The role of regulators to increase knowledge and confidence in biosimilar medicines

- a member state perspective

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Agenda

- Uptake of biosimilars in Denmark
- Legal framework
- Action plan on biologicals and biosimilars
- Raising awareness
  - Patients
  - Physicians
- Results of safety surveillance of biosimilars
- Continous work

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Uptake of new biosmilars in Denmark

- National recommendation to use biosmilars
- Nationwide tender process
- Biosimilars win the tender and are supplied to hospital pharmacies
- Both treatment naïve patients and patients in well established treatment can be treated with a biosimilar
- In case of specific, individual medical reasons for using the reference product this is possible

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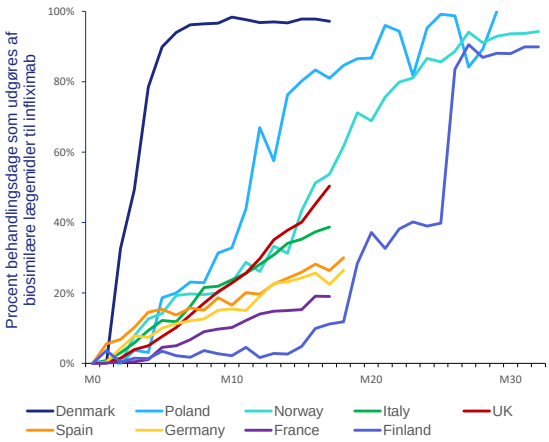
Uptake of biosimilar infliximab in some EU countries



Kilde: QuintilesIMS MIDAS MTH July 2016.

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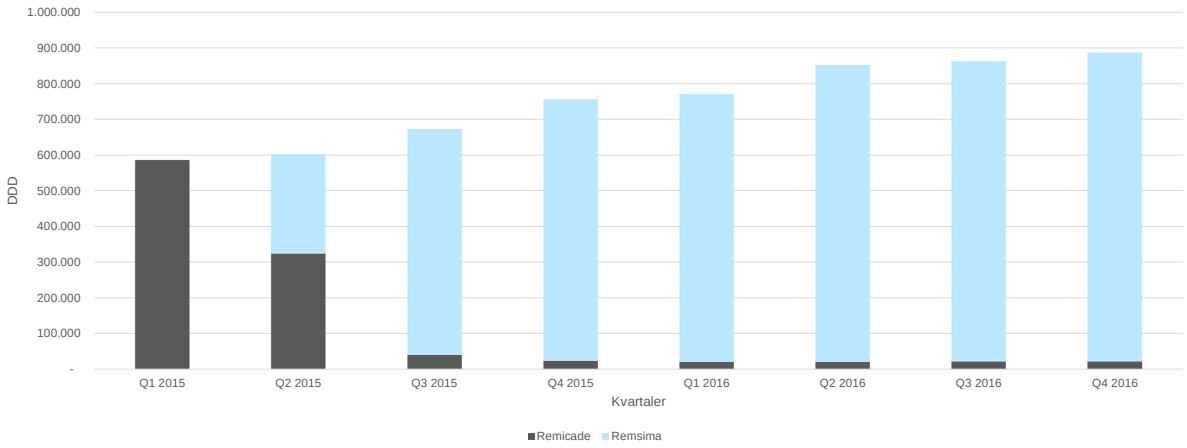
Infliximab consumption in DDD



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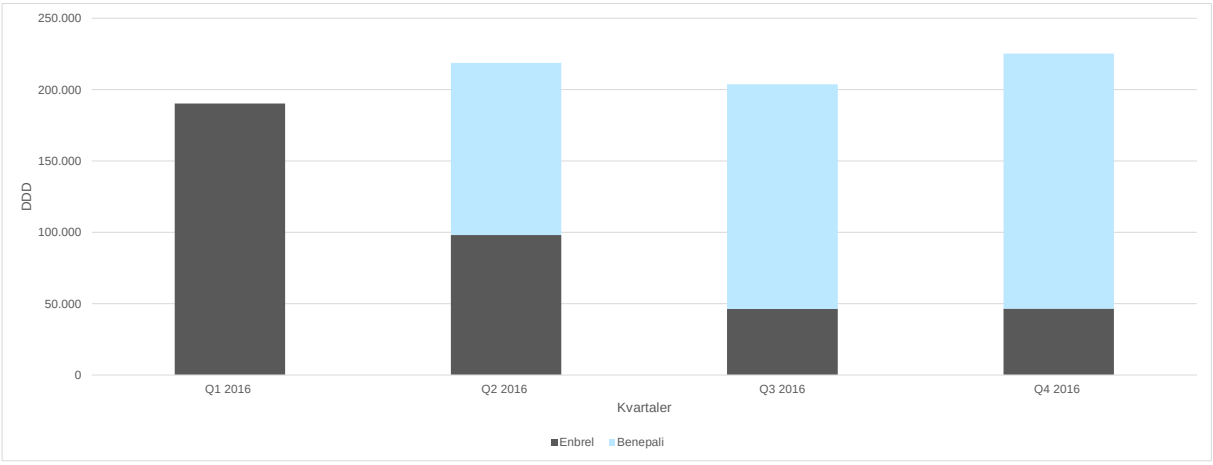
Etanercept consumption in DDD



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Legal framework

- European pharmacovigilance legislation
Regulation (EU) No 1235/2010 and Directive 2010/84/EU

- EU Good Vigilance Practices (GVP Modules) – including:
Product- or Population-Specific Considerations II: Biological medicinal products

- Danish national law, executive orders

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Focus on traceability of biologicals

- Member States obliged to ensure identification of biologicals
(Directive 2010/84/EU, art. 102)

- Member States may impose specific obligations on Healthcare proffessionals
(executive orders no. 1823 of 15 december 2015 re reporting of ADRs)

- Marketing Authorisation Holders obliged to ensure collection of ADR data incl follow-up (Directive 2010/84/EU, art. 107)

- Individual Case Safety Report content – for biologicals the batch number is obligatory (EC Implementing Regulation 520/2012)

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DK experience – Action Plan on Biologicals

– To meet patients' concern about biosmimilar medicines and to inform physicians about the principle of biosimilarity

– Four main focus areas:

- To Encourage surveillance on product level – traceability
- To raise awareness on biosmilarity
- To promote IT solutions to ease reporting of adverse drug reactions
- DKMA focus on the surveillance of biologicals incl biosimilars

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First initiatives to ensure traceability

New requirements in Danish Executive orders, December 2015

- Physicians shall make records of brand name and batch number in patient records
- Physicians shall, if possible, provide brand name and batch number when reporting ADRs – if included in the DKMA list of selected biologicals

DKMA list of biosimilars and reference products (http://laegemiddelstyrelsen.dk/en/sideeffects/biological-and-biosimilar-medicinal-products/list-of-selected-biological-medicinal-products)

Increased focus on product identification in reporting forms

- Pop up-message for biological medicinal products in HCP e-form
- Specific field for batch number in consumer e-form

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List of selected biologicals

Product name	Active substance
Elocta	Efmoroctocog alfa
Eprex®, Retacrit	Erytropoietin
Praluent	Alirocumab
Repatha	Evolocumab
Bemfola, Gonal-F®	Follitropin alfa
Genotropin®, Omnitrope®	Somatropin
Neupogen®, Nivestim, Zarzio	Filgrastim
Enbrel®, Benepali	Etanercept
Remicade, Remsima, Inflectra	Infliximab
Nucala®	Mepolizumab
Cosentyx	Secukinumab
Praxbind	Idarucizumab

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Raising awareness – dialogue with patients

Initial meeting with patient organisations

- Identification of information gaps
- Identification of suitable communication methods

Targeted communication

- Q&A on DKMA Website https://laegemiddelstyrelsen.dk/en/sideeffects/biological-and-biosimilar-medicinal-products/frequently-asked-questions/
- Leaflet
- Information videos in collaboration with patient organisations

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Key messages to patients

- Biological medicinal products can be either reference products or biosimilar
- The route of administration is the same for a biosimilar and its reference product
- Equal quality, efficacy and safety shall be demonstrated between a biosimilar and the reference product, just like equal quality, efficacy and safety has to be demonstrated before and after a manufacturing change of any biological product
- Therefore, switching from a reference biological product to a biosimilar product is not expected to cause changes in treatment response

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Raising awareness – dialogue with physicians

Aim

- To inform about new legal requirements (collaboration with Danish Patient Safety Authority)
- To raise awareness about biosimilarity and the uncertainties patients may feel

Communication methods

- Q&A on Website
- Email to all hospital CEOs, regional drug committees and relevant scientific medical colleges providing information
- Flyers, incl. the leaflet for distribution to patients

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Reporting of batch no, infliximab and etanercept

Product	Active substance	Number of reports	Batch number, initial report	Batch number, on follow up	Total batch no (% of reports)
Not specified	Infliximab	**9**	-	-	-
Remicade	Infliximab	**73**	2	3	**5 (6.8)**
Remsima	Infliximab	**142**	71	36	**107 (75.4)**
Not specified	Etanercept	**6**	-	-	**-**
Enbrel	Etanercept	**23**	4	2	**6 (26.1)**
Benepali	Etanercept	**22**	9	7	**16 (72.7)**
TOTAL		**275**	86	48	**134 (48.7)**

Review of selected biologicals, 2015-2016

1 September 2015 - 31 December 2016, DKMA received a total of 294 ADR reports possibly related to products on the list of selected biologicals

- 216 regarding infliximab; 73 on the reference product (Remicade) and 142 on the biosimilar (Remsima)
- 51 regarding etanercept; 23 on the reference product (Enbrel), 22 on the biosimilar (Benepali)
- Primarilly well-known ADRs were reported

– Switch

- We found that in 20 of 294 reports ADRs may be related to switching from reference to biosimilar
- Difficult to determine if a reaction is a consequence of a switch or simply occurring after a switch

Conclusions on surveillance of biosimilars in Denmark

- ADR data support equal safety profiles of biosimilars and their reference products
- No correlation between batches and reported ADRs
- Scientific litterature, including Norwegian Nor-Switch study looking at efficacy, safety and immunogenicity when switching patients from reference to biosimilar infliximab, support similar safety profiles of reference products and biosimilar products

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Continued dialogue with stakeholders is essential

Patients

- Meetings with pt organisations when biosimilars are introduced to new therapeutic areas, Facebook profile

HCPs

- Danish Pharmacovigilance Council (HCPs, patient representatives, pharmacists etc)

➢ To actively contribute to fostering dialogue between medicine users, healthcare professionals and authorities (among other things)

➢ To make recommendations to the DKMA about information for medicine users on medicines and side effects

- Forum for Quality of ICSRs – (hospital farmacists, physicians, industry, regions etc)

➢ Traceability and how to register data at the hospital (among other things)

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Thank you for your attention

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