boletim de FARMACO VIGILÂNCIA

VOLUME 23
NUMBER 6
JUNE 2019

Modafinil during pregnancy: risk of congenital malformations

Quick Read

Although data on exposure to modafinil during pregnancy are limited, there is evidence suggesting a risk of foetal malformations. Modafinil should therefore not be used by pregnant women and effective contraception should be ensured while this medicine is being taken.

Modafinil is indicated in adults for the treatment of excessive sleepiness associated with narcolepsy, with or without catalepsy. The mechanism through which modafinil promotes alertness is still not known but in vitro and in vivo data reveal that this substance, though not a direct dopamine agonist, binds to the dopamine transporter and inhibits reuptake of dopamine; an analogous though less marked mechanism occurs with norepinephrine.

Although there is only a limited number of cases of known exposure during pregnancy, use of modafinil is suspected of causing congenital malformations. Following on reported cases, this issue was recently reviewed by the European Medicines Agency (EMA) Pharmacovigilance Risk Assessment Committee (PRAC).

The reports of congenital malformations for which a causal relationship with modafinil was deemed possible came from a **pregnancy registry** based **observational study** in the USA with the products Nuvigil® (armodafinil) and Provigil® (modafinil), as well as from other sources of spontaneous reports. A definitive relation with the use of modafinil was however not possible to determine, since other potential causes could not be excluded.

EMA and **Infarmed** recommend:

- Modafinil should **not** be used **during pregnancy**;
- Doctors should make sure that every patient treated (or to be treated) with modafinil understands that there is:
  - potential risk of **foetal malformations** associated with the use of modafinil during pregnancy;
  - potential decrease in effectiveness of oral contraception by modafinil;
  - need to use an **effective additional or alternative contraceptive method**.
- Should a woman suffer from narcolepsy, with or without catalepsy, during pregnancy, **non-pharmacological treatment** options should be preferentially considered, such as behavioural changes, sleep hygiene and scheduled naps.

The texts of the **Summary of the Product's Characteristics (SmPC)** and corresponding **Information Leaflets** will be changed to reflect the above recommendations.

Ana Severiano

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Design and production: Letras & Sinais, Comunicação e Imagem, Lda.
ISSN: 0873-7118

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SNS SERVIÇO NACIONAL DE SAÚDE
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E-book – Clinical Records

In Chapter 4.8. (Miguel Antunes, Luís Pinheiro)

A clinical registry can be defined as "a repository of data concerning every case of one particular disease or health condition in a defined population and to which the cases can be related in such a way that an incidence rate of the phenomenon being studied can be calculated". In some cases, the main focus of attention determines by itself which medicinal products are to be observed – this is the case of the **pregnancy registries** in some countries, which are especially useful for monitoring the use of medicines with a pregnancy prevention plan attached. […]

As for any other type of study, registry-based studies may be affected by bias. Selection biases, on account of clinical and sociodemographic factors, are particularly relevant. A critical assessment of the selection criteria determined by the study's design is very important, in that those criteria may have an impact on the results obtained (incomplete records, loss of patients to follow-up, etc). The use of clinical registries can additionally be marred by other factors such as steep maintenance and quality control costs or the fact that they do not always contain adequate control groups for the problem at hand.

E-book – Pregnancy Prevention Programmes (PPP)

In Chapter 5.2. (Márcia Silva)

The goal of PPPs is to ensure that women are not pregnant before they start a treatment and that nor do they become pregnant whilst on therapy and for some time after its cessation. A PPP usually combines an educational programme with drug access control measures.

To find out more, look up these chapters or download the whole e-book (click on the picture)

New Pharmacovigilance Units

Central and Northern Alentejo Unit
(Évora and Portalegre districts)

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Escola Superior de Enfermagem de São João de Deus

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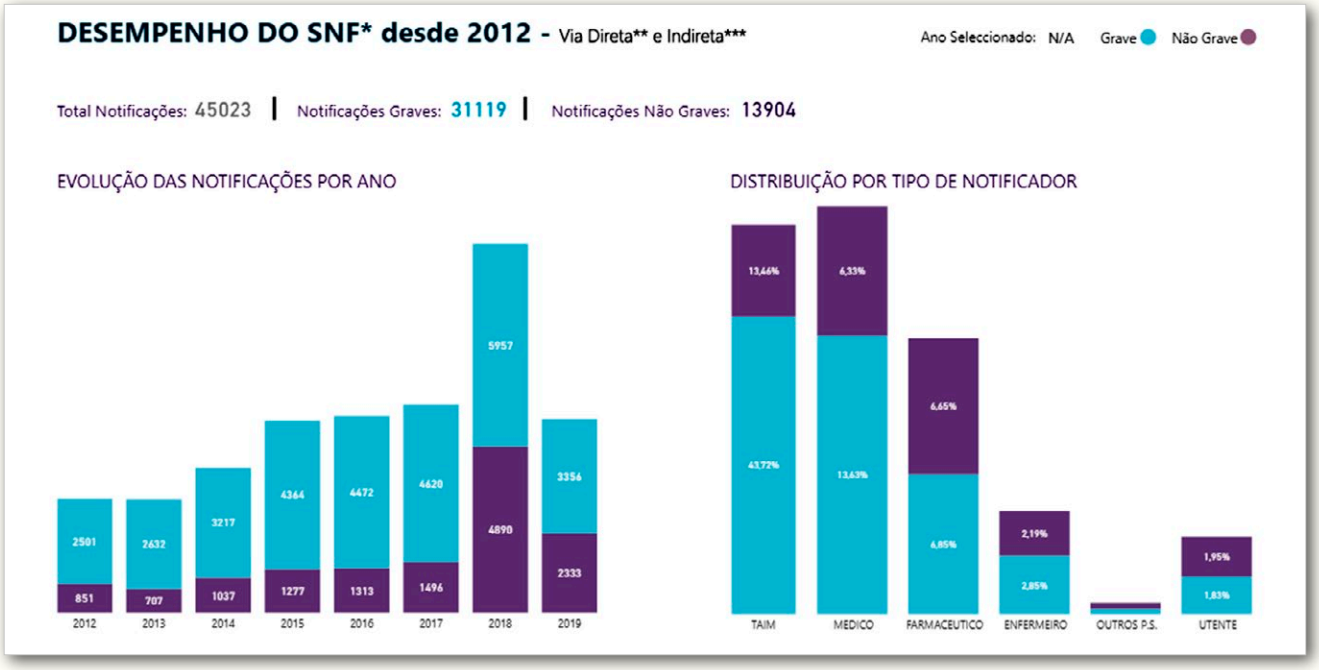
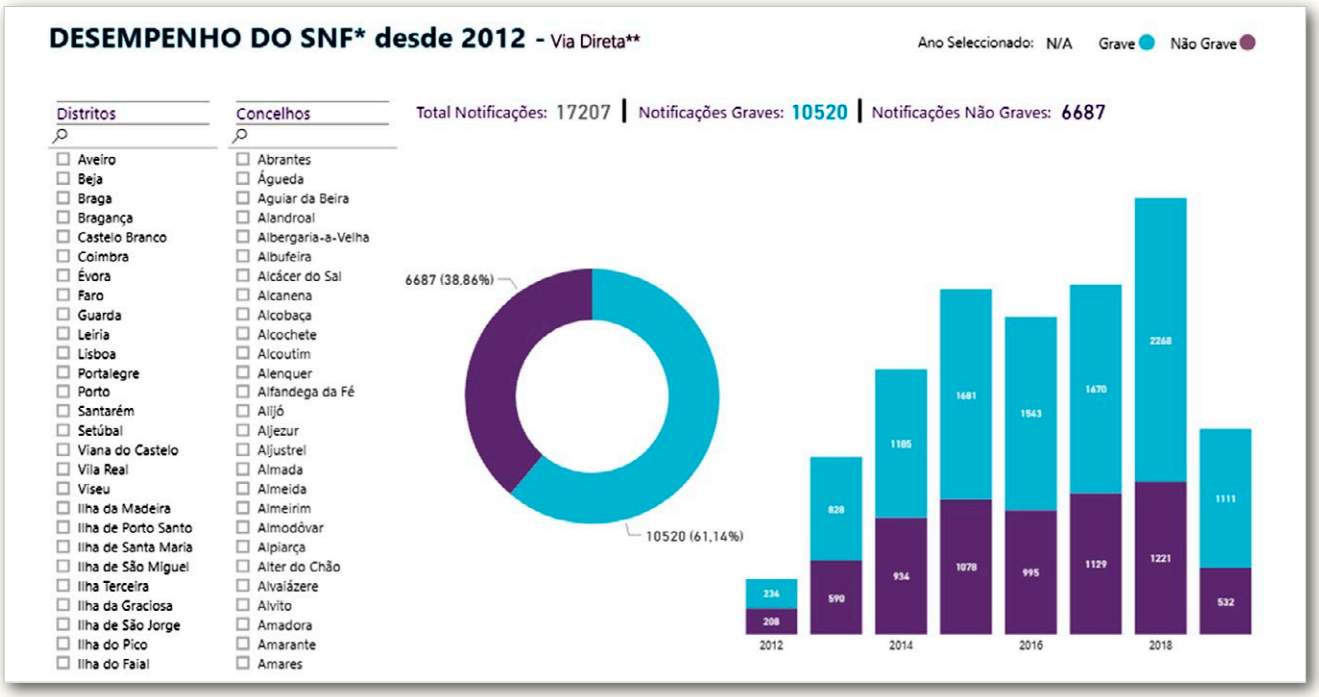
New Adverse Drug Reaction Reports Dashboard

The Infarmed Medicines Risk Management Department has just made available online a dashboard (in Portuguese) that you can look up to find out how the Portuguese National Pharmacovigilance System has been performing since 2012. The dashboard can be found **here**. It has been developed together with the agency's Information Technologies and Systems Department, gives a permanently up-to-date picture of the adverse drug reactions (ADRs) being submitted to Infarmed every day through **Portal RAM**, and is made up of three searchable boards that make it both a tool and a source of information for all those who need to access current pharmacovigilance data.

The first board shows an overview of data from all the reports entered into the system irrespective of source:



The second board shows the ADR reports sorted by reporting source – direct source from healthcare professionals and patients, and indirect source from marketing authorization holders (MAs). Finally, one can use the third board to search through ADR report data from direct sources by geographical region:



Ana Moreira

Communications to Healthcare Professionals published on the Infarmed website

Click on the links.

INN Medicinal product	Target	Comunication Online publication date
Daratumumab Darzalex	**Physicians:** haematology, oncology, and gastroenterology	Risk of hepatitis B virus reactivation 18-06-2019
Medicinal products containing febuxostat Adenuric Febuxostate Bluepharma, Generis, Krka, Farmoz, Pentafarma Urosat	**Physicians:** general/family medicine, rheumatology, orthopaedics, internal medicine, and cardiology **Pharmacists:** community	Increased risk of cardiovascular death and all-cause mortality (CARES study) 27-06-2019
Tocilizumab Roactemra	**Physicians:** : internal medicine, rheumatology, paediatrics, haematology, and oncology	Rare risk of serious liver injury, including hepatic failure requiring transplantation 18-06-2019

Compiled by Magda Pedro

Educational Materials published in the Infomed product information webpage

Click on the links.

INN Medicinal product	Target	Comunication Online publication date
Ambrisentan Volibris	**Patients**	Reminder card 12-06-2019
Atomoxetine Atomoxetina ratiopharm	**Physicians:** psychiatry, child psychiatry, and neurology	**Listas de verificação:** Before starting treatment During treatment Cardio- and cerebrovascular risk assessment and monitoring guide Cardiovascular record 07-05-2019
Vismodegib Erivedge	**Physicians:**specialists in dermatology, oncology, plastic surgery, and radiotherapy, at hospitals procuring this medicinal product	Information card Pregnancy Prevention Programme Verification of counselling form
	Patients	Pregnancy Prevention Pogramme: for women and men Information card 05-06-2019

Compiled by Magda Pedro