打擊不法藥物與生物相似藥的挑戰與機遇

大仁科技大學產學育成中心
林佩怡主任
2024.11.16

KEEP PATIENTS SAFE – SECURE THE GLOBAL MEDICINES SUPPLY CHAIN

Falsified and substandard medicines are a global issue yet low and middle-income countries carry the greatest burden with estimates suggesting 1 in 10 medical products in developing countries to be fake.

FIGHT THE FAKES ALLIANCE

SPEAK UP ABOUT FAKE MEDICINES

JOIN FIGHT THE FAKES WEEK BETWEEN 5-11 DECEMBER 2022 TO RAISE AWARENESS ABOUT SUBSTANDARD AND FALSIFIED MEDICINES

FIGHTTHEFAKES.ORG

#BeAFakeBuster #FTFweek

Fake news
Published in PharmaTimes magazine - March 2022

- An estimate by the World Customs Organization values the global annual market for fake medicines at approximately US$200 billion and as the legitimate pharmaceutical industry grows, so too does this shadow market.
- WHO estimated in 2015 that 50% of drugs for sale over the internet were fake and this is only increasing.
- in low-and middle-income countries where access to healthcare is widening, such as in Africa and Asia.

打擊不法藥物需要你我一起努力

公共政策網路參與平台連署活動

現況:網路偽藥猖獗 - 嚴重危害民眾健康

網路偽藥就在你我身邊

根據關務署報告顯示，
2022年海關於邊境緝獲仿冒及盜版品逾5萬件，
其中藥品合計近2.8萬件，又以威而鋼和犀利士佔大宗。

社區藥局淪為被冒名廣告的受害者

民眾透過偽藥廠商在網路上的假廣告，下單購買藥品後，
卻發現是偽藥，卻循線找到被冒用品牌的實體藥局通路，
甚至威脅找警察抓合法的實體藥局，被害藥師求助無門...

現行法規管不到也抓不到「非法業者」

非法偽藥透過海外架設網站，大規模廣告吸引民眾下單購買，
但是現行的法規卻管不著也罰不到，
導致偽藥廣告四處流竄，危害民眾健康。
正規合法在台設立的藥商，反而因為法規限制，
無法透過一般廣告教育民眾如何辨識偽藥，
只能眼看著非法偽藥業者繼續橫行無阻。

民眾對偽藥認知不足，以為網路上也可以買藥

一般民眾並不知道台灣現行法規並不允許在網路上購買藥品，
尤其偽藥廣告以假亂真，甚至在網路上教育民眾如何辨識偽藥，
讓民眾信以為真後下單購買，人財兩失!

網路偽藥的衝擊

危害民眾的健康

來源不明的偽藥，民眾吃了沒效，不僅傷荷包也傷身，
還有可能因為長年累積下來的傷害，
衍生出其他病症，進而耗費健保寶貴的資源。

減少政府財稅收入

政府可以透過財政稅收，
向合法經營的藥商和藥局通路收取營業稅或是所得稅。
但是，未經過合法管道販售的偽藥，政府則無法收取任何稅收，
進而影響財政收入。

增加執法人員額外的工作負擔

關務署一年緝獲仿冒及盜版品逾5萬件，其中偽藥就超過一半，
近2.8萬件。如果政府能落實偽藥的管制，
從源頭斷絕，則可大幅降低海關人員的工作負擔。

原開發廠生物製劑 VS 生物相似性藥品
台灣衛福部衛教資訊

衛教單張

TFDA: 生物相似性藥品專區
https://www.fda.gov.tw/TC/siteContent.aspx?sid=11262

2019年

護理在職課程

藥學生課程

2020年

新聞專訪

臨床科會

院內講座

部內課程

南區研討會

2022年

2021年

2020年

2019年

認知教育

健康醫療網

生物相似性藥 - 生物製劑長期『經濟毒性』的解方

近年來出現生物製劑可有效改善病況，不過費用卻不是人人負擔得起，幸好出現生物相似性藥可緩解這種「經濟毒性」。生物製劑改善自體免疫疾病困境惟『經濟 ...

4 小時前

健康醫療網

類風濕性關節炎治療不卡關生物相似藥降患者負擔

類風濕性關節炎在二十年前幾乎沒有很有效的治療藥物，甚至曾經有人將類風濕性關節炎形容成一種不會致命的癌症。高雄長庚紀念醫院風濕過敏免疫科鄭添財 ...

6 天前

新聞專訪

護理在職課程

臨床科會

藥學生課程

Biosimilars FORUM

The Importance of Dispelling Misinformation About Biosimilar Therapies

The promise of biosimilars is real. Biosimilars — which treat serious diseases, including cancers, rheumatoid arthritis, psoriasis, inflammatory bowel disease, and Crohn's Disease — are FDA-approved, equally safe, and have no clinically meaningful differences between their reference biologics. Yet biologic manufacturers have continued to sow doubt about the safety and efficacy of biosimilars. By creating confusion throughout the industry and hampering the biosimilars market, these tactics are only harming patients who are ultimately losing out on billions of dollars in potential cost-savings.

Today, the FDA and FTC are holding a public workshop exploring how best to increase patient access to biosimilars and help ensure that the biologics market is robust and competitive. As part of this interagency collaboration, the FDA and FTC are explicitly discussing the importance of "[discouraging] false or misleading communications about biosimilars, and [deterring] anticompetitive behaviors in the biologic product marketplace."

The Biosimilars Forum's Hillel Cohen, co-chair of the Forum's Education Committee, is participating in the panel, where he explains how biosimilar use is still limited in many health care systems because they are not well understood by many health care professionals and patients. This mistrust is exacerbated by negatively biased information or intentional misinformation disseminated by biologics manufacturers and other parties.

Why we should stop biosimilar misinformation?

Biosimilar(生物相似藥)

≠

Generic Drug(學名藥)??

台廠藥??

生物相似性藥也是種生物製劑

原開發廠

原創生物製劑

(又名: 原參考品，Reference product, Originator)

蛋白質氨基酸
序列專利過期

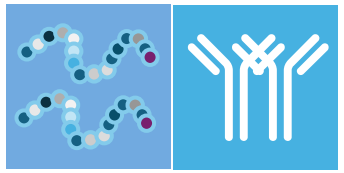
生物相似性藥開發廠

生物相似性藥 A

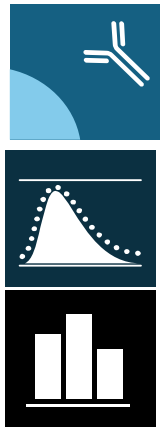
生物相似性藥 B

生物相似性藥 C

A biosimilar is designed to be comparable to the reference product in all parameters

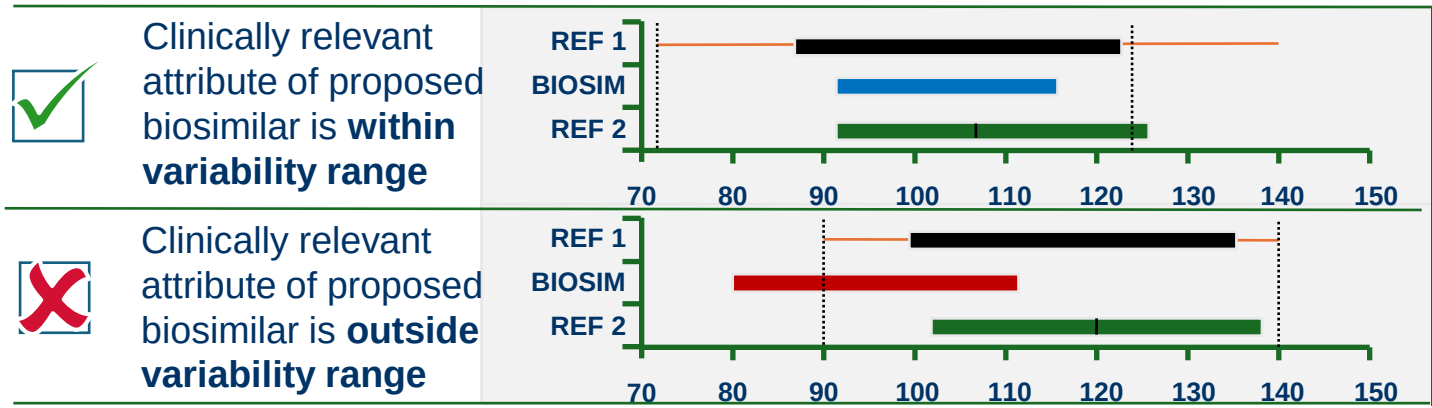


- ✔ Identical amino acid sequence
- ✔ Highly similar higher-order (spacial) structure



- ✔ Affinity
- ✔ Selectivity
- ✔ PK
- ✔ Effector function
- ✔ Solubility
- ✔ Immunogenicity

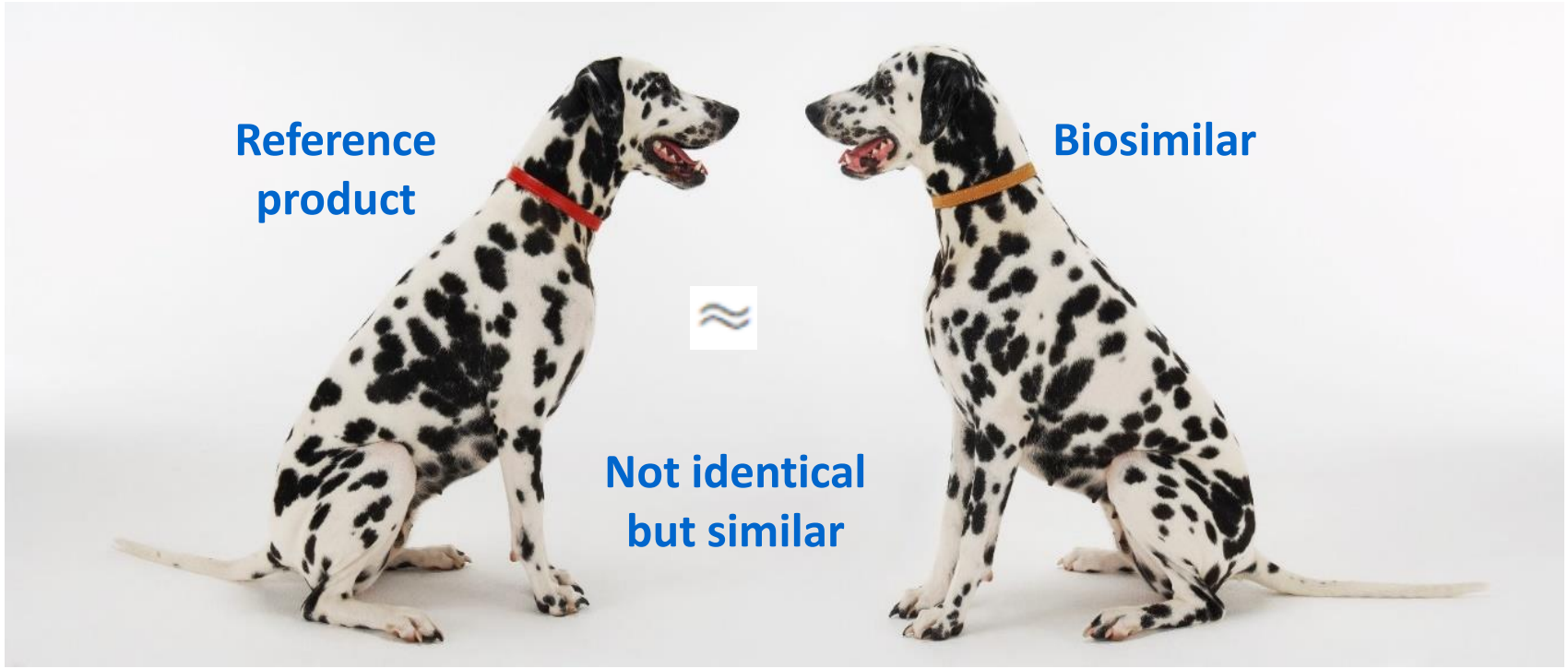
不同批次也有差異



The range, defined by the variability of the originator product, is very narrow

Schematic developed by Sandoz (18 November 2014).

原開發廠生物製劑也無法完全相同
生物相似性藥與原開發廠生物製劑在結構上相似，但功能無異



The issue people care is if they are both good dogs

專利適應症

藥廠 or 醫院端

UpToDate® rituximab

biosimilars 7/24

Contents Calculators Drug Interactions UpToDate Pathways

Back

Rituximab (intravenous) including biosimilars of rituximab: Drug information Lexicomp®

Access Lexicomp Online for additional drug information, tools, and databases.

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(For additional information see "Rituximab (intravenous) including biosimilars of rituximab: Patient drug information" and see "Rituximab (intravenous) ... mab: Pediatric drug information")

For abbreviations and symbols that may be used in Lexicomp (show table)

醫院端

臨床癌症治療指引:生物相似藥納入治療選項

National Comprehensive Cancer Network®

NCCN Guidelines Version 3.2024
Classic Follicular Lymphoma

NCCN Guidelines Index
Table of Contents
Discussion

SUGGESTED TREATMENT REGIMENS[a]

An FDA-approved biosimilar is an appropriate substitute for rituximab.[b]

An FDA-approved biosimilar is an appropriate substitute for rituximab.

Preferred regim
- Bendamustine [illegible]
- CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone) + obinutuzumab[e] or rituximab
- CVP (cyclophosphamide, vincristine, prednisone) + obinutuzumab[e] or rituximab
- Lenalidomide + rituximab

Preferred regimen, low tumor burden
- Rituximab (375 mg/m² weekly for 4 doses)[f]

Other recommended regimen
- Lenalidomide + obinutuzumab (category 2B)

FIRST-LINE THERAPY FOR OLDER OR INFIRM[b]
(if none of the above are expected to be tolerable in the opinion of treating physician)

Preferred regimen
- Rituximab (375 mg/m² weekly for 4 doses)

Other recommended regimens
- Chlorambucil ± rituximab
- Cyclophosphamide ± rituximab

[illegible] weeks for 2 years for patients initially presenting with high tumor burden (category 1)[g]
- Obinutuzumab maintenance (1 g every 8 weeks for 12 doses)

Other recommended regimens
- If initially treated with single-agent rituximab, rituximab maintenance 375 mg/m² one dose every 8 weeks for 4 doses

Footnotes on FOLL-B 4 of 6
See Second-line Therapy on FOLL-B 2 of 6
See Third-line and Subsequent Therapy on FOLL-B 3 of 6

Consider prophylaxis for tumor lysis syndrome (NHODG-B)
See monoclonal antibody and viral reactivation (NHODG-B)

Switching-related change in efficacy and safety: a case series study on trastuzumab

Ying-Ying Kang, Eric Kin-Lap Lee, Pei-Yi Lin
Department of Pharmacy, Kaohsiung Veterans General Hospital

Code name	Age	Prescriber	No. of Herceptin treatment received	No. of Ogivri treatment received	Switch from H to O (1), or O to H (2)	Switch date	Reason for switching	Reason for discontinuation after switching	ER visit
A	52	B	22	16	1	2020/9/11 & 2020/10/02	out-of-pocket & UP	TC	0
B	61	B	14	1	1	2021/3/12	out-of-pocket	PD, 2021/04/27 expired.	Twice, both of which non-drug-related
C	44	A	15	12	1	2020/2/3	out-of-pocket	PD, 2020/12/10 expired.	3 times, malignancy-related (non-drug related)
D	75	A	5	5	1	2021/1/14	commence combination treatment with pertuzumab	Loss to follow-up (last visit was on 2021/3/18 at OPD).	0
E	35	B	13	1	1	2021/06/12 & 2021/07/02	UP	TC	Twice, both unrelated to trastuzumab.
F	53	A	26	1	1	2021/5/13	CEM	PD, shifted to T-DM1	7 times, of which one was related to C/T.
G	65	A	9	8	1	2021/2/18	CEM	TC	Once on 2021/2/24 due to pathological fracture.
H	75	A	19	9	1	2021/1/25	CEM	TC	4 times, of which 3 was related to conventional chemotherapy (but not trastuzumab-related).
I	50	C	1	4	2, followed by 1	2021/3/20 & 2021/04/12	UP	PD, shifted to T-DM1	0

Note:
1. Age indicates most recent age or age at time of death.
2. Reason for switching: UP stands for unintended prescription. CEM stands for cost-effectiveness maximization.
3. Reason for discontinuation: TC indicates treatment continuation as of the end of the study period; PD indicates progressive disease according to RECIST 1.1.

- ✓ **2020-2021**
- ✓ **9 p’ts**
- ✓ **mean aged 57**

Efficacy and safety of Sandoz rituximab biosimilar (Rixathon®) in first-line treatment for patients with diffuse large B-cell lymphoma: a single center experience

Tzu-Chien Lin, Tsung-Hsien Tsai, Chang-Hong Yeh, Shyh-Jer Lin, Ying-Chung Hong

Division of Hematology and Oncology, Department of Medicine,
Kaohsiung Veterans General Hospital, Kaohsiung

ABSTRACT

We evaluated the real-world efficacy and safety of Rixathon®, a Sandoz rituximab biosimilar, in patients with diffuse large B-cell lymphoma (DLBCL) treatment. Since its introduction to our institute in 2021, 28 patients received Rixathon® in combination with chemotherapy as frontline treatment. The overall response rate was 96.4%, with complete responses in 71.4% of patients and partial responses in 25%. Infusion-related reactions occurred in 4 patients (14.3%), none of which resulted in treatment discontinuation. Febrile neutropenia occurred in 2 patients (7.1%), and five patients (17.9%) died during follow-up. Overall, Rixathon® appears to be an effective treatment with acceptable side effects.

INTRODUCTION

Diffuse large B-cell lymphoma (DLBCL) comprises about 30% of adult NHL cases worldwide[1]. Adding rituximab to standard CHOP chemotherapy has significantly improved DLBCL prognosis, boosting long-term survival rates by nearly 20%. However, rituximab's high cost limits accessibility, particularly in resource-limited regions. In Taiwan, rituximab is covered by National Health Insurance for DLBCL. To address financial constraints, biosimilar drugs like Rixathon® (a Sandoz rituximab biosimilar) are increasingly used. This study aimed to assess Rixathon®'s real-world clinical efficacy and safety in DLBCL patients.

Table 1. Baseline demographics and clinical characteristics of all patients.

Characteristics	N=28(%)	Characteristics	N=28(%)
Sex		**ECOG**	
Male	20(71.4)	0-1	25(89.3)
Age at transplantation, years		≥ 2	2(10.7)
Median (years)	68	Unknown	1
Range (years)	24-86	**LDH**	
20-40	4(14.3)	Normal	23(82.1)
40-60	3(10.7)	**β2-microglobulin**	
> 60	21(75)	Normal	18(64.3)
B symptoms	2(7.1)	**Molecular subtype**	
Stage		GCB	8(28.6)
I-II	14(50)	Non-GCB	17(60.7)
III-IV	14(50)	Unknown	3(10.7)
IPI risk group		**Regimen**	
Low	12(42.9)	R-CHOP	17(60.7)
Low-intermediate	5(17.9)	R-CEOP	7(25)
Intermediate-high	9(32.1)	R-EPOCH	3(10.7)
High	2(7.1)	R-miniCHOP	1(3.6)

CHOP: cyclophosphamide, doxorubicin, vincristine, and prednisone; CEOP: cyclophosphamide, epirubicin, vincristine, and prednisone; EPOCH: etoposide, prednisone, vincristine, cyclophosphamide and doxorubicin

Efficacy and safety of Sandoz rituximab biosimilar (Rixathon®) in first-line treatment for patients with diffuse large B-cell lymphoma: a single center experience

Tzu-Chien Lin, Tsung-Hsien Tsai, Chang-Hong Yeh, Shyh-Jer Lin, Ying-Chung Hong

Division of Hematology and Oncology, Department of Medicine,
Kaohsiung Veterans General Hospital, Kaohsiung

Table 2. Efficacy outcomes by all patients.

	N=28(%)
Number of cycles received	
1-3	5(17.9)
4	2(7.1)
5	3(10.7)
6	18(64.3)
Cause of incompletion	
Intolerance	4
Progression/Expire	6
Best response	
Complete response	20(71.4)
Partial response	7(25)
Progressive disease	1(3.6)
Overall response	96.4%

Table 3. Safety outcomes by all patients.

	N=28(%)
Infusion-related reaction	4(14.3)
Any grade	4
Grade ≥ 3	0
Febrile neutropenia	2(7.1)
Neutropenia	13(46.4)
Thrombocytopenia	7(25)
Liver enzyme increased	8(28.6)
Creatinine increased	4(14.3)
Infection	4(14.3)
Mortality	5(17.9)
Cause of death	
Lymphoma	3(60)
Infection	2(40)

Table 4. Indirect comparison of clinical study of reference Rituximab and Real-world evidence of Rixathon® in Patients with previously untreated DLBCL (The table should be interpreted with caution, as direct head-to-head comparisons were not conducted)

Parameter	Study		
	GOYA (2020)[2]	REFLECT	Taiwanese RWE (current study)
Study			
Design	**Phase III** International, prospective, open-label, randomized trial of R-CHOP vs. CHOP plus obinutuzumab	**RWE** Prospective, observational, multi-center, non-interventional study (Oct 19, 2017 to Mar 31, 2021)	**RWE** single center (Taiwan), retrospective study (2021-2023)
Population	Previously untreated CD20+ DLBCL treated with R-CHOP	Previously untreated CD20+ DLBCL treated with R-CHOP	Patients with previously untreated DLBCL treated with Rixathon®of patients
N	710	169	28
Endpoints			
Primary endpoint	Investigator-assessed PFS	CR at end of treatment assessed by treating physician	Treatment response
ORR, %	77.6	94.7 (95% CI 90.1, 97.5)	96.4
CR, %	CT with PET: 59.1 CT without PET: 33.9	65.1 (95% CI 57.4, 72.3)	71.4
PR, %	N/A	29.6 (95% CI 22.8, 27.1)	25
PFS/EFS, %	5-year PFS: 62.6 (95% CI 58.1, 66.8)	24-month est. PFS: 78.5 (95% CI 70.9, 84.4)	N/A
AEs, %	94.0	84.6	N/A
SAEs, %	38.4	37.3	N/A

Policy review

RIXATHON®
rituximab
Power in your hands

先進國家推動biosimilar鼓勵政策與策略

強制轉換	**挪威**：醫院**強制統一採購**，低價藥得標後列入處方選項中。
	加拿大：特定適應症**強制轉換**，biosimilar列為**新病人**處方項目。
處方獎勵	**英國**：醫師開立單一成分biosimilar達標後可有**藥品1%合約價格獎勵**。新病人90%、舊病人80%
	日本：醫師衛教且開立biosimilar，每次可得**1500日圓**獎勵。
簡化流程	**澳洲**：**事前審查**作業簡化。
替代獎勵	**澳洲**：**鼓勵但不強制**醫師開立biosimilar於新病人。
收益共享	**英國**：地方臨床委任小組與醫院收益共享，**醫院可保留處方較低價的藥品所節省的成本之固定百分比**。

台灣醫藥品法規學會生物相似藥品政策建言 https://tsrap.org.tw/medicine_detail.php?id=516

全民健康保險推動使用生物相似藥之鼓勵試辦計畫

113 年 6 月 14 日健保審字第 1130111063 號公告

壹、計畫依據

全民健康保險會(下稱健保會)協定年度醫療給付費用總額事項辦理。

貳、現況分析

近年全球藥品研發朝向大分子生物藥，據 Nature 報導，111 年最暢銷

全民健康保險推動使用生物相似藥之鼓勵試辦計畫

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引進，得以治療更多病人。

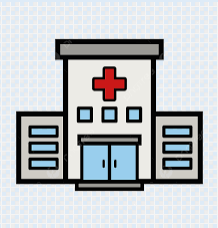
全民健康保險保險人(下稱保險人)為提升生物相似性藥品之使用，已推動 3 大措施，分別為：於官網建立生物相似性藥品專區、無須提報專家諮詢會議討論以加速收載，及無財務衝擊或可容許之財務衝擊下，得「免除事前審查」、「放寬使用期限」或「擴增給付規定」等給付策略。112 年健保收載之生物相似性藥品計有 11 個成分、41 個品項，其中生物相似性藥品之醫令量占整體同成分藥品之醫令量占率為 7.38%。

全民健康保險
推動使用生物相似藥之鼓勵試辦計畫

計畫試辦3 年，實施目標: ⬆ 醫療院所開立生物相似性藥品之處方數 ⬆ 本計畫藥品醫令量占率達30%以上

(一) 處方開立獎勵

每一處方獎勵150點 → 按季勾稽撥付予個別院所 → 以浮動點值計算

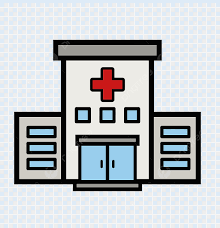


應用於推動生物相似性藥
之相關照護使用

(二) 藥費差額回饋：

(原廠支付價-生物相似藥支付價) X 醫令量 → 按季統計個別院所藥費差額回饋點數

交由各分區業務組
回饋方案由各分區因地制宜



列入年度自主管理方案之目標管理點數校正，得以100%方式回饋

Ref:全民健康保險推動使用生物相似藥之鼓勵試辦計畫 113 年6 月14 日健保審字第1130111063 號公告

附表

全民健康保險推動使用生物相似藥之鼓勵試辦計畫
鼓勵處方藥品清單

成分項次	藥品成分	分類分組名稱	藥品項次	藥品商品名	藥品健保代碼
1	**adalimumab**	adalimumab，注射劑，40 mg	1	Amgevita	KC01098283
			2	Idacio 玻璃小瓶(瑞士廠)	KC01153283
			3	Idacio 預充填針筒(義大利廠)	KC01154283
			4	Abrilada	KC01157283
			5	Hulio	KC01149283
			6	Hyrimoz	KC01181283
			7	Yuflyma	KC0
2	**etanercept**	etanercept，注射劑，25.00 mg	1	Erelzi	KC0
			2	Nepexto	KC0
		etanercept，注射劑，50.00 mg	3	Erelzi	KC0
			4	Nepexto	KC0
3	**pegfilgrastim**	pegfilgrastim，注射劑，6.00 mg	1	Fulphila	KC0
			2	Ziextenzo	KC0
4	**rituximab**	rituximab，注射劑，100mg	1	Truxima 100 mg	KC01094229
			2	Rixathon 100 mg	KC01118229
			3	Ruxience 100 mg	KC01165229
		rituximab，注射劑，500 mg	4	Truxima 500 mg	KC01094248
			5	Rixathon 500 mg	KC01118248
			6	Ruxience 500 mg	KC01165248
5	**teriparatide**	teriparatide，注射劑，600 mcg	1	Alvosteo	KC01151213
6	**trastuzumab**	trastuzumab，注射劑，420~440 mg	1	Kanjinti	KC011112DE
			2	Ogivri	KC010892B5
			3	Herzuma	KC011162B5
			4	Trazimera	KC011362B5
		trastuzumab，注射劑，150 mg	5	Eirgasun	JC00154261

註：試辦期間，本表如有新暫予收載或異動之生物相似性藥品品項，保險人得於每月 25 日前修正公告附表品項資訊。

Rixathon®洛希隆注射劑 可減少醫療體系的支出與負擔[1]

RIXATHON rituximab
Power in your hands

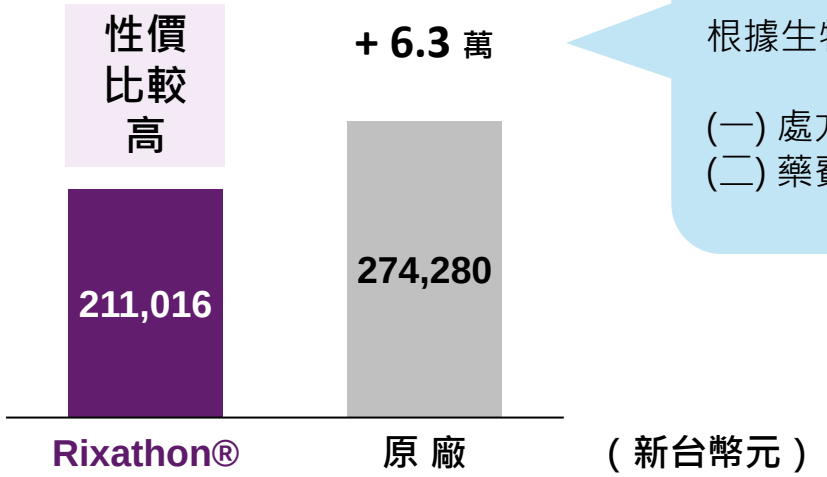
規格 (瓶)	Rixathon®	原廠	藥價差
100 mg 健保代碼	5,275 KC01118229	7,098	1,823
500 mg 健保代碼	26,377 KC01118248	34,285	7,908

以類風濕性關節炎假設案例推估

Rituximab IV 劑型
總用量 4,000 mg/年

*類風濕性關節炎一個療程含兩次靜脈輸注，
每次輸注500-1000 mg，
此處以每次輸注1000 mg、
24週後施打一個重複療程推算

藥價試算總療程費用*



根據生物相似藥鼓勵計畫[2]

(一) 處方開立獎勵 600點
(二) 藥費差額回饋 6.3萬點

SANDOZ

Ref. 1. 藥品價格皆參考 衛生福利部中央健康保險署-健保用藥品項查詢 (2024.06 查詢) 2.全民健康保險推動使用生物相似藥之鼓勵試辦計畫 113 年6 月14 日健保審字第1130111063 號公告

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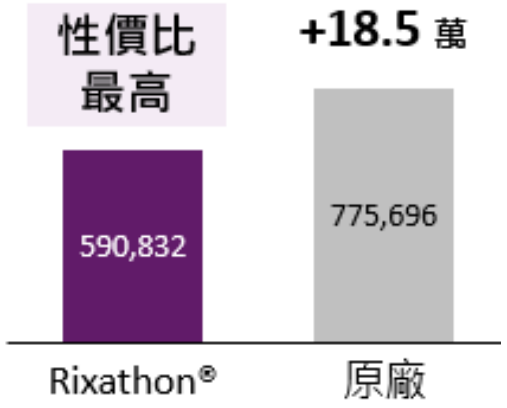
藥價試算總療程費用*

以濾泡性淋巴瘤假設案例推估

身高 170 cm
體重 65 kg
體表面積 1.75 m^2

Rituximab IV 劑型
總用量 657 mg*

*濾泡型淋巴瘤 誘導治療 +
維持治療一共 16 劑（**約 2 年半**）



根據生物相似藥鼓勵計畫[2]

(一) 處方開立獎勵 2,400點
(二) 藥費差額回饋 18.5萬點

SANDOZ

Ref. 1. 藥品價格皆參考 衛生福利部中央健康保險署-健保用藥品項查詢 (2024.06 查詢) 2.全民健康保險推動使用生物相似藥之鼓勵試辦計畫 113 年6 月14 日健保審字第1130111063 號公告


Thank you