure
- Angina pectoris, recent myocardial infarction or past history of cerebrovascular condition
- History of mania
- Suicidal ideation or history of suicide attempt
- Depression
- Risk factors for seizures (history of head trauma, hypoglycaemic episodes associated with diabetes therapy, concomitant medicines that may lower the seizure threshold).

Treatment with Mysimba® should only be started or maintained provided a full assessment of benefits and risks has been undertaken, and its safety and tolerability evaluated at regular intervals.

Patrícia Catalão

Educational Materials published on the Infomed product information webpage
Click on the links.

INN Medicinal product	Target	Comunication Online publication date
Bupropion + Naltrexone Mysimba	**Physicians:** general/family medicine, endocrinology, general surgery, psychiatry	Prescriber's checklist 24/02/2020

Educational Materials published on the Infomed product information webpage

Click on the links.

INN Medicinal product	Target	Comunication Online publication date
Avelumab Bavencio	**Patients**	Information brochure Alert card 17-02-2020
Dibotermin alfa InductOs	**Dibotermin alfa:** who prepare and administer InductOs, including surgeons, surgical nurses and hospital pharmacists	Surgical preparation and application instructions for lumbar intersomatic arthrodesis and acute exposed tibial fractures Preparation and application instruction video for lumbar intersomatic arthrodesis Surgical preparation and application instruction video for acute exposed tibial fracture 21-01-2020
Mecasermin Increlex	**Physicians:** specialists in paediatric endocrinology and paediatricians who undertake hospital paediatric endocrinology consultations hospitais	Safety information for physicians
	Patients /caregivers	Safety information for patients 24-02-2020
Methotrexate Ledertrexato	**Physicians:** : rheumatology, internal medicine (autoimmune conditions) and dermatology **Nurses:** working with specialities using methotrexate **Pharmacists:** community and hospital	Safety information for healthcare professionals 07-02-2020
Tocilizumab Roactemra	**Physicians:** internal medicine, rheumatology, paediatrics, haematology and oncology (who can be expected to prescribe this medicinal product)	Brochure
	Nurses: who administer this medicinal product	Administration guide
	Patients	Brochure Alert card 12-02-2020

Compiled by Patrícia Catalão

Communications to Healthcare Professionals published on the Infomed product information webpage

Click on the links.

INN Medicinal product	Target	Comunication Online publication date
Tofacitinib Xeljanz	**Physicians:** rheumatology, internal medicine and dermatology (rheumatoid and psoriatic arthritis clinics); gastroenterology (for the ulcerative colitis indication)	Increased risk of venous thromboembolism and serious and fatal infections 12-02-2020

Compiled by Patrícia Catalão

What do they mean?

ADR	Adverse Drug Reaction
EMA	European Medicines Agency
MA	Marketing Authorization
PIL	Patient Information Leaflet
PRAC	Pharmacovigilance Risk Assessment Committee (EMA)
SmPC	Summary of Product Characteristics