Implementation of the Lenalidomide Pregnancy Prevention Programme (PPP) for Generic Products

1 Background

Lenalidomide is structurally related to thalidomide, a known human teratogenic substance that causes severe and life-threatening birth defects. Given the potential serious risks associated, risk minimisation measures are required as part of the marketing authorisation holder's (MAH) licensing conditions for lenalidomide. These measures include a pregnancy prevention programme (PPP) and a national controlled distribution system established in collaboration with the EU member state's National Competent Authority (i.e. the HPRA in Ireland). The controlled distribution system for lenalidomide, as agreed by the HPRA, includes the use of a prescription authorisation form (PAF) for prescribing and dispensing controls, and the collecting of detailed data relating to the indication in order to monitor the effectiveness of the implementation of the PPP and off-label use.

2 Generic Lenalidomide Products

The EU patent for lenalidomide expired Q1 2022. Six MAHs have launched generic lenalidomide products on the Irish market with the possibility of new entrants to the market in the future. As part of the conditions for the marketing of these products with the EMA and HPRA each of the MAHs are required to implement a PPP.

The Health Products Regulatory Agency (HPRA) has engaged with MAHs as well as with the NCCP and the HSE Corporate Pharmaceutical Unit in order to facilitate harmonised implementation of the PPPs for the various products in Ireland.

Two MAHs (Krka and Rowex) are implementing paper-based systems to fulfil the requirements of their PPPs. These are similar to what is already in place for the originator product i.e. Revlimid®.

Another four MAHs, Accord, Clonmel, Mylan and Teva, are implementing a shared online platform for their products. This online platform, the Patient Safety Hub, facilitates certain requirements of the lenalidomide PPP including the use of a digital PAF and a product-specific electronic ordering process and is available at www.patientsafetyhub.ie. The MAHs will liaise directly with clinicians and pharmacies regarding user access to the online platform.

All healthcare professionals prescribing or dispensing these products must ensure they read and understand the Healthcare Professional's Information Guide and should comply with all of the PPP requirements for each of the MAHs. The educational materials have been proactively distributed by MAHs and are also available either directly from the MAH or on www.hpra.ie.

3 Key elements of the PPP for generic lenalidomide products

1. The forms have been harmonised.
2. Prescriber registration with generic MAHs is not required. Instead MAHs are required to keep a record of all prescribers they have distributed materials to. This distribution list will be provided to their relevant wholesale distributor and will be regularly updated.
3. In order to measure effectiveness of implementation of the PPP, the pharmacy self-audit of paper-based systems is still required. For products ordered via the online platform, the concerned MAHs will fulfil this obligation.

Table 1. Key elements of the generic PPP process

	Previous PPP Steps	**Generic PPP Steps**
Registration	Clinician and pharmacy register with Celgene/BMS using forms from HCP Information Pack	• Prescribers do not need to register with generic MAHs, however all prescribers are required to read and understand the relevant HCP Information Guide and to adhere to the PPP. • MAHs will proactively check sources of prescribers details for any new potential prescribers and distribute the materials to them • Pharmacies must register with the MAH of **each** brand of lenalidomide they intend to dispense.
Prescribing	Clinician writes High Tech prescription and completes prescription authorisation form (PAF) for each script	• Clinician prescribes lenalidomide using international non-proprietary name (INN) (generic name) on High Tech prescription and completes PAF using paper PAF or digital PAF on the online platform.
Dispensing	Pharmacy receives prescription with PAF and submits order distributor using specific order form PAF is retained for 2 years	• The patient presents the prescription to the pharmacy with the PAF as a paper copy or if the PAF has been sent via the online platform, the pharmacy will receive a notification via email (Healthmail account). If a lenalidomide brand is not specified on the prescription, provision is made for using a different PAF if the content is aligned and this has not changed. Although each MAH has produced a PAF, the content has been harmonised across all PAFs and a pharmacy can dispense in line with the accompanying prescription irrespective of any logo/branding on a PAF. A new step for generics is that the pharmacy should now record the brand they order on the PAF as this will be needed for the self-audit process. • An order can still be placed via the online platform (for the applicable MAHs) if a paper PAF is received. In this case the pharmacists will need to transfer the details provided on the paper PAF into a digital PAF on the online system if they wish to order these specific products. • The pharmacy orders the lenalidomide product using a MAH specific order form thereby maintaining controlled distribution. • All paper PAFs received by the pharmacy must still be retained for 2 years.

Audit	Pharmacy complete annual self-audit on adherence to PPP and submit data to MAH	• "Patient Safety Hub" online platform: Pharmacy does not complete self audit. • Paper-based system: Completion of pharmacy self-audit required for these MAHs.
Ordering	Distributor only supplies product if both the prescriber and pharmacy are registered	• The distributor will continue to check if the pharmacy is registered and will not supply the product to an unregistered pharmacy. • The distributor will check the prescriber's name on the PAF against the distribution list for the relevant MAH. If the prescriber name is not listed, the distributor can continue to supply the product but they must alert the MAH who will contact this prescriber and provide them with any materials they need. This prescriber will then be added to the list of prescribers who have been distributed the materials by the MAH.

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