

NCCP Guidance on the use of Biosimilar Medicines in Cancer Treatment

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All comments and feedback are welcome at oncologydrugs@cancercontrol.ie

1 Background

1.1 What is a biosimilar?

A biosimilar¹ is a biological medicine that is highly similar to another biological medicine (also known as a reference medicinal product) which already has a marketing authorisation and has been approved for use in patients. As such, biosimilars contain a version of the active substance of an approved biological medicine and generally should be used in the same way for its own approved indications (1). The focus of development of biosimilars has been to establish similarity to the reference medicinal product through a rigorous comparability exercise which is carried out at the quality, non-clinical and clinical levels. It should be remembered that “biosimilar” is a regulatory term, not a scientific one. Because biosimilars are biological medicines, they are not the same as generic medicines. Therefore they are not currently included in the HPRA ‘list of interchangeable medicines’ which refer to generic medicines that can be substituted for each other at pharmacy level. Biosimilars can be used in the place of the reference products (2, 3). This should be done in line with the hospital’s biosimilar policy.

1.2 How are biosimilars approved?

Biosimilar medicines must be manufactured to the same quality standards as the reference medicine. The majority of biosimilars are authorised through a centralised procedure, co-ordinated by the EMA. The approval process involves a complete scientific evaluation of the biosimilar comparability exercise. This is a tiered approach, based on three steps (4):

1. Quality comparability (physicochemical and biological)
2. Pre-clinical comparability (in vitro and more rarely with in vivo studies)
3. Clinical comparability (pharmacokinetics, pharmacodynamics, safety (including immunogenicity) and efficacy)

1.3 How are indications extrapolated?

For a biosimilar product to be approved, it needs to be demonstrated that there are no clinically meaningful differences relative to the reference medicine in a sensitive patient population. Once comparability has been demonstrated in one indication (i.e. the most sensitive), confirmative clinical studies are not required for all other approved indications.

¹ The term biosimilar is used to describe a medicine which is highly similar to a reference biological medicine in terms of its quality, safety and efficacy (1)

When the same mechanism of action applies, the other indications may be approved for the biosimilar on the basis of extrapolation, as efficacy and safety in each indication has already been established with the reference product. Extrapolation to other indications is evaluated as part of the marketing authorisation assessment process on a case-by-case basis (4, 5) and will be reflected in the biosimilar marketing authorisation. This means that the biosimilar may be approved for all the indications for which the reference medicine is approved. This needs to be communicated to all healthcare professionals who would be more familiar with the approval of medicines being based on clinical trials in each individual indication.

2 Use of Biosimilar Medicines

2.1 Medicines Optimisation

All persons involved in the prescribing, administration and utilisation of biosimilars, including clinicians, nurses, pharmacists and patients, need to be informed of the safety and the therapeutic equivalence of biosimilars to the reference medicine. Staff need to be informed of any prescribing recommendations as well as safety measures put in place to ensure correct prescribing, adverse event reporting and traceability. The implementation of a hospital biosimilar policy should follow a methodical, staged approach with engagement of the relevant stakeholders, which may include clinicians, nurses, pharmacists, other healthcare professionals, those involved in hospital procurement as well as patients.

2.2 Interchangeability

Interchangeability refers to the possibility of exchanging one medicine for another medicine that is expected to have the same clinical effect (6). In Ireland, unlike the generics of chemical medicines, the substitution of biosimilars by a pharmacist is currently not included in the legislation (7). The hospital biosimilar policy should detail the changeover process to be followed when changing from the reference product to a biosimilar (or vice versa). This may include supplying a patient with dedicated patient information on the use of biosimilars and/or a discussion between patients and the prescribing physician. Once a biosimilar has been approved, it can be considered appropriate to switch, should the patient's clinician wish to do so. (1)

A reference medicinal product and its biosimilar may have the same international non-proprietary name. The biosimilar has been shown to be highly similar but not necessarily identical to the reference product. Therefore, all biological medicines should be clearly identifiable by brand name to ensure traceability. This will also ensure that substitution of biosimilar medicines does not inadvertently occur when the medicine is dispensed by a pharmacist.

2.3 Safety and Adverse reaction reporting

As for all medicines, it is essential to report any suspected adverse reactions that are potentially linked to the usage of biosimilar medicines. Records maintained should allow for full traceability, including brand name and batch number. As for all newly licensed biological medicines, biosimilars will be subject to additional monitoring following approval. This is indicated by the black inverted triangle symbol displayed in the SmPC and package leaflet. This does not imply that there are any additional safety concerns for biosimilars, as all newly authorised biological medicines are subject to this additional monitoring. A medicine remains under additional monitoring for five years or until the EMA's Pharmacovigilance Risk Assessment Committee decides to remove it from the Additional Monitoring list.

As for all medicines, healthcare professionals are asked to report any suspected adverse reactions associated with the use of biosimilars. The brand name and batch number should be included in any report of a suspected adverse reaction to a biological medicine (including biosimilars). Suspected adverse reactions should be reported to the HPRA (see www.hpra.ie for further details) (1). Clear identification of biological medicines is of particular importance and national legislation highlights the requirement to identify the brand name and batch number of the biological medicine concerned in adverse reaction reports submitted (8).

3 Cost Efficiencies

In line with the 2016 Framework Agreement on the Supply and Pricing of Medicines (The Agreement) the price of a biologic medicine which becomes a patent-expired non-exclusive biologic medicine after 1st August 2016, shall reduce to 80% of the ex-factory price of that Biologic Medicine as of the 31st July 2016. In addition to this price reduction there is a further rebate of 12.5% (9).

The Agreement also allows for the HSE and/or hospitals to procure these medicines through tender processes or public procurement procedures (9). This will allow hospitals to achieve best value on price in line with their local recommendations on the use of biological medicines and biosimilars in cancer treatment.

Such supply or reimbursement may also be to the HSE or publicly-funded entities and State Agencies whose functions include the provision of medicines. Reference to State-funded hospitals in the Agreement should be taken to refer to all such possible entities.

4 Recommendations

4.1 Use of biosimilars

- Biosimilars are suitable for use in the treatment of cancer patients in line with their licensed indication(s).
- The use of a biosimilar should be in line with the licensed indication and the hospital's biosimilar policy.
- Implementation of a hospital biosimilar policy should follow a methodical, staged approach with engagement of the relevant stakeholders, which may include clinicians, nurses, pharmacists, other healthcare professionals, those involved in hospital procurement as well as patients.

4.2 Prescribing of biosimilars

- Any medicine for which a biosimilar is available will need to be prescribed using brand name e.g. Mabthera[®], Truxima[®] in order to ensure a patient receives the intended product and to ensure correct reporting of any adverse events, unless the hospital policy ensures that dispensing of the product safeguards this process.

4.3 Switching to and between biosimilars

- Any new patient can be considered for treatment with a biosimilar in line with the changeover process detailed in the hospital's biosimilar policy. Any patient on an existing treatment with a reference product or a biosimilar can be considered for switching to a biosimilar. The process to be followed for switching should be detailed in the hospital's biosimilar policy.

- Once a biosimilar has been approved, it can be considered appropriate to switch, should the patient's clinician wish to do so. (1) Patients should be maintained on their current brand unless a switching decision has been made in line with the local policy on switching. This includes situations where a patient may require treatment temporarily in another hospital.

4.4 Patient Information leaflets

- Information for patients should be supplied to all patients and they should be encouraged to read these leaflets to ensure they are familiar with their medicine. The HPRA have developed general information material on biosimilars for patients (3) which is available on its website at the following link: <http://www.hpra.ie/homepage/medicines/special-topics/biosimilar-medicines/questions-and-answers-for-patients>. This may be used as a source of information for patients.

5 Conclusion

The introduction of biosimilar products into the healthcare market in Ireland is welcomed by the NCCP. Many bodies in Europe and in Ireland have issued positive recommendations on their use (4, 11-15).

The issue of sustainability of the cost of Systemic Anti-Cancer Therapy has been much discussed. Biosimilars and generics represent some of the ways forward to obtain sustainability and maximise the funding for new medicines to be made available for patient treatment.

6 References

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15. Tabernero J, Vyas M, Giuliani R, Arnold D, Cardoso F, Casali PG, et al. Biosimilars: a position paper of the European Society for Medical Oncology, with particular reference to oncology prescribers. 2017.

Appendix 1. Bibliography

| Publication Name | Publication Organisation |
|--|---|
| Guideline on Similar Biological Medicinal Products | European Medicines Agency |
| Biosimilar Medicines: Overview | European Medicines Agency |
| Biosimilars in the EU: Information Guide for Healthcare Professionals | European Medicines Agency |
| What I need to know about Biosimilar Medicines: Information for patients | European Medicines Agency |
| Fourth stakeholder conference on biosimilar medicines | European Commission and European Medicines Agency |
| Guide to Biosimilars for Healthcare Professionals | Health Products Regulatory Authority |
| Biosimilar Medicines in the Irish healthcare setting | HSE Medicines Management Programme |
| Biosimilars: a position paper of the European Society for Medical Oncology, with particular reference to oncology prescribers | European Society for Medical Oncologists |
| The Cancer Vanguard. Biosimilars - Getting it right first time <ul style="list-style-type: none"> Contains a number of tools and templates on topics including education and implementation | NHS England |
| EAHP Position paper on Biosimilar Medicines | European Association of Hospital Pharmacists |
| Biological and Biosimilar Medicines: What patients should know | Health Products Regulatory Authority |

Appendix 2. Members of NCCP Biosimilar Medicines in Cancer Group

| Organisation | Member |
|---|---|
| NCCP | Ms Patricia Heckmann, NCCP Chief Pharmacist (Chair) Ms AnneMarie De Frein, NCCP Deputy Pharmacist |
| Consultant medical oncologist (ISMO rep.) | Dr. Maccon Keane, Galway University Hospital Dr. Patrick Morris, Beaumont Hospital |
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| Health Products Regulatory Authority | Ms. Joan O'Callaghan |