Understanding lenalidomide generic equivalents

Scope

Lenalidomide is available as a branded medicine (Revlimid®▼) and generic equivalents, for example lenalidomide Accord®. Sometimes the manufacturer's name is not used in the product name. The Welsh Medicines Advice Service (WMAS) supports Haematology, medical and nursing specialists and pharmacy teams in managing the introduction of generic lenalidomide by providing information on the impact of the change on storage, supply, administration and the Pregnancy Prevention Programme (PPP).

Please note that:

- We do not cover the legal authority and regulatory framework under which medicines are administered to patients.
- It is advised that the information below is used in conjunction with the information provided in the Summaries of Product Characteristics (SmPCs) for lenalidomide products.

Purpose

WMAS supports the clinical introduction of lenalidomide generic equivalents by

- Summarising information about lenalidomide generic equivalents in relation to the originator product Revlimid®▼, for consideration by specialist Haematology and pharmacy teams when preparing to use generic lenalidomide products.

- Providing pertinent information on
    - the similarities and differences in the licensed indications and product information for generic lenalidomide products and the originator product Revlimid®▼
    - the change to supply processes including the PPP.

- Providing high level information about
    - the characteristics of Revlimid®▼ and generic lenalidomide products in the form of a comparison table.

Contents

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1. Lenalidomide use in NHS Wales

Lenalidomide is licensed for the following indications

- Newly diagnosed multiple myeloma in patients who have undergone autologous stem cell transplantation
- Newly diagnosed multiple myeloma in patients not eligible for transplant (in combination with dexamethasone)
- Multiple myeloma in patients who have received at least one prior therapy (in combination with dexamethasone)
- Newly diagnosed multiple myeloma in patients not eligible for transplant (in combination with melphalan and prednisone)
- Newly diagnosed multiple myeloma in patients not eligible for transplant (in combination with bortezomib and dexamethasone)
- Myelodysplastic syndromes
- Mantle cell lymphoma
- Follicular lymphoma (in combination with rituximab)

NICE approves the use of lenalidomide for

- Previously treated follicular lymphoma (with rituximab) [TA627]

NICE approves the use of lenalidomide with restrictions for

- Multiple myeloma in people who have received at least 2 prior therapies [TA171]
- Myelodysplastic syndromes associated with an isolated deletion 5q cytogenetic abnormality [TA322]
- Relapsed or refractory multiple myeloma (with ixazomib and dexamethasone) [TA505]
- The treatment of multiple myeloma (with dexamethasone) after 1 treatment with bortezomib [TA586]
- Previously untreated multiple myeloma (with dexamethasone) [TA587]
- Maintenance treatment after an autologous stem cell transplant for newly diagnosed multiple myeloma [TA680]
- Previously treated multiple myeloma (with dexamethasone and carfilzomib) [TA695]

The NICE advice applies to the generic products in the same way as the originator product, Revlimid®▼.

The All Wales Medicines Strategy Group (AWMSG) currently make no additional recommendations.

2. Product Information

a. Presentation

Lenalidomide 2.5mg, 5mg, 7.5mg, 10mg, 15mg, 20mg, 25mg hard capsules.

The capsules are packaged in plastic and aluminium foil for all available formulations (Revlimid®▼ and generic). Each manufacturer produces packs containing 7 or 21 capsules. Additional pack sizes of 14, 28 or 42 capsules may be available for some brands, however not not all sizes are marketed in the UK. Healthcare teams are advised to check which strengths are available in a specific manufacturer's product range before prescribing. Some manufacturers do not manufacturer every strength.

b. Dose

The initial dose of lenalidomide for specific indications varies. Dosing regimens are cyclical and doses are adjusted according to clinical and laboratory responses. Refer to current prescribing information in the SmPC or the BNF. Lenalidomide is often used as part of multi-drug regimens which may include dexamethasone or rituximab for example.

The recommended dose of lenalidomide capsules should be taken orally at about the same time on the scheduled days. The capsules should not be opened, broken or chewed. The capsules should be swallowed whole, preferably with water, either with or without food.

c. Excipients

Revlimid®▼ does not contain excipients with known effect except for lactose.

The amount of lactose may vary by manufacturer, product, formulation, or strength. The lactose content of most generic lenalidomide capsules is similar to, or less than, that of Revlimid®▼, which contains up to 300mg per capsule. Lenalidomide Zentiva® 25mg capsules contain a slightly higher amount of lactose (322mg). Mylan and Teva brands do not contain lactose.

Some strengths of the generic capsules made by Piramal and Thornton and Ross contain tartrazine (E102), Sunset yellow FCF (E110) and Allura red AC (E129). There is a possible link between these colourings and hyperactivity in children.

d. Storage and stability

Lenalidomide generic products have similar storage conditions to Revlimid®▼.

- The manufacturers of Revlimid®▼ and some of the generic products do not make any special storage recommendations. However, some generic manufacturers state that the product should be stored under 25°C. The Mylan brand states that the product may be stored at temperatures up to 30 °C.

Some lenalidomide generic products have a different shelf life to Revlimid® ▼

- Revlimid® ▼ has a shelf life of 3 years
- The shelf life of generic lenalidomide products varies between 2 and 3 years

3. Evidence supporting safety and efficacy of generic lenalidomide

The European Medicines Agency (EMA) require the manufacturer of a generic medicine to show that it is comparable to the reference medicine in order for it to be given a marketing authorisation. In most cases, bioequivalence data is required to show that the generic medicine produces the same levels of the active substance in the body as the reference medicine.

4. Considerations for implementation

Shelf life

Some generic lenalidomide formulations have a shelf life of 2 years. This is 1 year shorter than that of Revlimid® ▼. It is anticipated that the impact of this difference on services is minimal.

Pregnancy Prevention Programme

Lenalidomide is structurally related to thalidomide, and if taken during pregnancy is expected to cause a teratogenic effect. All UK manufacturers must therefore have a validated PPP in place. The conditions of the PPP must be fulfilled for **all** patients unless there is reliable evidence that the patient does not have childbearing potential.

Before generic lenalidomide can be received by, or dispensed from a pharmacy, the premises must be registered with the generic supplier to agree compliance to the risk minimisation measures of their specific PPP. Education and training needs of staff involved in the prescribing and supply of lenalidomide must be addressed using the supporting materials of the PPP specific to the manufacturer's product.

Patients must be informed about the new PPP platform (as it will hold information about them) and the switch in brand of their medicine.

Patients, prescribers, and pharmacists must comply with the conditions set out in the manufacturer's PPP. A new treatment initiation form (TIF) must be completed for each patient. Where a face to face consultation is held, patients should sign the appropriate TIF to confirm their entry into the manufacturer's PPP and consent to information sharing as necessary. The TIF should be filed in the patient record. Where a telephone or virtual consultation is held, the prescriber should take verbal agreement from the patient, and clearly document this on a copy of the TIF which should be filed in the patient record. Every prescription must be accompanied by a completed Prescription Authorisation Form (PAF).

> The manufacturer's specific PPP system must be used when their product is prescribed and supplied.

Several manufacturers use the Pathfinder Risk Management Platform (RMP), an electronic PPP system developed in partnership with the NHS. It is not linked to any single company, and any manufacturer who holds a Market Authorisation for lenalidomide can sign up to use it. It enables healthcare professionals to register, initiate patients and complete and approve prescription authorisation forms as part of the risk minimisation requirements necessary for the prescribing and dispensing of lenalidomide. One of the expected benefits of this system is to drive standardisation and compliance; thereby improving patient safety. This single system supports the implementation of future contracts and any subsequent switching between products that might be necessary. Doctors, nurses and pharmacist independent

prescribers must complete the PAF at each consultation, and the dispensing team must select which supplier the product is from, supporting robust medicine reconciliation. The Pathfinder RMP cannot be used for non-registered suppliers.

Wherever possible generic lenalidomide products used in Wales will be those from manufacturers using the Pathfinder RMP. It is recognised however, that potential future supply chain problems may mean that an alternative manufacturer's product, and therefore PPP may need to be used.

Haematology and pharmacy teams must work together to ensure that the correct PPP is always used for the generic product supplied.

Stock management

When switching between Revlimid®▼and generic lenalidomide, health boards should establish a safe, efficient strategy to ensure that stock wastage is minimal.

Stock levels will continue to be reconciled by the appropriate RMP PPP pharmacovigilance team.

Table 1. Comparison of lenalidomide products

Brand	**REVLIMID®▼**	**Lenalidomide Zentiva®**	**Lenalidomide Sandoz®**	**Lenalidomide Mylan®**	**Lenalidomide Accord®**	**Lenalidomide** (Teva)	**Lenalidomide** (Thornton & Ross)	**Lenalidomide** (Ranbaxy (UK) Ltd.)	**Lenalidomide** (Piramal Critical Care Ltd.)
Pregnancy prevention programme	Bristol Myers Squibb RMP	Zentiva PPP	Pathfinder RMP	Pathfinder RMP	Accord PPP	Teva RMP	Pathfinder RMP	Pathfinder RMP	Pathfinder RMP
Lactose content	74-294mg	66-332 mg	66-332 mg	Nil	33-134 mg	Nil	54-200mg	54-215mg	52-214mg
Storage	No special storage requirement	No special storage requirement	No special storage requirement	Do not store above 30°C	No special storage requirement	No special storage requirement	No special storage requirement	Store below 25°C	No special storage requirement
Shelf life	3 years	3 years	3 years	2 years	3 years	3 years	3 years	2 years	3 years
Strengths available	2.5mg, 5mg, 7.5mg, 10mg, 15mg, 20mg, 25mg	5mg, 10mg, 15mg, 25mg	5mg, 7.5mg, 10mg, 15mg, 20mg, 25mg	2.5mg, 5mg, 7.5mg, 10mg, 15mg, 20mg, 25mg					
Presentation	Hard capsules								
Licensed indications	• Newly diagnosed multiple myeloma in patients who have undergone autologous stem cell transplantation • Newly diagnosed multiple myeloma in patients not eligible for transplant (in combination with dexamethasone) • Multiple myeloma in patients who have received at least one prior therapy (in combination with dexamethasone) • Newly diagnosed multiple myeloma in patients not eligible for transplant (in combination with melphalan and prednisone) • Newly diagnosed multiple myeloma in patients not eligible for transplant (in combination with bortezomib and dexamethasone) • Myelodysplastic syndromes* • Mantle cell lymphoma* • Follicular lymphoma (in combination with rituximab)								

Healthcare professionals are reminded of the importance of reporting suspected adverse drug reactions to the Yellow Card scheme. [Yellow Card | Making medicines and medical devices safer (mhra.gov.uk)]

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