mode, a Hazard Score (HS) was calculated by multiplying the probability of occurrence (Remote = 1, Uncommon = 2, Occasional = 3, Frequent = 4) and severity of effect (Minor = 1, Moderate = 2, Major = 3, Catastrophic = 4). If \( HS \geq 8 \), corrective actions were proposed. If \( HS < 8 \), failure mode was evaluated based on: lack of detection, criticality and absence of effective control measures. All data were collected in a validated worksheet.

**Results** A flow diagram was obtained. Twenty-seven failure modes were identified, and twenty had a \( HS > 8 \). Failure modes with the highest HS were: wrong dose calculation and wrong protocol (Prescribing); incorrect production protocol in the computer system and non-detection of wrong dose calculation (Pharmaceutical validation); wrong medicine is chosen, incorrect volume of drug added to diluent and labelling error (Compounding); Delivered to wrong nursing unit or patient (Dispensing). Corrective actions proposed were: policy of weighing patient for proper dose calculation, chemotherapy database updated, double checking, gravimetric control on prepared chemotherapy, procedures for proper patient identification (barcode identification system or radiofrequency dispensing system).

**Conclusions** FMEA contributes to the development of a very clear and shared vision of the chemotherapy process, taking into account different perspectives: oncologist, pharmacist, technician and nurse.

FMEA is a useful tool for identifying critical parts of the chemotherapy process, prioritising corrective actions, minimising potential risks and improving the quality and safety of patient care.

No conflict of interest.

---

**FREQUENCY OF VALPROIC ACID-INDUCED HYPERAMMONEMIA IN ADULT PSYCHIATRIC SETTINGS**

doi:10.1136/ejhpharm-2013-000276.074

B HUE, N Chaumartin, P Beauvoir. EPS Paul Guiraud, Pharmacy, Villejuif, France; EPS Paul Guiraud, General Practitioner, Villejuif, France.

**Background** Valproic acid (VPA) is widely prescribed by paediatric neurologists as an antiepileptic drug. VPA-induced hyperammonaemia can lead to encephalopathy and coma; it is well documented among the paediatric population. Severe urea cycle enzyme deficiencies are often revealed in early youth when VPA is administered. Such mild genetic deficiencies can remain unnoticed until adulthood and be discovered if VPA is taken for bipolar disorder.

**Purpose** To evaluate the frequency of VPA-induced hyperammonaemia in adult psychiatric settings and to sensitize the medical community to a potentially severe adverse effect of a widely-prescribed drug.

**Materials and Methods** The study was carried out a two-week period in a psychiatric hospital. It included every full-time hospitalised patient treated with VPA for at least 4 days (corresponding to 5 drug half-lives). Ammonia and VPA blood measurements were performed once and an electroencephalogram when ammonia exceeded 70 µM (normal range: 10 to 35 µM). Ethics committee approval was obtained before starting the study.

**Results** 122 patients were included in this study. 68 patients (55.8%) presented ammonia blood levels exceeding 35 µM and 4 of them (3.3%) exceeded 70 µM. One patient reached 118 µM one week after VPA initiation. No encephalographic abnormalities were observed. No correlation was found between ammonia and total VPA levels. Different oral forms of VPA were used and this study showed that they affected VPA blood levels.

**Conclusions** VPA-induced hyperammonaemia is a frequent, generally well-tolerated, adverse effect. Ammonia blood level monitoring combined with clinical monitoring are essential to avoid hyperammonaemic encephalopathy. Communication within the hospital led to the medical community becoming aware of the problem and new monitoring recommendations were defined including initial ammonia level measurement after VPA initiation and bimonthly monitoring of this biological parameter. Total VPA level determination doesn’t seem to be useful for predicting hyperammonaemia whereas the importance of measuring the free VPA has recently been highlighted.

No conflict of interest.
General and risk management, patient safety

Agency): gastro-duodenal ulcers (including NSAIDs and steroid-related ulcers), reflux oesophagitis, Zollinger-Ellison’s syndrome, and Helicobacter pylori eradication. Inclusion criteria: patients >65 years old on at least four home medicines and an anti-ulcer prescription in the ER. Pharmaceutical interventions were recorded and their degree of acceptance calculated. The cost resulting from drug misuse was calculated considering a mean stay in the unit of one day.

Results 111 patients, 70.2% male, median age 78.9 years-old [65–94]. 94.6% of patients (92.9% FPI, 1.7% H2 antagonists) received one of these agents upon presentation (95.5% of them were prescribed de novo), with intravenous pantoprazole the agent mainly involved (82% of cases). 29.7% of prescriptions did not meet the indications, while this percentage decreased to 12.5% upon ward admission. The pharmaceutical interventions were accepted in 16.2% of cases. Monthly, the estimated cost of the off-label use was $185,000.

Conclusions Gastro-protection in the ER did not meet the criteria in nearly 1/3 of patients. This contrasted with the poor acceptance of the pharmaceutical recommendations of discontinuation. The rationale might be the so-perceived harmless profile of these drugs with the short-term use. The rate of off-label prescriptions dropped to half upon ward admission, likely due to thorough revision by the prescriber. Since only patients at a higher risk of suffering from a medicines-related problem were included, the cost resulting from the misuse of anti-ulcer drugs was probably underestimated. In conclusion, forthcoming pharmacy policies should focus on improving the adherence to the indications of both widely-used and expensive drugs, given their financial and health-care impact.

No conflict of interest.

Conclusions Most suspected ADRs identified corresponded to MMF’s profile ADRs described in the summary of product characteristics. The switch to generic from innovator drug should have a surveillance strategy that includes medical monitoring, patient education and the contribution of all health professionals involved in the patient immunosuppressant regimen in order to create a system that allows reverse reactions to be detected, with the ultimate goal of maximising benefit and minimising risk by promoting safer use of medicines.

No conflict of interest.

Conclusions Gastro-protection in the ER did not meet the criteria in nearly 1/3 of patients. This contrasted with the poor acceptance of the pharmaceutical recommendations of discontinuation. The rationale might be the so-perceived harmless profile of these drugs with the short-term use. The rate of off-label prescriptions dropped to half upon ward admission, likely due to thorough revision by the prescriber. Since only patients at a higher risk of suffering from a medicines-related problem were included, the cost resulting from the misuse of anti-ulcer drugs was probably underestimated. In conclusion, forthcoming pharmacy policies should focus on improving the adherence to the indications of both widely-used and expensive drugs, given their financial and health-care impact.

No conflict of interest.

Background Immunossuppressant drugs have an important role in the prophylaxis of transplant rejection, so they are considered ‘critical dose drugs’. Use of a generic immunossuppressant represents a significant cost savings to the medical system. Since safety data for new medicines are always limited, post-marketing surveillance is essential to determine medicines’ safety in real life use. With the introduction of generic mycophenolate mofetil (MMF) in CHLO, EPE–HSC, the pharmaceutical services (PHS) have implemented an app to monitor ADRs identified with an app implemented by the PHS. Notification were reported to the Portuguese National Pharmacovigilance Unit.

Notifications were reported to the Portuguese National Pharmacovigilance Unit.

Results 111 patients, 70.2% male, median age 78.9 years-old [65–94]. 94.6% of patients (92.9% FPI, 1.7% H2 antagonists) received one of these agents upon presentation (95.5% of them were prescribed de novo), with intravenous pantoprazole the agent mainly involved (82% of cases). 29.7% of prescriptions did not meet the indications, while this percentage decreased to 12.5% upon ward admission. The pharmaceutical interventions were accepted in 16.2% of cases. Monthly, the estimated cost of the off-label use was $185,000.

Conclusions Gastro-protection in the ER did not meet the criteria in nearly 1/3 of patients. This contrasted with the poor acceptance of the pharmaceutical recommendations of discontinuation. The rationale might be the so-perceived harmless profile of these drugs with the short-term use. The rate of off-label prescriptions dropped to half upon ward admission, likely due to thorough revision by the prescriber. Since only patients at a higher risk of suffering from a medicines-related problem were included, the cost resulting from the misuse of anti-ulcer drugs was probably underestimated. In conclusion, forthcoming pharmacy policies should focus on improving the adherence to the indications of both widely-used and expensive drugs, given their financial and health-care impact.

No conflict of interest.

Materials and Methods Between 11/2011 and 09/2012, all adult HT recipients who switched from innovator to the generic MMF recipients who switched from innovator to the generic MMF were included in the MMF APP. This substitution was made under EPE–HSC, the pharmaceutical services (PHS) have implemented an app to monitor ADRs identified with an app implemented by the PHS. Notification were reported to the Portuguese National Pharmacovigilance Unit.

Purpose To describe and quantify suspected adverse drug reactions (ADRs) identified with an app implemented by the PHS.

Materials and Methods Between 11/2011 and 09/2012, all adult HT recipients who switched from innovator to the generic MMF were included in the MMF APP. This substitution was made under medical supervision and the pharmacist provided the patients with all necessary explanations. Subsequent pharmaceutical assessment was done with a questionnaire (in person or telephone), which identified demographic data, concomitant treatment and suspected ADRs.

Results 55 patients were included in the MMF APP, 78% male, average age 55 ± 13 (22–76) years. 14 patients (25%) reported ADRs at MMF switch. These patients had not experienced ADRs with the innovator drug. The most common ADRs identified were diarrhoea (25%), stomach ache (12.5%) and asthenia (12.5%). All ADRs notifications were reported to the Portuguese National Pharmacovigilance Unit.