

# Isotretinoin : Review of the Pregnancy Prevention Programme

HCP WG meeting October 2011: Dr Sarah Mee  
Isotretinoin: UK RMS

# Introduction

- In 2003, European referral led to introduction of the isotretinoin pregnancy prevention programme (PPP).
- Guidelines for prescribers, pharmacists and patients were issued regarding the safe use of isotretinoin.
- Harmonized, consistent and accurate product information essential with the generic market - avoid potential for confusion and inconsistencies.
- The European guidelines had to be implemented under national responsibility in the European Member States with a supporting PPP.

# The current Isotretinoin PPP

The PPP consists of

## Educational programme

- physicians, pharmacist and patient guideline documents
- brochure for patients on contraception
- acknowledgement form for female patients)

## Therapy management

- Mandatory pregnancy testing
- Mandatory effective contraception
- Obligations for the prescriber)

## Distribution control

- Prescription limited to 30 days and 7 day validity

## Additional measures

- Clear SmPC labelling- not to share medication
- Registration of all isotretinoin exposed pregnancies)

Updates on the PPP - submitted six-monthly up to July 2010, now annually.

## Schaefer et al: Observational Study Of The Berlin Institute For Clinical Teratology And Drug Risk Assessment In Pregnancy.

A total of 108 pregnancies exposed to systemic isotretinoin (median dosage 20 mg/day) during the contraindicated period were registered.

Where outcome known - 76% (69/91) of the pregnancies electively terminated.

Terminations mainly for fear of medication risk – none due to abnormal prenatal ultrasound findings.

None of the infants showed symptoms of retinoid embryopathy.

Contraception use – where known 70% (48/69) did not use any method !!!  
In 30% contraception failed

Of 18 live births including one pair of twins, one major birth defect (small ventricular septal defect) was observed.

# Conclusion on the Isotretinoin PPP



- The number of new pregnancies remains small and stable.
- German study highlighted lack of use and compliance with contraception. Key concern and a stimulus for further examination of implementation and effectiveness of the PPP.
- Important to engage with healthcare professional to further investigate the implementation and effectiveness of the PPP  
-> list of questions was proposed to the HCPWG

# The List of Questions and Responses

## 1. Are you aware of the requirements of the EU approved PPP for isotretinoin?

All responded with 'yes'.

## 2. If you are aware of the documentation associated with the isotretinoin PPP, are you broadly happy with the contents of the isotretinoin PPP documentation?

All responded with 'yes'.

## 3. In what way do you think the PPP could be improved to enhance its utility in clinical practice and in particular how could the importance of compliance with the use of contraception be emphasised?

Proposals made were:

The information sources should be promoted

Implementation in HCP software

More involvement of professional associations and societies

Information should be provided through regulatory channels, such as the EMA or competent authorities

Patient information should be enhanced by visuals

Flagged tool for the pharmacist to check with the prescriber on the pregnancy test

Contraceptive supply should also be dispensed for 30 days together with isotretinoin

The awareness of HCPs and patients should be improved

HCP should discuss teratogenicity and use of contraception with the patient instead of just providing the educational material.

# List of Questions and responses

## **4. Does the documentation support a common understanding of roles and responsibilities for all healthcare professional involved (i.e. pharmacist, prescriber, dermatologist, primary care physician)?**

Nine responders were positive on this question.

There should be information or a register which can be checked by pharmacists which prescribers are qualified. There should a website for consultation for complex drugs such as isotretinoin. Furthermore, all stakeholders should approve the communication.

## **5. In your opinion, how could healthcare professional awareness of the components of the PPP be further heightened?**

Proposals made were:

By academic societies

By medical journals

By e-mails to GPs

Implementation of HCP software

Online training followed by a test and a certificate

Pharmacists should inform the patients

PPP should be part of the education / the curriculum

Post-graduate training

Frequently asked Questions document / website

Information meetings by the MAH

SMS reminders for daily intake of oral contraceptives

Specify the roles of HCPs

Availability of a pharmaceutical dossier for each patient which also includes OTC product use

Mandatory compliance for HCP and patient

# List of Questions and responses

## **6. Do you think it is important that the content and format of all documentation should be the same for all products containing isotretinoin? If yes, why?**

All responded with 'yes'. Remarks were made that it was dose depending and several other mentioned that topical formulation should be excluded.

## **7. What particular aspects of the PPP are important to ensure its utility and effectiveness?**

Two times this question was not answered. Remarks were:

Insist on oral contraceptives

There should be a structured checklist

Effectiveness of contraception should be divided in method failure vs. user failure

Consistent information should be given by both prescriber and pharmacist

Simultaneous dispensing of barrier methods and pregnancy test

More emphasis on the 30 day supply and 7 days validity

Clarification of the different roles of HCPs

Only patient themselves may collect the drug to provide good information by pharmacists

Material should have involvement of all stakeholders



# List of questions and responses

## **8. Where could the plan be improved? Material to the patients? Material to the healthcare professionals?**

Proposals for improvement were:

Patient material should be improved

HCP material should be improved

Electronic reminders such as sms or by e-mail

Pharmacist involvement with contraceptive check

Availability of different types of material; paper and online

Information should be provided through regulatory channels, such as EMA or competent authorities

Patient information should be enhanced by visuals

Specify the role of the individual HCP

Annual reminders to HCPs on the PPP

Software should give a pop-up for complex drugs

Method to ensure that the patient gets the educational material to be supported by IT programme

## **9. In your view, what is a measure of success for a PPP?**

Four responders mentioned pregnancy reports or pregnancy rate or the number of abortions. Three mentioned the prevalence or the rate of contraceptive use. A proposal was made that regular interaction between HCP and patient could be measure. Some responders did not answer this question.

# Further Work on the PPP to take forward

**Feedback from the Group on the LoQs has been extremely valuable**

**Some valuable recommendations but some clearly need careful thought about how to take forward – not necessarily issues that can be taken forward by the MAHs**

**Careful consideration is required on the practicality of taking recommendations forward**

**Competent authorities will need to work closely with relevant professional bodies at both EU and national level to further evaluate the practicalities of the proposals for improvement of the Isotretinoin PPP.**