CHINA'S 2019 NRDL UPDATE: IMPLICATIONS ON GLOBAL & LOCAL MANUFACTURER STRATEGY

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INTRODUCTION

China's 2019 NRDL update marked a critical turning point for manufacturers seeking market access with the successful Category B listing of 70 drugs for national reimbursement: 52 were manufactured by multinational corporations and 18 by domestic manufacturers.

The final negotiated prices reflect an average discount of 60.7% from the list prices – the largest average reduction from an NRDL update to date. For innovative medicines with comparable clinical benefit, the tender-like negotiation model intensified competition and formed a steep price cliff.

OBJECTIVE

The objective of this research was to evaluate 2019 NRDL negotiation outcomes as indicators of potential strategic approaches for multinational and domestic manufacturers to achieve NRDL listing.

METHODOLOGY

A review of published 2019 NRDL results – along with secondary research on the competitive landscape for listed products in Hepatitis C and rheumatoid arthritis – was conducted.

RESULTS

HCV CASE STUDY: MANUFACTURER POSITIONING AMID COMPETITIVE THERAPEUTIC AREA

LOCAL HCV LANDSCAPE

One of the most competitive NRDL negotiations occurred in the disease area of HCV due to the local landscape and market opportunity. China has the highest HCV burden worldwide, with an estimated 8.9 million people living with chronic HCV infection.[1] However, current HCV treatments have high efficacy and are considered curative, which has contributed to the diminishing patient pool and increasing competition.

Given interferon and ribavirin treatment remains the local standard of care, patient access to more effective HCV medications has been limited due to high price points. For example, a standard twelve-week regimen of EPCLUSA® costs around CNY 75,000 (USD 10,892) while the average annual disposable income in 2019 was CNY 26,523 (USD 3,833) according to the National Bureau of Statistics.

NRDL NEGOTIATIONS AND OUTCOMES

Four companies, three multinationals (GILEAD, MERCK, and ABBVIE), and one domestic (ASCLETIS PHARMA), competed for coverage of HCV drugs on the NRDL. MERCK's ZEPATIER® (elbasvir / grazoprevir) and GILEAD's HARVONI® (ledipasvir / sofosbuvir) successfully gained NRDL listing after the two multinational manufacturers negotiated the lowest two full-course cost, an average price cut of 85%. GILEAD's EPCLUSA® (sofosbuvir / velpatasvir) entered the NRDL with a slightly lower price cut due to the unmet need captured by its broader indication (HCV genotype 1 to 6).

MANUFACTURER SPOTLIGHT

Antiviral manufacturer ASCLETIS PHARMA was negatively impacted by the NRDL update. Its product GANOVO® is the first locally developed direct-acting antiviral and previously maintained a significant pricing advantage on the market at approximately half of EPCLUSA®'s pre-NRDL negotiated price (Figure 1).

Prior to GANOVO®'s launch in 2018, ASCLETIS partnered with ROCHE and obtained exclusive marketing and sales promotion rights in China for PEGASYS®, a pegylated interferon to be used in combination with GANOVO®. Even though ASCLETIS went into the negotiation with a very large price cut, the price of PEGASYS® was considered during the process; the combination pricing ultimately exceeded the discounted prices agreed upon by MERCK and GILEAD for their monotherapies. GANOVO®'s market share will be undercut, as the listed HCV drugs will receive national reimbursement market exclusivity for the next two years.

ASCLETIS' stock price plunged 25% upon the release of NRDL results, and the company has since pivoted its sales strategy to focus on third- and fourth-tier cities in hopes of capturing the limited self-pay market from patients with poor outpatient medical insurance coverage.

	Multinational Corporation Product					China Domestic Product
Brand Name	ZEPATIER®	HARVONI®	EPCLUSA®	EXVIERA®	VIEKIRAX®	GANOVO®
Generic Name	elbasvir / grazoprevir	ledipasvir / sofosbuvir	velpatasvir / sofosbuvir	dasabuvir	ombitasvir / paritaprevir / ritonavir	danoprevir
Manufacturer	MERCK	GILEAD	GILEAD	ABBVIE	ABBVIE	ASCLETIS
Treatment Description & Indication	Monotherapy for HCV genotype 1b	Monotherapy for HCV genotype 1b	Monotherapy HCV genotype except 1b	In combination with VIEKIRAX® for HCV genotype 1	In combination with EXVIERA® for HCV genotype 1 and 4	In combination with PEGASYS® for HCV genotype 1b
2019 NRDL Inclusion	YES	YES	YES	NO	NO	NO
Pricing Calculation Assumptions	One pill daily for 14 weeks	One pill daily for 12 weeks	One pill daily for 12 weeks	Two pills daily for 12 weeks	Two pills daily for 12 weeks	Two pills daily for 12 weeks
Per Course Cost Prior to 2019 NRDL (CNY)	74,861	69,623	74,571	3,703*	42,583*	42,853**
Per Course Cost After 2019 NRDL (CNY)	8,225	7,033	14,040			
NRDL % Price Cut	89%	90%	81%	N/A	N/A	N/A

*EXVIERA® and VIEKIRAX® are used in combination with each other for HCV genotype 1a and 1b patients thus the per course cost would be 3703 + 42,583 = 46,286

**PEGASYS® and GANOVO® are used in combination with each other for HCV genotype 1b thus the per course cost would be 11,940 + 42,853 = 54,793

FIGURE 1: HCV DRUG NEGOTIATION OUTCOMES AND ESTIMATED PRE-/POST-NRDL COSTS

FUTURE MANUFACTURER STRATEGIES

With more frequent NRDL updates, local manufacturers should consider the risk posed by the entry of global branded products. Both local and multinational manufacturers should not underestimate their competitors' willingness to negotiate price in exchange for broader patient access.

Among products lacking value differentiation (e.g., efficacy, patient subpopulation), price competition is inevitable. A well-developed and realistic pricing plan with base-case and lower-case scenarios will help secure the best opportunity for NRDL listing.

As exclusivity may be leveraged by the NHSA to secure high price discounts, a trade-off analysis of price decrease vs. volume expansion will be essential for manufacturers when making pricing decisions.

RA CASE STUDY: STEEP PRICE DISCOUNTS & BIOSIMILAR THREATS

LOCAL RA LANDSCAPE

There are around five million RA patients in China yet effective treatments are limited due to the late entry of biologics into the market, high drug prices, low patient consultation rates, as well as limited access to novel treatments.[2]

RA is considered one of the main causes of labor loss and disability in China. The local standard of care has primarily been methotrexate, a conventional DMARD with significant side effects, and traditional Chinese medicines.

NRDL NEGOTIATIONS AND OUTCOMES

Five branded RA drugs from global manufacturers are included on the NRDL: HUMIRA®, REMICADE®, and XELJANZ® were listed through pricing negotiations, while ACTEMRA® and SIMPONI® went through routine update.

In particular, ABBVIE's blockbuster drug HUMIRA® saw low uptake in China prior to its 2019 NRDL listing, with only four of seventeen indications approved. Although China has a large patient population, HUMIRA®'s sales in China accounted for only 0.1-0.2% of its global sales. During the 2019 NRDL negotiations, HUMIRA® enlisted with an 83% price cut, resulting in a price of approximately CNY 2,795 (USD 409) per month (Figure 2).

ACTEMRA® and SIMPONI® entered the 2019 NRDL via routine update, due to their relatively low pricing. Noticeably, ACTEMRA® underwent a significant voluntary price cut from CNY 14,598 (USD 2,138) to CNY 6,294 (USD 121) per month in May 2019 right before the NRDL negotiations. With this 57% price drop, ACTEMRA® entered the listing and avoided the risks of pricing negotiation.

	Multinational Corporation Product					China Domestic Product		
Brand Name	HUMIRA®	REMICADE®	XELJANZ®	ACTEMRA®	SIMPONI®	YISAIPU	ANBAINUO	QIANGKE
Generic Name	adalimumab	infliximab	tofacitinib	tocilizumab	golimumab	TNF RII: IgG Fc Fusion Protein	TNF RII: IgG Fc Fusion Protein	TNF RII: IgG Fc Fusion Protein
Manufacturer	ABBVIE	JANSSEN	PFIZER	ROCHE	JANSSEN	3SBio	HISUN	CELGEN
NRDL Status	Listed through negotiation	Listed through negotiation	Listed through negotiation	Listed through routine update	Listed through routine update	Entered NRDL in 2017, renewed in 2019	Entered NRDL in 2017, renewed in 2019	Entered NRDL in 2017, renewed in 2019
Pricing Calculation Assumptions	40mg injection / two weeks	3mg/kg injection at week 0, 2, and 6; 3mg/kg every 8 weeks afterwards; average weight 65kg	5mg pill twice daily	8mg/kg injection every 4 weeks; average weight 65kg	50mg injection monthly	25mg injection, twice weekly	25mg injection, twice weekly	50mg injection weekly
Monthly Cost Before 2019 NRDL (CNY)	16,467	7,830	3,977	14,598	4,900	5,547	4,437	5,113
Monthly Cost After 2019 NRDL (CNY)	2,795	3,009	2,100	6,294	4,900			
Price Discount	83%	62%	47%	57%	N/A	N/A	N/A	N/A

FIGURE 2: RA DRUG NEGOTIATION OUTCOMES AND ESTIMATED PRE-/POST-NRDL COSTS

FUTURE MANUFACTURER STRATEGIES

Biosimilars will ultimately drive down the price once a product loses exclusivity. Thus, manufacturers should track biosimilar timelines and consider earlier NRDL inclusion to fully leverage the exclusivity, achieving early and broad patient access.

Future product launches with similar efficacy need to consider the potential price ceilings set through NRDL negotiations. In 2019, the three newly listed drugs have a monthly cost between approximately CNY 2,000 and 3,000 (USD 291 and 436), and this can be used as a benchmark for future "me too" drugs in the RA space.

CONCLUSION

Entering the Chinese market requires strategic consideration of key opportunities and risks. In order to maintain a positive margin, both local and global pharmaceuticals need to focus on value differentiation and tailored pricing strategies to fit the dynamic landscape.

Manufacturers need to be mindful of the possible pricing benchmark set by enlisted products and undergo in-depth analysis of the price and volume trade off scenarios when choosing a launch price.

ABBREVIATIONS

CNY: Renminbi; DMARD; Disease-Modifying Antirheumatic Drug; HCV: Hepatitis C Virus; IgG: Immunoglobulin; kg: Kilogram; mg: Milligram; N / A: Not Applicable; NHSA: National Healthcare Security Administration; NRDL: National Reimbursement Drug List; RA: Rheumatoid Arthritis; TNF RII: Recombinant Human Tumor Necrosis Factor - Receptor II; USD: US Dollar

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