Important Safety Information on Sotrovimab for Injection - Risk of Treatment Failure due to Circulation of SARS-CoV-2 Omicron BA.2 Subvariant

2022-04-14

Audience
Healthcare professionals responsible for treating patients infected with SARS-CoV-2, including general practitioners, infectious disease physicians, intensive care unit and emergency room physicians, internal medicine physicians, critical care physicians, respirologists, pharmacists, hospital pharmacy departments, and chiefs of medicine in hospitals.

Key messages

- **Sotrovimab, 500 mg IV, is unlikely to maintain efficacy against the Omicron BA.2 subvariant.**
- **Current data indicates that sotrovimab continues to be effective against the Omicron BA.1 and BA.1.1 subvariants.**
- **Healthcare professionals are advised that:**
  - **Local epidemiology and individual exposure to variants should be taken into consideration before use of sotrovimab.**
  - **Use of sotrovimab 500 mg IV should be limited to when the patient is likely to have been infected with a variant that is susceptible to the authorized dose.**
- **The Canadian Product Monograph for sotrovimab, which is available in French and English on Health Canada's Drug Product Database, at www.gsk.ca or www.sotrovimabinfo.com, will be updated to include new information concerning the Omicron BA.2 subvariant.**

What is the Issue?
Sotrovimab, 500 mg IV, is unlikely to maintain efficacy against the Omicron BA.2 subvariant. Sotrovimab demonstrates reduced *in vitro* neutralization against the Omicron BA.2 subvariant.

Products Affected
Sotrovimab for injection, anti-SARS-CoV-2 spike protein monoclonal antibody, solution for infusion, 500 mg / 8 mL, single-use vial, DIN 02518341.

Background Information
Sotrovimab is indicated for the treatment of mild to moderate coronavirus disease 2019 (COVID-19), confirmed by direct SARS-CoV-2 viral testing, in adults and adolescents (12 years of age and older weighing at least 40 kg) who are at high risk for progressing to hospitalization and/or death.

Sotrovimab is NOT authorized for use in patients:
- who are hospitalized due to COVID-19, OR
- who require oxygen therapy due to COVID-19, OR
- who require an increase in baseline oxygen flow rate due to COVID-19 (in those on chronic oxygen therapy due to underlying non-COVID-19 related comorbidity).

The antiviral activity of sotrovimab against SARS-CoV-2 variants, including the Omicron BA.2 subvariant, has been evaluated using *in vitro* assays. Sotrovimab exhibited a reduction in activity against the Omicron BA.2 subvariant live virus (15.7-fold change in EC_{50} value, 25.3 to 48.1-fold change in EC_{90} value, relative to wild-type SARS-CoV-2 live virus) (see Table 1).

Table 1: Sotrovimab Authentic SARS-CoV-2 Neutralization Data for SARS-CoV-2 Variants

SARS-CoV-2 Lineage	WHO Nomenclature	Key Substitutions[a]	Fold Reduction in Susceptibility
B.1.1.7	Alpha	N501Y	No change[b]
B.1.351	Beta	K417N+E484K+ N501Y	No change[b]
P.1	Gamma	K417T+E484K+ N501Y	No change[b]
B.1.617.1	Kappa	L452R+E484Q	No change[b]
B.1.617.2	Delta	L452R+T478K	No change[b]
B.1.1.529/BA.1	Omicron	G339D+S371L+ S373P+S375F+ K417N+N440K+ G446S+S477N+ T478K+E484A+ Q493R+G496S+ Q498R+N501Y+ Y505H	No change[b]

SARS-CoV-2 Lineage	WHO Nomenclature	Key Substitutions[a]	Fold Reduction in Susceptibility
B.1.1.529/BA.1.1	Omicron	G339D+R346K+ S371L+S373P+ S375F+K417N+ N440K+G446S+ S477N+T478K+ E484A+Q493R+ G496S+Q498R+ N501Y+Y505H	No change[b]
B.1.1.529/BA.2	Omicron	G339D+S371F+ S373P+S375F+ T376A+D405N+ R408S+K417N+ N440K+S477N+ T478K+E484A+ Q493R+Q498R+ N501Y+Y505H	15.7[c] 25.3 to 48.1[d]

[a] For variants with more than one substitution of concern, only the one(s) with the greatest impact on activity is (are) listed. [b] No change: <5-fold reduction in susceptibility. [c] EC_{50} value fold reduction in activity relative to wild-type. [d] EC_{90} value fold reduction in activity relative to wild-type based on two independent SARSCoV-2 Omicron B.1.1.529/BA.2 isolates.

Information for healthcare professionals

Sotrovimab, 500 mg IV, is unlikely to maintain efficacy against the Omicron BA.2 subvariant. Current data indicates that sotrovimab continues to be effective against the Omicron BA.1 and BA.1.1 subvariants.

Healthcare professionals are advised that:

- Local epidemiology and individual exposure to variants should be taken into consideration before use of sotrovimab.
- Use of sotrovimab 500 mg IV should be limited to when the patient is likely to have been infected with a variant that is susceptible to the authorized dose.

The Canadian Product Monograph for sotrovimab, which is available in French and English on Health Canada's Drug Product Database, at www.gsk.ca or www.sotrovimabinfo.com, will be updated to include new information concerning the Omicron BA.2 subvariant.

Action taken by Health Canada

Health Canada has worked with GlaxoSmithKline Inc. to prepare this alert for sotrovimab, 500 mg IV. Health Canada is communicating this important safety

information to healthcare professionals and Canadians via the Recalls and Safety Alerts Database on the Healthy Canadians Web Site. This communication update will be further distributed through the MedEffect™ e-Notice email notification system, as well as through social media channels, including LinkedIn and Twitter.

Report health or safety concerns

Managing marketed health product-related side effects depends on healthcare professionals and consumers reporting them. Any serious or unexpected side effects in patients receiving sotrovimab should be reported to GlaxoSmithKline Inc. or Health Canada.

GlaxoSmithKline Inc.
100 Milverton Drive
Suite 800
Mississauga, Ontario
L5R 4H1
Tel: 1-800-387-7374

To correct your mailing address or fax number, contact GlaxoSmithKline Inc.

You can report any suspected adverse reactions associated with the use of health products to Health Canada by:

- Calling toll-free at 1-866-234-2345; or
- Visiting MedEffect Canada's Web page on Adverse Reaction Reporting (http://www.hc-sc.gc.ca/dhp-mps/medeff/report-declaration/index-eng.php) for information on how to report online, by mail or by fax.

For other health product inquiries related to this communication, contact Health Canada at:

Marketed Health Products Directorate
E-mail: mhpd-dpsc@hc-sc.gc.ca
Telephone: 613-954-6522
Fax: 613-952-7738

Original signed by

Marni Freeman
Country Medical Director, Canada
GlaxoSmithKline Inc.