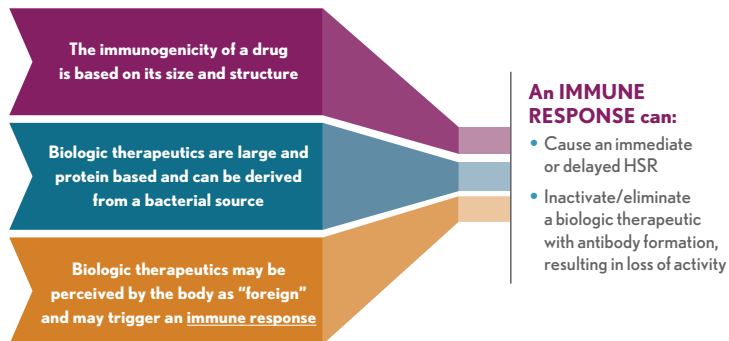


HSR OVERVIEW

Hypersensitivity reactions (HSRs)
are immune responses that can occur in
response to biologic therapeutics.

Hypersensitivity reactions (HSRs) to biologic therapeutics

Why are biologic therapeutics immunogenic?¹



Clinical manifestations of an HSR²

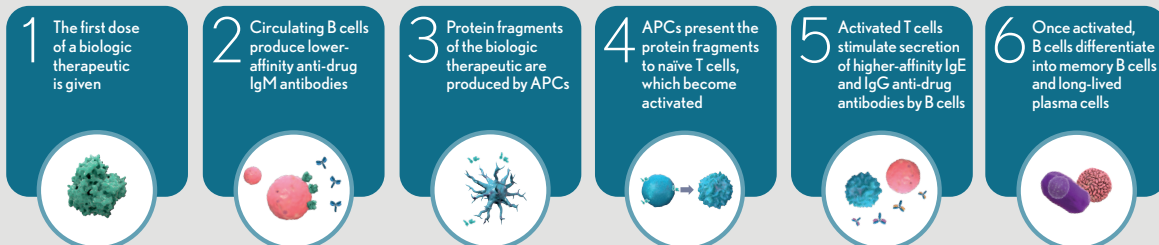
Symptoms of HSRs²:

| | |
|--|--|
| Chest pain, hypotension, arrhythmia, edema | Renal impairment |
| Dizziness and loss of consciousness | Arthralgias, myalgias, hypotonia |
| Diaphoresis and fever | Cough, dyspnea, rhinitis, tachypnea, hypoxemia, bronchospasm, oropharyngeal or laryngeal edema, cyanosis, acute respiratory syndrome |
| Nausea, vomiting, diarrhea, abdominal cramping | Pruritus, urticaria, erythema, angioedema |

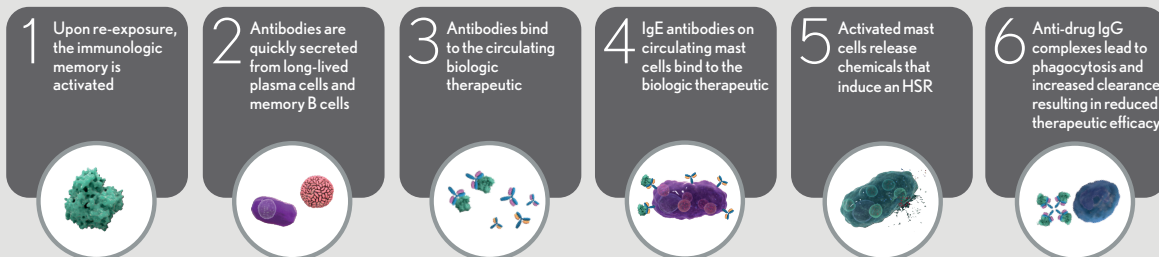
Reduced treatment efficacy due to:

- Failure to receive a full course of treatment
- Development of drug-neutralizing antibodies, which result in:
 - Altered drug pharmacokinetics
 - Antibody-mediated drug inactivation

PRIMARY IMMUNE RESPONSE to an immunogenic biologic therapeutic¹



SECONDARY IMMUNE RESPONSE to an immunogenic biologic therapeutic¹



Differentiating HSRs from infusion reactions²

Antibody-mediated reactions

- Clinical HSRs are antibody mediated
- Reactions can occur after repeated exposure
- May occur without overt clinical symptoms (subclinical hypersensitivity or silent inactivation)

Infusion-related reactions

- Occur independently of the development of anti-drug antibodies
- Can occur on a patient's first exposure
- Often present with symptoms similar to clinical HSRs

Non-cross-reactive therapies can rescue treatment after an HSR³



Following an HSR, alternative biologic therapeutics with distinct immunogenetic profiles can be administered



This can allow a patient to complete their recommended therapy without exacerbating HSRs or diminishing therapeutic efficacy

Abbreviations: HSR, hypersensitivity reaction; IgM, immunoglobulin M; APC, antigen-presenting cell; IgE, immunoglobulin E; IgG, immunoglobulin G.

Footnote: *Common symptoms of HSRs are shown; other symptoms can occur.

References: 1. Leach MW, et al. *Toxicol Pathol*. 2014;42(1):293-300. 2. Burke MJ, Rheingold SR. *Leuk Lymphoma*. 2017;58(3):540-551. 3. van der Sluis IM, et al. *Haematologica*. 2016;101(3):279-285.