



**World Health
Organization**

Evidence Assessment: Sinopharm/BBIBP COVID-19 vaccine

**FOR RECOMMENDATION BY THE STRATEGIC ADVISORY GROUP OF EXPERTS (SAGE)
ON IMMUNIZATION**

Prepared by the SAGE Working Group on COVID-19 vaccines

EVIDENCE ASSESSMENT: BBIBP-CorV

Key evidence to inform policy recommendations on the use of BBIBP-CorV

Background

- 2-dose β -propiolactone-inactivated, aluminium hydroxide-adjuvanted COVID-19 vaccine administered on a 0/21-28-day schedule for the prevention of COVID-19 disease
- Authorized by the China National Medical Products Administration on December 31, 2020
- Authorized by 45 countries/jurisdictions for use in adults ≥ 18 years
- >65 million doses administered through emergency use programs
- EUL pending

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1. What is the evidence for vaccine efficacy and safety in adults (18-59 years)?
2. What is the evidence for use in older age groups?
3. What is the evidence for efficacy and safety for certain comorbidities and health states?
4. GRADEing of the evidence assessment

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Clinical database available at the time of review

Total Data Package	Age Group (Years)	Authorized dose/schedule	Alternative dose/schedule	Total by age	Total all ages
Safety	18-59	15,789	336	16,125	16,671
	≥60	378	168	546	
Immunogenicity	18-59	2,267	334	2,601	2,890
	≥60	125	164	289	
Efficacy	18-59	13,556	0	13,556	13,765
	≥60	209	0	209	

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Summary of clinical trials reporting to date

Study Name Trial Registration	Phase Type (primary outcome)	Location(s)	Participants N Ages eligible	Dosing Regimens	Study Status
COVIV-01 ChiCTR2000032459	Phase 1/2 Safety	China	2,128 healthy subjects ≥3Y	Multiple	Interim results available for aged ≥18y
COVIV-02 NCT04510207	Phase 3 Efficacy*	UAE, Bahrain, Egypt, Jordan	45,000 healthy subjects ≥18Y	2-dose regimen, 0/21(+7)-day schedule	Interim results available
COVIV-05 CTR20201998	Phase 3 Immuno- bridging pilot and commercial scale product	China	2,100 healthy subjects 18-59Y	2-dose regimen, 0/21-day schedule	Interim results available

*Evaluated BBIBP-CorV & WIBP-CorV

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Vaccine efficacy in multi-country Phase 3 Trial (median follow up time 112 days)

Group/Subgroup	BBIBP-CorV Group		Placebo Group		Vaccine Efficacy % (95% CI)
	No. at risk	No. of cases	No. at risk	No. of cases	
Overall	13,765	21	13,765	95	78.1 (64.9, 86.3)
Hospitalization	13,765	3	13,765	14	78.7 (26.0, 93.9)
Severe	13,765	0	13,765	2	NE
Sex					
Male	11,598	18	11,642	83	78.4 (64.1, 87.0)
Female	2,167	2	2,123	13	75.6 (13.3, 93.1)
Age group					
18-59 years	13,556	21	13,559	95	78.1 (64.9, 86.3)
≥60 years	209	0	206	0	NE
Comorbidities					
Hypertension	374	0	367	4	NE
Diabetes	300	2	308	6	63.7 (-79.8, 92.7)
Obesity	3,040	7	3,080	36	80.7 (56.7, 91.4)
Baseline SARS-CoV-2 serostatus					
Baseline positive	NR	0	NR	1	NE
Baseline negative	NR	16	NR	83	80.8 (67.2, 88.8)

NE=Not estimated

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Clinical development safety summary

- No safety concerns identified from pre-clinical or repro/tox studies
- Clinical safety database: 16,671 participants who received any dose/schedule of BBIBP-CorV product, of which 97% received authorized dose/schedule
- Most AEs were mild to moderate: most common adverse events were pain at the injection site, headache, and fatigue
- No imbalance in the number of reported serious adverse events, adverse events of special interest (neurological diseases), or Grade 3+ adverse event between BBIBP-CorV and placebo group
- Two Serious Adverse Events assessed to be possibly linked to vaccination (serious nausea and inflammatory demyelination syndrome/acute disseminated encephalomyelitis)
- One death occurred in the Phase 3 trial, in the placebo group
- One participant with a diagnosis of thrombus was identified in the Phase 3 trial, in the BBIBP-CorV group
- All acute allergic reactions were Grade 1 and 2 in BBIBP-CorV group (no anaphylaxis) and no difference in frequency between vaccine and placebo groups

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Post-authorization safety summary

Current post-authorization safety data limited to domestic use in China (data cut off December 30, 2020)

- Data report based on 5.9 million people vaccinated in China
 - 1,453 reported adverse events for a reporting rate of 24.6/100,000 doses
 - Of 108 local reactions reported, there were 2 reports of severe induration and 6 reports of severe redness and swelling
 - Of 202 cases of fever reported, 86 were classified as severe (≥ 38.6 degrees Celsius)
 - 11 cases of facial nerve symptoms – all assessed to be unrelated to the vaccine
 - Other reports included allergic rash/urticaria

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Use in older age groups (≥60 years)

- Clinical Protection
 - Vaccine efficacy was not demonstrated in Phase 3 trial (0 cases in 415 participants in BBIBP-CorV and placebo groups)
 - Immunogenicity showed high seropositivity in older adults but lower GMTs (both for binding antibody and neutralizing antibody) compared to younger adults
- Safety
 - Clinical trials (N=546):
 - Similar safety profile compared to younger adults, but with lower reactogenicity in older adults
 - No SAEs occurred in adults ≥60 years in the vaccine group
 - Post-authorization:
 - 1.1 million doses of BBIBP-CorV vaccine have been administered to people 60 years of age or older in China
 - AEFIs were reported 79 individuals, with 45 adverse reactions considered related to vaccination
 - Most common were dizziness (n=23), headache (n=9), fatigue (n=9), nausea (n=7), fever (n=6), vomiting (n=6), allergic dermatitis (n=6)

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Vaccine effectiveness in Bahrain

- Test-negative design, rt-PCR case confirmation
- PCR+ cases and PCR- controls identified through the national public health database, matched on test time frame
- Primary analysis based on 14 days post-2nd dose

	Total	COVID +ve	COVID -ve	Odds Ratio (95%CI)	Vaccine Effectiveness (95%CI)
≥18 years	Vaccinated	282	2178	0.10	90%
	Not vaccinated	2949	2373	(0.09-0.12)	(88-91%)
≥60 years	Vaccinated	65	238	0.09	91%
	Not vaccinated	328	110	(0.06-0.13)	(87-94%)

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Use in individuals with underlying disease

- Clinical protection
 - Efficacy not reported amongst participants with any comorbidity
 - Participants with BMI over 30: VE = 80.7 (95%CI 56.7, 91.4)
 - Analysis of efficacy amongst participants with comorbidities limited by the low number of participants with comorbidities (other than obesity) in the Phase 3 trial
- Safety
 - Analysis of safety amongst participants with comorbidities limited by the low number of participants with comorbidities (other than obesity) in the Phase 3 trial

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Protection against variants of concern

- Cross-neutralization study suggest neutralization but with reduced titers against B.1.351
- Interim efficacy against variants of concern could not be assessed in the Phase 3 clinical trials
- No vaccine effectiveness studies yet to inform protection against variants of concern

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Evidence gaps

- Protection against severe disease
- Duration of protection, need for booster doses, and future risk of vaccine-associated enhanced disease
- Protection against variants of concern
- Safety in pregnancy
- Safety and clinical protection in older adults, those with underlying disease and other subpopulations
- Identification and evaluation of rare adverse events detected through post-authorization safety monitoring

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Ongoing/planned studies

- Follow up of existing clinical trial participants (Phase 3: 12 months follow up)
- Vaccine efficacy in Peru and Argentina
- Vaccine effectiveness in UAE, Bahrain, and Pakistan
- Pediatric immunogenicity and safety trial in China
- Vaccine co-administration (23-valent pneumococcal polysaccharide vaccine or quadrivalent inactivated influenza vaccine) study in China
- Active safety monitoring cohort (N>100,000) in China, including monitoring for anaphylaxis, 40% adults ≥60 years of age, and adults with comorbidities (6 months follow up)
- Active safety monitoring cohort (N=1,000) in China, including special populations such as immunocompromised and elderly patients with chronic bronchitis, thrombocytopenia, or vital organ damage (6 months follow up)
- Passive safety monitoring (N=1,000,000) in China
- Additional passive safety surveillance through China's National AEFI system

GRADEing of Evidence	Statement on quality of evidence	SAGE Working Group Judgement
Efficacy against PCR confirmed COVID-19 (Adults)	High level of confidence	We are very confident that 2 doses of BBIBP-CorV are efficacious in preventing PCR confirmed COVID-19 in adults (18-59 years).
Safety-serious adverse events (Adults)	Moderate level of confidence	We are moderately confident that the risk of serious adverse events following one or two doses of BBIBP-CorV in adults (18-59 years) is low.
Efficacy PCR confirmed COVID-19 (Older adults)	Low level of confidence	We have low confidence in the quality of evidence that 2 doses of BBIBP-CorV are efficacious in preventing PCR confirmed COVID-19 in older adults (≥60 years).
Safety-serious adverse events (Older adults)	Very low level of confidence	We have very low confidence in the quality of evidence that the risk of serious adverse events following one or two doses of BBIBP-CorV in older adults (≥60 years) is low.
Efficacy PCR confirmed COVID-19 (<i>Individuals with comorbidities or health states that increase risk for severe COVID-19</i>)	Very low level of confidence	We have very low confidence in the quality of evidence that 2 doses of BBIBP-CorV are efficacious in preventing PCR confirmed COVID-19 in individuals with comorbidities or health states that increase risk for severe COVID-19 as included in the clinical trial.
Safety-serious adverse events (<i>Individuals with comorbidities or health states that increase risk for severe COVID-19</i>)	Very low level of confidence	We have very low confidence in the quality of evidence that the risk of serious adverse events in individuals with comorbidities or health states that increase risk for severe COVID-19 following one or two doses of BBIBP-CorV is low.