



# BENZATHINE PENICILLIN G



**Benzathine penicillin G (BPG) is an antibiotic administered by injection into muscle. BPG mixes only very slowly with water, ensuring that low levels of the penicillin stay in the blood for weeks. This makes BPG suitable for treating and preventing specific bacterial infections sensitive to penicillin.**

BPG was developed in 1951 and has been considered an Essential Medicine by the World Health Organization since the first Essential Medicines list was developed in 1977. It is also on the World Health Organization Essential Medicines List for Children and for Reproductive Health.

The human cost of inadequate BPG supplies accrues most clearly for pregnant women in low- and middle-income countries. At risk of maternal death from untreated rheumatic heart disease (RHD) and at risk of transmitting congenital syphilis infections to their unborn babies, vulnerable mothers are the most in need of this essential medicine.

## FORMULATIONS OF BPG

There are two formulations of BPG:

- A branded liquid formulation which requires a cold chain is relatively expensive and licensed in a small number of high-income countries.
- Powdered formulations are produced by a number of generic manufacturers around the world. Powdered formulations are less expensive and do not require a cold chain. However, the powder must be mixed with a sterile liquid before it is administered as a suspension. Anecdotal reports indicate that administration is difficult and that large particle sizes can block even large-gauge needles.

## ADMINISTRATION OF BPG

Injection of BPG into muscle is painful. Pain and fear of pain is a barrier to adherence, particularly when multiple doses of BPG are required as in advanced syphilis and RHD. Severe allergy and anaphylaxis to RHD has been relatively rare in formal studies.<sup>1</sup> However, anecdotal reports of poorly characterized adverse reactions are not uncommon, prompting concern about the quality and safety of BPG products.

## LIMITED SUPPLY OF BPG

Reports of stockouts and shortages of BPG have increased in recent years, affecting a wide range of low- and middle-income countries. Purchasing supplies of BPG remains a challenge even for pooled procurement agencies such as UNICEF. The number of manufacturers producing powdered formulations has decreased, and there are no clear signals of market intent to increase production.

## DEMAND FOR BPG

Despite the significant clinical need for BPG, demand to actually purchase the product is relatively small.

- Diagnosis and treatment of people who need BPG remains challenging in low-resource settings where the need is greatest.
- Countries where the drug is needed most have relatively weak health systems for delivering syphilis and RHD control strategies.
- Disparate procurement and distribution channels between clinical indications further fragments the global market for BPG.
- Consumer demand is limited given that the primary indications for BPG are diseases of vulnerable populations in low-resource settings who are not necessarily aware of critical need for the product.



## INDICATIONS FOR BPG

BACTERIA	DISEASE	GLOBAL BURDEN	GLOBAL DISTRIBUTION	DESCRIPTION	USUAL ADULT DOSE
TREPONEMAL INFECTIONS	Syphilis treatment	<b>36 million people living with syphilis (2005)<sup>2</sup></b>	Low- and middle-income countries. Some cases in high-risk communities and high-risk populations	Syphilis is a sexually transmitted treponemal infection which causes disease of the reproductive system, eyes, skin, and neurologic systems.	Early syphilis: A single injection of 2.4 million units of BPG
	Congenital syphilis treatment	<b>1.5 million pregnant women with active syphilis annually (2013)<sup>4</sup></b>		Mother-to-child transmission of syphilis occurs during pregnancy. This transmission is a major cause of stillbirth, premature, and serious abnormalities of infected babies.	Late syphilis: Three injections of 2.4 million units of BPG over 15 days <sup>3</sup>
	Yaws treatment	<b>65,000 cases per year in 13 endemic countries (2015)<sup>5</sup></b>	Low-income countries	Yaws is a neglected tropical disease which causes destruction of skin and bone. Three-quarters of cases of yaws occur in young people aged less than 15 years.	A single injection of 1.2 million units of BPG cures yaws
GROUP A STREPTOCOCCAL INFECTIONS	Sore throat treatment	<b>616 million episodes annually (2005)<sup>6</sup></b>	Global	Strep throat causes up to 30% of sore throat infections in young people. 3–5% of these infections spark the autoimmune reaction of acute rheumatic fever (ARF). A single dose of BPG reduces the risk of developing ARF by 80%. <sup>7</sup> Antibiotics for strep throat are recommended in low-resource settings with an endemic burden of RHD.	A single injection of 1.2 million units of BPG
	ARF prevention in rheumatic heart disease	<b>32 million people living with RHD (2015)<sup>8</sup></b>	80% of cases in developing countries <sup>6</sup>	Recurrent episodes of ARF culminate in chronic heart valve damage known as RHD. RHD progresses to heart failure in young people and increases the risk of stroke, abnormal heart rhythms, and heart valve infections. Women with RHD are at risk of catastrophic cardiovascular collapse during pregnancy.	Injections of 1.2 million units of BPG every 2–4 weeks for a minimum of 10 years
Other uses			Low- and middle-income countries	In some countries, BPG is widely used in the treatment of skin sores. BPG may also be used for prophylaxis of encapsulated bacteria infections in people with spleen disorders including sickle cell anemia.	



## CLINICAL NEED FOR BPG

There are no comparably effective drugs for treatment of congenital syphilis or prevention of ARF. BPG is the mainstay of treatment for these conditions. Alternative antibiotics do exist for other indications but may be more expensive, difficult to access, or contributors to antibiotic resistance. Focusing primarily on congenital syphilis and ARF indications alone illustrates the scale of global need for BPG.

TARGET	NUMBER OF CASES ANNUALLY	% NEEDING TREATMENT	ANNUAL NEED FOR BPG	% CURRENTLY RECEIVING TREATMENT
Prevention of congenital syphilis	1.5 million pregnant women <sup>4</sup>	100% need at least one dose of BPG	<b>1.5 million cases x 1–3 doses each = 1.5–4.5 million doses</b>	30–70% <sup>9</sup> of women tested and treated worldwide
Prevention of acute rheumatic fever cases	32 million <sup>8</sup>	Estimated 70% require monthly doses = 13 injections annually	<b>32 million cases x 70% x 13 doses each = 291 million doses</b>	Unknown—experts estimate only 2% of people with RHD are receiving necessary treatment

**A minimum of 292 million doses of BPG needed each year to provide recommended treatment for serious medical conditions.**

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**RHD Action**

United to End  
Rheumatic Heart Disease

[www.RHDACTION.org](http://www.RHDACTION.org)