IPU Submission to the Department of Health on a National Biosimilar Medicines Policy

September 2017

1. Introduction

The Irish Pharmacy Union (IPU), with almost 2,200 members working in over 1,700 pharmacies, is the representative and professional body for community pharmacists. Our mission is to promote the professional and economic interests of our members. Members of the IPU are committed to delivering a quality, accessible, personal and professional service that puts the patient first and has, as its primary goal, the optimisation of the health and wellbeing of society. Community pharmacies are located in every town, village and community in the country. Research shows that consumers and patients visit their pharmacies far more frequently than any other part of the healthcare system, with 85 million visits to pharmacies each year, making pharmacists the most accessible healthcare providers.

We welcome the opportunity to make a submission to the Department of Health on its National Biosimilar Medicines Policy.

2. Pharmacy High Tech Scheme

Most biological and biosimilar medicines are classified as high tech medicines for the purposes of reimbursement. It is worth noting that Ireland is one of the few EU countries where high tech medicines are supplied through community pharmacies; in most other Member States, patients must, at great inconvenience, go to a hospital pharmacy to collect their high tech medicines. Commenced in 1996, the High Tech Scheme provides for the supply and dispensing of high tech medicines through community pharmacies.

2.1 High Tech Eligibility

The scheme operates as a patient-specific pharmaceutical care and treatment programme, with a nominated pharmacy responsible for a specific patient and their complete and complex medication and health needs. To be eligible for the High Tech Scheme, the initial prescription for the high tech medicine must be initiated by a consultant in an Irish hospital; subsequent prescriptions may be written by a GP or registered nurse prescriber. Typically, the patient is referred back to the consultant for review at prescribed intervals.

2.2 Nominated Pharmacy

When a patient is first prescribed with a high tech medicine, the hospital clinic makes contact with the patient's preferred pharmacy, typically by faxing a copy of the prescription, to give the pharmacy notice to allow the pharmacist to order the high tech medicine for the patient. The pharmacy must then fax a copy of the prescription to the HSE local office to ensure that the nomination of the pharmacy is recorded for reimbursement purposes. The patient can only collect their high tech medicine from their nominated pharmacy.

2.3 High Tech Ordering

The pharmacy orders the high tech medicine from the appropriate manufacturer or wholesaler or agent. For some medicines, this can take several days due to the direct-to-pharmacy distribution methods imposed by some pharma companies and the lack of availability of these products through the usual wholesale channels. This fragmentation of the supply chain means that the least efficient and poorest service levels to pharmacies apply to the delivery of high tech medicines, which are the most expensive and often most critical medicines dispensed. The supplier of the high tech medicine is paid directly by the HSE Primary Care Reimbursement Service (PCRS). The pharmacy must sign the delivery docket on receipt of the medicine and PCRS will audit suppliers on a regular basis. The High Tech Medicines Scheme currently operates as in Figure 1 below.

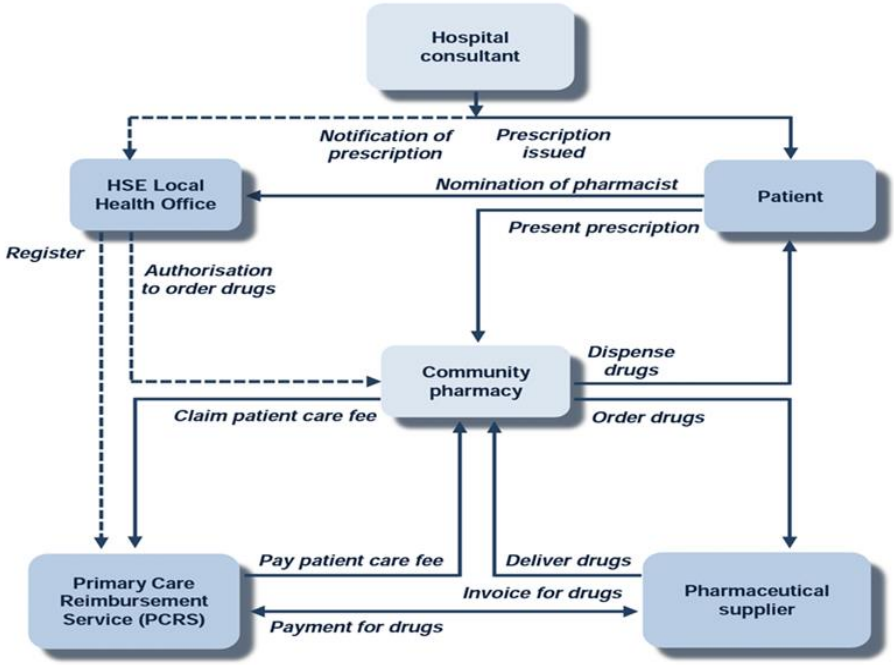

Figure 1: High Tech Medicines Scheme - current process

The HSE PCRS is currently developing a High Tech Hub Ordering and Management System to streamline administration of the scheme for pharmacists and to provide the HSE with enhanced visibility of stock management and spending on this scheme. The IPU has engaged with the HSE on the design and development of the High Tech Hub, which has a targeted 'go live' date, in a phased approach, beginning in December 2017. This new High Tech Hub must ensure nationwide best in class service levels in respect of all supplies of high tech medicines to pharmacies.

2.4 Role of the Pharmacist

Patients receiving care and treatment under the High Tech Scheme have complex medical and health needs, and management frequently involves vital treatment regimens with novel and/or toxic medicines. Patient-specific monitoring is required on an ongoing basis and the pharmacist monitors overall medicines therapy, notwithstanding that a high tech medicine may not be required at a particular patient visit. Comprehensive patient counselling on the correct use, adverse effects, warnings on precautions and storage of the medicine is required to ensure a patient is aware of the appropriate use of the medicine. There must be constant vigilance around adverse drug reactions, drug interactions and other adverse events, especially where the high tech medicine has been designated for extra pharmacovigilance by the European Medicines Agency (EMA). Such high-risk medicines are identified in practice by an inverted black triangle ▼ on their package leaflet and Summary of Product Characteristics (SmPC). Rather than a dispensing fee or a margin on the cost of the medicine, pharmacists are paid a monthly patient care fee by the PCRS for each patient, which is halved in months when there is no dispensing.

2.5 Benefits to HSE and Patients

These arrangements are designed to provide a quality community-based service to patients by ensuring the active involvement of community pharmacists in the dispensing of high tech medicines that were previously supplied, in the main, through hospitals or local health offices. The scheme has proved to be the most cost-effective distribution method for the HSE and the most convenient to the patient, whilst, at the same time, safeguarding patient safety and health outcomes through the comprehensive role undertaken by the community pharmacist.

3. Interchangeability, Switching and Substitution

The terms interchangeable, switching and substitution all mean quite different things.

- Interchangeable refers to the medical practice of replacing one medicine with another medicine and expecting to get the same clinical effect. This can happen in any clinical setting and with any patient.
- Switching refers to the practice of a prescriber making a decision to change a medicine a patient is receiving mid-treatment.
- Substitution refers to the practice of changing the brand of medicine a patient is taking at pharmacy level without requiring knowledge or consent of the prescriber.

3.1 Interchangeability

The European Medicines Agency (EMA) has acknowledged that there are no clinically meaningful differences between a biosimilar and the reference biological medicine and has stated that the evidence acquired over 10 years of clinical experience shows that biosimilars approved through the EMA can be used as safely and effectively in all their approved indications as other biological medicines[1].

A systematic review by Chingcuanco et al, published in the Annals of Internal Medicine, concluded that the existing evidence supports the biosimilarity and interchangeability of Tumour Necrosis Factor-α (TNF-α) Inhibitors[2]. Consequently, there should be no concerns about the safety or efficacy of biosimilars and their increased use should be encouraged; the only consideration should be whether this is done through switching or substitution.

3.2 Switching

Biosimilars have been authorised in Ireland since 2006, in line with all other Member States. The Department has acknowledged in the consultation paper that uptake of biosimilars in Ireland has been low relative to other EU countries. There is no reason, therefore, to believe that encouraging prescribers to prescribe biosimilars initially would increase the uptake since prescribers have always had the right to do this; they just haven't. However, knowing

[1] European Medicines Agency, Biosimilars in the EU: Information Guide for Healthcare Professionals, 2017

[2] Chingcuanco et al, Bioequivalence of Biosimilar TNF-α Inhibitors Compared with Their Reference Biologics.

that pharmacists will have the right to substitute for new patients, as described in Section 3.3, prescribers should be encouraged to switch existing patients from a biological reference product to a biosimilar, ensuring that the patient's pharmacy is informed of this switch at least one month in advance, to save the pharmacy from ordering the biological which then typically cannot be returned to the wholesaler.

3.3 Substitution

The Health (Pricing and Supply of Medical Goods) Act 2013 lays out the rules and regulations for generic substitution of medicinal products, identified as interchangeable by the Health Products Regulatory Authority (HPRA). Pharmacists have demonstrated that they have the competence and capability to implement this legislation, resulting in a significant increase in the usage of generic medicines in Ireland, from 11% by volume pre-2013 to 53% by 2016.

In our opinion, it was a mistake at the time the Act was being passed to exclude the substitution from a biological reference product to a biosimilar. It would have been preferable for the legislation to have remained silent on the matter, since such substitution could only have been enabled if the HPRA published an interchangeable list for the biological reference product. Now, however, an amendment to primary legislation is required to facilitate substitution by a pharmacist from a biological reference product to a biosimilar, the most effective and easily implemented option to achieve increased uptake of biosimilars in Ireland.

The HPRA does not recommend that patients switch back and forth between a biosimilar and a biological reference medicine[3]. In our proposal, a pharmacist, on receiving the initial high tech prescription for a patient, will make the decision to dispense and supply a biosimilar or the biological reference medicine. A note of this will be made in the patient's medication record (PMR) and, because the patient nominates a single specific pharmacy for their high tech medicine, subsequent supplies will be for the same product and no further switching will occur.

[3] Health Products Regulatory Authority, Guide to Biosimilars for Healthcare Professionals and Patients, 2015

3.4 International Biosimilar Policies

The Department's consultation paper reviews switching and substitution policies in other Member States but does not highlight that, as outlined in Section 2, Ireland is one of the few EU countries where high tech medicines are supplied through community pharmacies; in most other Member States, patients must go to a hospital pharmacy to collect their high tech medicines. Consequently, any switching or substitution policy in those Member States would be agreed by a multi-professional team in a hospital, probably through a Drugs and Therapeutics Committee, and the agreed medicine would be dispensed by the hospital pharmacy.

4. Legislation and Guidelines

4.1 Legislation

In Ireland, the high tech medicine will be dispensed in a community pharmacy. To enable pharmacist substitution of biological reference products, Section 5(7)(d) of the Health (Pricing and Supply of Medical Goods) Act 2013, which prohibits substitution of biologicals, would need to be amended.

4.2 Guidelines

Any National Biosimilar Medicines Policy should contain a table, mapping the reference product to the relevant biosimilars, thus providing community pharmacists with a guide on which biosimilar to choose. An example of such a guide is laid out in Table 1 below.

Therapy Area	Active Ingredient	Reference Product	Biosimilar
G-CSF	Filgrastim	Neupogen	Accofil Grastofil Nivestim Ratiograstim Tevagrastim
TNF-α Inhibitor	Infliximab	Remicade	Inflectra
TNF-α Inhibitor	Etanercept	Enbrel	Benepali
Erythropoietin EPO	Epoetin Zeta	Erypo/Eprex	Retacrit
Gonadotropin	Follitropin Alfa	Gonal-F	Bemfola

Table 1: Biosimilars reimbursable in Ireland mapped against the Reference Product: Source IPU Product File

4.3 ePrescribing

Another option to consider is that when ePrescribing is eventually rolled out in Ireland, the National Medicinal Product Catalogue that will support ePrescribing should facilitate prescribing by Virtual Medicinal Product (VMP), thus encouraging generic and biosimilar prescribing by the initiating consultant. The IPU Product File is already coded for VMPs so would be an ideal source for the National Medicinal Product Catalogue.

5. Support and Education

5.1 Current Support

Currently, when a high tech injectable is prescribed for a patient for the first time, the pharma company pays, through a third party, for a nurse to go to the patient's home, after the patient has collected the new medicine from the pharmacy, to instruct the patient on how to administer the medicine. The pharma company also sends a nurse to the patient's home every 6 months to collect used needles and issue a personal sharps bin. These activities are often a condition of the high tech medicine being eligible for GMS reimbursement. There is no reason why community pharmacists couldn't carry out this role.

5.2 Pharmacycare

Hibernian Healthcare, with the support of the IPU, has produced an online platform called Pharmacycare, to facilitate community pharmacists in offering a range of Patient Support Programmes (PSPs) to patients on high tech medicines. Examples of such programmes include Patient Education, Sharps Service and Compliance Support. Current Patient Support Programmes often fall short in supporting the patient on their journey with a life-changing chronic illness. The PSP services are typically front-ended and can leave the patient to their own devices for several months until their next consultant appointment at the hospital. Pharmacycare offers a range of pharmacy-led services that bridges those gaps, improves engagement with the medication and supports compliance. Patients are enrolled, following consent, onto Pharmacycare, either by the hospital clinic or by the pharmacy. Both the consultant and the pharmacist have access to the patient record.

Pharmacycare is already available in a significant number of pharmacies; the initial Pharmacycare service is a sharps service for injectable devices for Roche (RoActemra), Novo

Nordisk (Norditropin), Biogen (Benepali) and Nordimet (Nordic Pharma). The patient brings their full sharps bin to the pharmacy and is provided with a new sharps bin. Future planned services include:

- Prescription updates – the pharmacist will update the patient record on the Pharmacycare system each time the prescription is dispensed. This allows the consultant to check patient compliance.
- Patient education – training programmes to help patients learn how to inject their high tech medicine.
- Compliance coaching – pharmacists will receive training in compliance and coaching and will then conduct compliance coaching by appointment with patients.
- Patient outcome measure – this will include testing of various health metrics to establish post-medication efficacy.

Pharmacycare can ensure that both the consultant and pharmacist are aware of the exact medicine (biological reference product or biosimilar) that a patient is taking and can provide the pharmacist with the tools to deliver education and support. Pharmacycare also facilitates pharmacists in reporting adverse drug reactions to the prescriber, the HPRA and the pharma company.

5.3 Pharmacists' CPD

Continuing Professional Development (CPD) for pharmacists is mandatory and is regulated by the Pharmaceutical Society of Ireland (PSI) and monitored by the Irish Institute of Pharmacy (IIOP). Pharmacists are obliged to keep up to date with new therapies and treatments. The IPU provides continuing education to pharmacists, through IPU Academy, in the form of face-to-face courses, online courses, podcasts, webinars and written articles. Examples of courses that IPU Academy has produced recently in relation to biologicals and biosimilars include Biosimilars, Rheumatology, Monoclonal Antibodies and Cancer Therapy.

The IIOP offers a face-to-face course on Quality Improvement in the Supply of High Risk Medicines. On successful completion of this programme participants should be able to:

- Identify what are high-risk medicines and the factors that increase the relative risk in relation to other medicines;
- Recognise process errors which occur in the prescribing, dispensing, administration and/or supply of high-risk medicines as defined in this programme;
- Outline the principle side-effects and symptoms of toxicity associated with high-risk medicines;
- Identify what specific information is required to complete a thorough review of a prescription for a high-risk medicine;
- Identify the points in the medication use process where medication error is at increased relative risk with a view to informing patients regarding the safe use of high-risk medicines;
- Develop a procedure to ensure the appropriate counselling of patients regarding the importance of regular therapeutic review by a physician and the monitoring associated with long-term use of high-risk medicines;
- Evaluate the quality of the supply of high-risk medicines in their current practice using risk analysis tools to identify deficits and risks in quality provision;
- Devise a continuous quality improvement system to reduce the risk of error occurring in the dispensing/supply of high-risk medicines, which includes review of quality related adverse events, e.g. dispensing errors, near misses, complaints;
- Develop an action plan to engage all members of their pharmacy team in quality improvement processes including the training of pharmacy staff to identify high-risk medicines and take appropriate steps to reduce associate risks.

It should be clear from the above that any new policy on biosimilars would be incorporated into the relevant continuing education courses.

6. Incentives and Disincentives

6.1 Prescriber Incentive

The consultation paper questions whether there should be some form of financial incentive for prescribers, either to prescribe biosimilars to new patients or to switch existing patients. The Indicative Drug Target Savings Scheme, IDTS, was introduced by the Department of

Health in 1993, following agreement with the Irish Medical Organisation (IMO). The purpose of the scheme was to assist GPs in achieving cost-effective prescribing and was considered an integral part of the blueprint for general practice. The scheme was suspended in 2006, following an independent review by the National Centre for Pharmacoeconomics, which concluded that there was no evidence to show that the IDTS was achieving its objectives. There is no reason to suppose that if a similar scheme were to be introduced for biosimilars it would achieve its objectives.

6.2 Patient Co-payment

Under the current legislation which provides for generic substitution for non-biological medicines, the patient must pay the difference in cost between the generic and the brand medicine if they wish to have the brand medicine, unless the prescriber specifically states that no substitution should occur. The introduction of a similar policy for biosimilars could be considered.

6.3 Pharmacist Incentive

Pharmacists are experts in the use and effects of medicines and are perfectly placed to implement a national substitution policy for biosimilar medicines. There is, however, a significant difference between interchangeability of small-molecule medicines with identical active ingredients and substitution of biosimilars which contain highly similar molecules and provide clinically equivalent effects. Given the complexity of these patients' medical conditions and medicine regimes, implementing biosimilar substitution would require a meaningful consultation with the patient at the point of first dispensing of the biosimilar. Pharmacists, given their accessibility and the high levels of trust[4] that the public places in them, are perfectly placed to have that consultation with the patient and to provide all the advice, information and counselling that is required to reassure the patient and facilitate the substitution. Pharmacists' increased professional obligations in this regard, as well as the substantial additional time and resource costs involved in delivering these savings for the State, must be adequately recognised by way of a properly constructed gain-sharing agreement.

[4] Pharmaceutical Society of Ireland News Release 24 July 2017: "Public trust in pharmacists remains high"

7. Cost of High Tech Medicines

7.1 Cost of Drugs Bill

Much hype is given to the cost of the drugs bill in Ireland, without acknowledgment of the reasons why the drugs bill continues to increase. Ireland prides itself on the improvement in life expectancy, which has improved significantly in the past decade. Between 2003 and 2014, life expectancy in Ireland for males increased from 75.7 to 79.3 years and for females from 80.7 to 83.5 years[5]. This is a positive development which reflects improvements in healthcare. It is not rocket science to conclude that, if life expectancy increases, the number of older people increases and those older people typically need medicines to keep them in good health. The number of people aged 65 years and over increased by 30.2% between 2006 and 2015 (compared with an increase of 15.1% for the EU 28 over the same period). This trend in ageing is set to continue, with CSO projections showing a 37% increase in the 65+ age group between 2015 and 2026.

Furthermore, the drugs bill should not be looked at in isolation. At present, chronic diseases account for a significant proportion of hospital activity, including 40% of hospital admissions and 75% of hospital bed days. Whilst high tech medicines, in particular, are expensive, they keep people healthier and out of hospital. Therefore, the reduction in the cost of A&E attendances and hospital admissions must be given mention when assessing and reporting on the drugs bill.

In addition, people who would previously have died from diseases such as cancer now survive due to the new medicines available, as demonstrated in Figure 2. If life expectancy is the measure by which the Government wishes to reflect the health of its citizens, then it must accept that spending on medicines will of necessity continue to increase over time.

[5] Department of Health Capacity Review 2017: Public Consultation

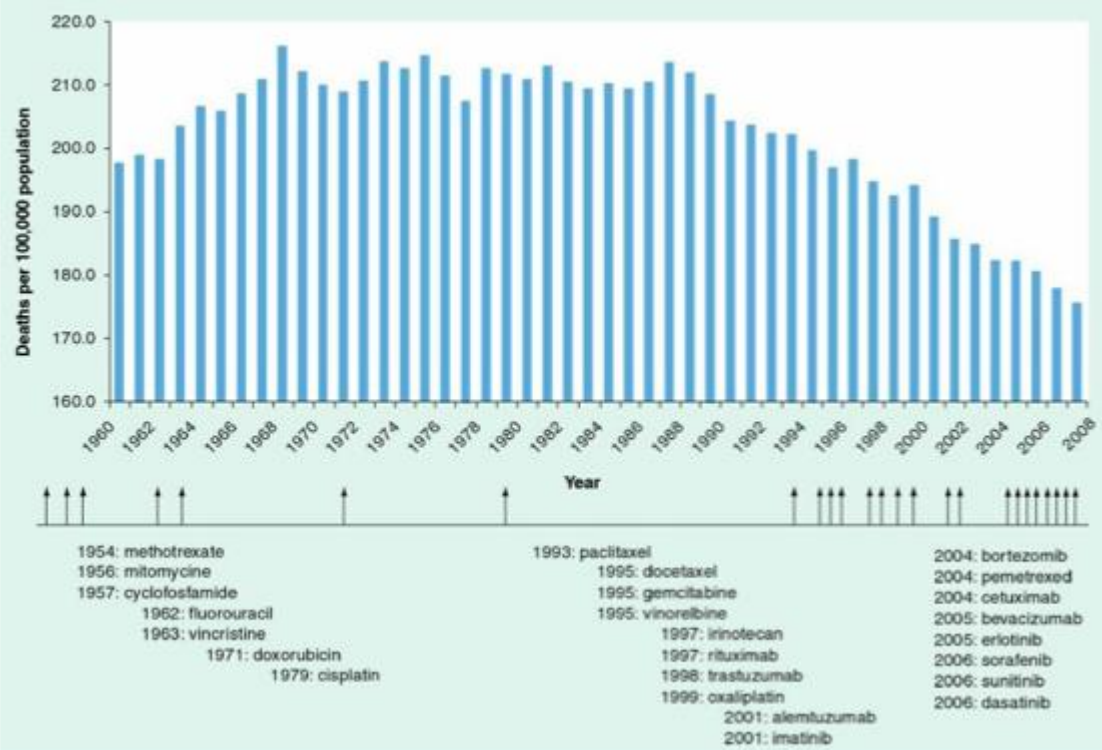

Figure 2: Carin A Uyl-de Groot et al. The Economics of Improved Cancer Survival Rates: Better Outcomes, Higher Costs. Expert Rev Pharmacoeconomics Outcomes Res. 2010;10(3): 283-292

As mentioned in Section 2, Ireland is one of the few EU countries where high tech medicines are supplied through community pharmacies; in most other Member States, patients must go to a hospital pharmacy to collect their high tech medicines. Nevertheless, when comparing Ireland's primary care drugs bill to that of other Member States, it is never mentioned that high tech medicine costs are reported under secondary care in those other Member States, thus making it seem that Ireland's primary care drugs spend is out of kilter.

7.2 Biosimilar Cost Saving Opportunity

Applied Strategic, a UK consultancy firm with expertise in biosimilar markets, conducted an initial assessment of the savings opportunity presented by biosimilars in the Irish health system. Using published PCRS data, they concluded that, in the absence of specific steps being taken to improve biosimilar uptake, spending on biologics can be expected to reach €740 million in 2019. Even though biosimilars can provide more cost effective treatment, thus broadening patient access to treatment for a given budget, uptake has been historically low in Ireland, with biosimilars representing less than 10% market share, which is significantly lower than the EU average.

Applied Strategic's assessment of the Irish biologics and biosimilar market identified a potential saving of €370 million over the next 3 years with optimum biosimilar entry and penetration.

Three types of opportunities for existing biologics are identified. Early biosimilars are those which are currently available (for more than one year) but have a market share significantly lower than EU average and could provide immediate potential savings. Evolving biosimilars are those which have recently been approved (less than one year) or are under review in EU and could enter Ireland in the near future. Potential current savings could be achieved, with even greater future savings possible. Future biosimilars are those which are not yet available but many of which are in development with future opportunity to enter the market. Significant future savings are possible, given the right policies.

The potential savings estimate of €370 million over the next three years is made up of €90 million in year one, €120 million in year two and €160 million in year three. It is based on assumptions of biosimilar prices which are 30%, 40% and 50% lower than the originator's full price in years one, two and three respectively, with biosimilar market share of 20%, 40% and then to 60% in those first three years. This is combined with the originator price drop of 30% when biosimilars become available, which is provided for in the IPHA Agreement, while the originator's market share reduces to 80%, 60% and then to 40% in years one, two and three.

7.3 Reimbursement Policy

Under the *Framework Agreement on the Supply and Pricing of Medicines 2016* (the IPHA Agreement), the price of patent-expired non-exclusive biological medicines is reduced by 80% once a biosimilar is available for sale and supply in Ireland. However, only 10 out of the 28 biosimilars centrally authorised by the EMA are currently reimbursable in Ireland. Because biological reference products which don't have a biosimilar available for sale and supply in Ireland do not have to reduce their price, the savings envisaged under the IPHA Agreement may not be realised.

€62 billion worth of biological medicines are expected to go off patent by 2020[6]. There is no incentive for industry to market biosimilars in Ireland unless they can be assured of a high volume of the market. Because prescribers tend to prescribe the biological reference product rather than the biosimilar, sales of the biosimilar remain very low. For example, Enbrel sold 14,157 packs during May 2017, with its biosimilar, Benepali, selling just 36. There is danger that a policy that involves poor outcomes for the pharmaceutical industry will result in many players not placing their biosimilars on the Irish market. The most effective and efficient way to reverse this trend and increase biosimilar usage is to allow pharmacists to substitute.

7.4 Tendering

Tendering for medicines may lead to a price war resulting in smaller companies which provide medicines being driven out of the Irish market because it makes no financial sense for them to remain. In those circumstances, the power to supply could rest with one company only and the risk of medicine shortages could increase, as has been seen in other EU countries.

7.5 Pricing Policies

Similarly, if the reimbursable or reference price of a medicine is set too low, there will be no incentive for manufacturers to market their products in Ireland, given the relatively small size of the Irish market. There should be an obligation on the Department of Health to make sure that there is a sufficient security of supply of medicinal products for patients and that any decisions taken will not lead to increased shortage of medicines. We need to encourage industry to market their products, including biologics and the associated biosimilars, in Ireland.

[6] Medicines for Ireland Policy Manifesto 2017

8. Conclusion

It is timely that the Department intends to produce a National Biosimilar Medicines Policy as it dovetails nicely with the Department's health service capacity review which acknowledges the interdependent nature of capacity across primary care and acute care and the ongoing developments in the way care is delivered.

As outlined in this submission, €62 billion worth of biological medicines are expected to go off patent by 2020 globally, providing significant savings possibilities, and there is already a potential three year saving of €370 million for the Irish health system – none of which will be realised if biosimilar usage in Ireland is not brought to European norms. As the experience of generic substitution since 2013 has demonstrated, allowing community pharmacists to substitute is the fastest and most effective way to ensure a rapid and meaningful increase in the usage of biosimilars.

We would welcome the opportunity to meet with the Department to discuss the issues outlined in this submission in greater detail.